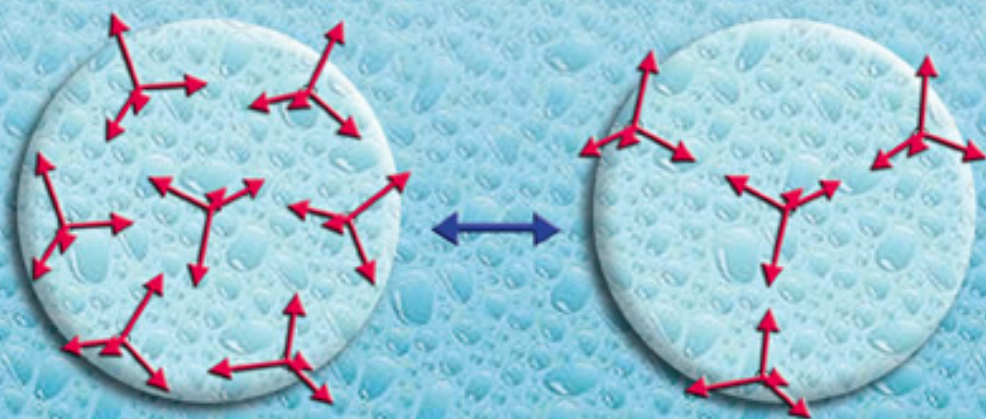


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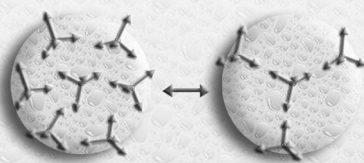
Molecular Theory of Water and Aqueous Solutions



Part I: Understanding Water

Arieh Ben-Naim

Molecular Theory of Water and Aqueous Solutions



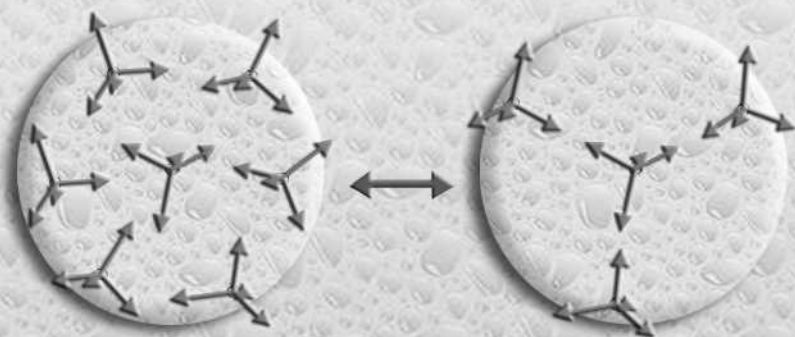
Part I: Understanding Water

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Molecular Theory of Water and Aqueous Solutions



Part I: Understanding Water

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To Ruby

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PREFACE

This book is addressed to anyone who is interested in understanding the unusual properties of liquid water in its pure state, in its solutions, and in its role in biological systems.

More than 35 years have passed since I published my first book on “Water and Aqueous Solutions.” In 1974, there was a need to summarize the new approach to the theory of water that had been developed at that time; instead of *ad hoc* models of liquid water, Frank Stillinger and I proposed a model of a single water molecule along with a pair interaction to study the properties of liquid water. In most of the older theories, some types of *structures* were introduced as *input* in the theory. In the new approach, *structures* were obtained as *output* of the theory.

Since then, much has been done in the field of water and aqueous solutions. New experimental data have become available, new theories have been developed, and a great number of simulations have been carried out on these model systems. All these studies have greatly enriched our knowledge and deepened our understanding of the properties of liquid water and its role in biological systems.

The field of aqueous solutions has become so huge that it is impossible to review the whole field in a single book. Therefore, I have selected only a few topics, giving preference to those that have contributed the most to our *understanding* of the molecular reasons underlying the outstanding properties of liquid water and its solutions.

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The views expressed in this book are highly personal, in the sense that they are based either on my own work, or on the works that I am familiar with and are deemed to be helpful in understanding water. There is a vast literature that contains important studies of aqueous systems. I believe, however, that I have presented in this book a fair survey of what we have learned and understood in the past 30 years on this unique and vital liquid.

The book conveys several messages that I believe justify its writing. First, contrary to numerous statements in the literature, I am convinced that the behavior of water and aqueous solutions of simple solutes is reasonably well understood and that this understanding was achieved mainly by studying very simplified models for water. Even in very recent articles one can find statements like “the peculiar properties of water are still not well understood.” Of course, this kind of statement can be made about every subject that has ever been investigated. One can always choose to look at the half-full or at the half-empty glass with regard to the understanding of water. Personally, I prefer the half-full view, which in my opinion is much more than half full. I also hope that this understanding of the properties of water and simple aqueous solutions will contribute to the much needed understanding of the role of water in the biological sciences.

For many years, various mixture-model (MM) approaches were used to explain the properties of water. The problem with the MM theories was that they were considered *ad hoc* models for water, having neither experimental nor theoretical support. However, once the MM approach was firmly anchored in statistical mechanical grounds, it gained legitimacy, and as a result of which it became a powerful and reliable tool for the interpretation of the properties of water and aqueous solutions. It is puzzling to see, even in relatively recent publications, authors

categorizing their theory as “belonging” to the mixture-model or the continuous approach. I believe this distinction is now obsolete; the two approaches are completely equivalent. They differ in their interpretative power. Again, contrary to the commonly held opinion, the understanding of aqueous systems is mainly due to these simple MM models, and not to the more recent sophisticated simulated results.

The second, no less important, message consists of the repeated emphasis of a fundamental *principle* underlying most of the unique properties of water and aqueous solutions. The principle states that the unique properties of water can be explained as emanating from the unique mode of packing of water molecules in such a way that *low local density* is correlated with *strong binding energy*. This key feature of liquid water was first formulated in 1973^a in terms of generalized molecular distribution functions. This principle was *implicitly* used for constructing the first successful pair potential for liquid water in 1972.^b It was later used *explicitly* for constructing models of water-like particles in one and two dimensions. In my view, this principle is so fundamental that it deserves to be referred to as *the principle* of liquid water, and therefore, was justifiably chosen for the cover design of this book.

As is well known, statistical thermodynamics is a theory that links the molecular properties and the macroscopic properties of matter. Specifically, for water, it provides the relationship between some specific features of the pair potential, and some of the outstanding properties of water and aqueous solutions.

^aBen-Naim (1973).

^bSuccessful in the sense that it produces the correct features of the pair correlation function and some anomalous properties of water. See Ben-Naim and Stillinger (1972).

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It has long been known that water is a “structured” liquid, and that this structure is a result of the tendency of water molecules to form hydrogen bonds. What is less recognized is that the specific correlation between local density and binding energy is a more fundamental principle of the interaction between water molecules. This feature, when implemented in a model system in any dimension can produce most of the outstanding properties of aqueous systems.

In the earlier mixture-model theories of liquid water, this principle was introduced implicitly into the theory by choosing two components: an open structure, but highly hydrogen-bonded (*HBed*), and a close-packed form but of weakly interacting molecules. In the modern era, the principle was used either implicitly or explicitly in the construction of many models of water-like particles in one, two, and three dimensions.

Therefore, I feel confident in claiming that this principle is both *necessary* and *sufficient* for the manifestation of water-like behavior. It is necessary in the sense that any model that shows water-like behavior contains, as far as we know, this principle. It is sufficient in the sense that even extremely simple models, which have almost nothing more than this principle, do show the outstanding behavior of real liquid water. It was the astonishing success of the 1-D model to explain various properties of water that lent overwhelming support to the crucial importance of the principle.

I have used the terms “necessary” and “sufficient” not in the precise way they are used in mathematics. The principle is not *necessary* in the sense that there might be a future model of water that does show all the characteristic behavior of water but does not include this principle. Also, the principle is not *sufficient* in the sense that its implementation might not be sufficient to explain *all* the properties of water.

In the three-dimensional model, the implementation of the principle leads to the tetrahedral-open structure-geometry which is associated with highly *H*Bed molecules (and similarly in the 2-D model). In the 1-D model, the principle is reduced to a stronger interaction associated with larger distance.

The third message might sound as if it were bordering on semantics. Nevertheless, I believe it is important not only in the study of water but also in any study of any thermodynamic system where the concept of entropy is involved.

Ever since the unique properties of water were recognized, the concept of the *structure* of water was involved in all of the interpretations of the properties of water. Furthermore, the concept of structure was also useful in interpreting the entropy of solvation of simple solutes in water.

However, the concept of “structure,” as order and disorder, is not a well-defined concept. While it is true that sometimes the association between structure and entropy is useful, it might also be misleading. The association of changes in entropy with changes in structure (or changes in order) is not a necessity. The important association is between changes in entropy and changes in the Shannon’s measure of missing information.^c It so happens that what we conceive as the more structured or more ordered species in water is also the species with stronger binding energy. As we shall show in several examples throughout the book, it is the change in the strength of *binding energies* that explains the solvation entropy and not the change of the structure itself. The structure may or may not be relevant to the explanation of entropy changes. This is demonstrated for a one-dimensional model discussed in Sec. 2.5, and for a lattice model discussed in Sec. 2.4.

^cSee Ben-Naim (2008a).

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The previous paragraph should not be misunderstood as implying that water is not a structural liquid. Water is indeed a highly structured liquid, and the concept of structure was, and still is, very useful in discussing the properties of water. In fact, I will be using this concept, as well as the term “structural changes” induced by processes carried out in water, quite often throughout the book. What I do claim here is that the concept of “structure,” though useful in many cases, is not *essential* for the interpretation and understanding of the unusual properties of water.

It should be noted that though it is true that in both the 2-D and 3-D models, the low density form is the more *structured* form, the structure in itself is not the important aspect of that form. This comment is obvious in the 1-D model for water, where one cannot claim that a sequence of *HBed* molecules is more structured than a series of non-*HBed* particles.

Thus, as will be abundantly illustrated throughout the book, the concept of *structure*, though very useful in *describing* water, is not *essential* for understanding the properties of water and aqueous solutions. In fact, one can rewrite the entire book without ever invoking arguments based on *structure*. This is similar to the understanding of entropy without ever mentioning order or disorder.

The fourth and perhaps the most important message of this book is that contrary to the almost universal belief that hydrophobic interactions are the most important driving forces in biochemical forces, I believe that *hydrophilic* interactions are far more important in biochemistry. In a sense what I am proposing is an inversion of the Hydrophobic/Hydrophilic paradigm. This proposal is similar to but not exactly the same as the “side-chain/backbone paradigm” inversion proposed by Rose *et al.* (2006). As will be shown in Chapter 4, hydrophilic groups exhibit a richer and a more powerful repertoire of effects than

hydrophobic groups. This message is discussed only briefly at the end of Chapter 4. I hope to further elaborate on the relative importance of hydrophilic versus hydrophobic effects in specific biochemical processes in a future book.

Finally, a very personal message. While researching the literature in preparation for writing this book, I was pleased and gratified to see so many works that were based on and developed upon ideas that I published more than 30 years ago. On the other hand, I was, of course, not so pleased to come across some publications presenting “original” ideas that I had actually published myself. I shall give only two examples here.

To the best of my knowledge, the formulation of the *principle* and its significance to the understanding of the anomalous properties of water was first published in 1972.^d This principle and its implications were repeatedly used later by many authors who “rediscovered” it. Similarly, the *exact entropy-enthalpy compensation* theorem and its implications for the theory of aqueous solutions were first discussed in terms of a mixture-model approach in 1965.^e Later, it was proved in a much more general form in Ben-Naim (1975b, 1978b). This theorem was “reproved” several times by several authors using different nomenclature and different notations.

For over 30 years, I have suggested several pair potentials for water-like particles. I have never referred to any pair potential I have devised as the *Ben-Naim potential*. I was dismayed to learn that through the years, authors have used these pair potentials and either presented them as “their own,” or simply renamed them, and as a result of which completely obliterating the roots of their origins.

^dBen-Naim (1972c).

^eBen-Naim (1965b).

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To set the record straight, I have decided to designate the following names for the potentials I had devised as: the BN1D, BN2D, and BN3D potentials.

The Ben-Naim 1-D potential (BN1D) was published in 1992. The Ben-Naim 2-D potential (BN2D) published in 1971 was renamed the “Mercedes Benz” (MB) potential. Subsequent users of the MB potential continued to use the MB term, ignoring the existence of the original BN2D. Very recently, in a flagrant disregard for the proper provenance of the 3-D potential (BN3D), which I designed and published in 1974, it was not only renamed the 3-D version of the MB potential (which it is not) but also “claimed” by some authors as their own design (see Sec. 2.7). Another pair potential on which I had spent nearly two years was initially referred to as the Ben-Naim and Stillinger (BNS) potential. It was later modified and renamed the ST2 potential (see Sec. 2.7).

This book is organized into four chapters. The first includes some historical notes and a survey of the main outstanding properties of water. The second chapter presents the theories that have contributed to our understanding of liquid water. Chapter 3 is devoted to extremely dilute solutions of simple solutes in water. This chapter is strictly concerned with the solvation properties of a single solute in pure liquid water. Chapter 4 is an extension of Chapter 3. It contains a discussion of slightly more concentrated aqueous solutions, where pairwise correlations between two solutes are the main subject of interest.

All the numerical examples presented in tables and plots in this book are for illustration only. These are given in whatever units they were published in the original source from which they were taken.

The content of the entire book, though very relevant to the understanding of the role of water in biological systems, does not include any discussion of biological systems. The literature

on biological fluids is voluminous, and since most of our understanding of biological fluid is still far from satisfactory, I have decided to exclude this topic from the present book. I hope to devote a special book on this topic in the future.

The book does not discuss kinetic or transport quantities — diffusion, viscosity, rate of chemical reaction, rate of dielectric relaxation, and so on — all of which cannot be dealt with in the framework of equilibrium thermodynamics.

Although this book is written in a textbook style, it is not a textbook. Throughout the book, I have added a few exercises. Some to help the reader grasp the subject, and others to encourage critical reading of published statements.

The emphasis is mainly on theoretical results that have enriched our understanding of the properties of water. There exists a voluminous literature on the simulation of water and aqueous solutions. I shall discuss only a very small fraction of these results.

In my view, the simulation of water is more closely related to an experiment rather than to a theory. The only theoretical ingredient in the simulated experiment (besides the methodology of simulation itself) is the model pair potential. As in experiments, simulated results do not provide any explanation of the properties of water. Unlike an experiment that is carried out on a *real* system, the simulation is performed on hypothetical model particles. Therefore, whatever results one obtains from the simulation, they strictly pertain to these hypothetical model particles.

It is well known that in the theory of simple liquids, simulations have contributed to our understanding of the main features of the pair potential. A good agreement between computed macroscopic quantities, and the corresponding experimental data provides us with a sense of how close the pair potential used in the calculation is to the real pair potential.

The reason for this is that the properties of simple liquids are largely *determined* by the pair potential. Therefore, agreement between simulated results and experimental results lend support to the “reality” of the pair potential.

This is not the case for water. Even when a proposed pair potential leads to very good agreement between experimental and computed results, it does not mean that the pair potential is close to the real one. Conversely, even if we had the exact pair potential operating between two water molecules, it is doubtful that this will lead to better agreement between computed and experimental results. The reason is that the properties of water are not *determined* by the pair potential only. Higher order potentials are important and have significant effects on the behavior of liquid water.^f

Thus, even the most successful simulation that gives very good agreement between experimental and computed quantities, does not say anything about the *real* pair potential. All it can say is that some characteristics of the water-like model potential are important to the manifestation of some characterizing behavior of water. Judging from this point of view, the 1-D model has a definite advantage. Like the 3-D model, it does say something about the relationship between some characteristic properties of water, and some features of the pair potential, but unlike the 3-D case, the 1-D model says the same thing but exactly!

Guillot (2002) has recently reviewed the achievements of the various model potentials for water. In this review, Guillot focuses on the “philosophy which underlies the models and their ability to yield useful results.”

After thoroughly comparing the results of simulations for some 45 different potentials with experimental results, he asks

^fThis topic will be discussed further in Chapter 2.

the intriguing question: “What have we learnt?” His answer is *negative*: “The fact that no model potential is able to reproduce in every detail the properties of real water despite the 30 years of active research leaves a taste of incompleteness.” Having said that, he posed the next question: “Is there still room for improvement?” His answer to this question is *yes*.

I fully concur with Guillot’s “philosophy” as presented in his review. I also agree that the time has come to ask these questions. Yet I feel there is also room for another, perhaps more crucial, question to be asked: “Is it worthwhile searching for improvements?”

Guillot discusses several directions along which one can “improve” the results of the models. I believe that his “guidance for improvement” could indeed lead to better agreement with experimental results. It seems to me that Guillot believes that with such improvements, we could learn more about water. If this is true, then my views are quite different. I believe that even when one can achieve the ultimate improvement, there will still be room for asking the question: “*What can be learned from such improvement?*”

My answer to this question is: “*not much more than what we already have learned.*”

Postscript

After I have finished proofreading this book, I heard the sad news about Walter Kauzmann’s passing away on January 27, 2009.

I met Walter Kauzmann in one of the first Gordon conferences on Water back in the late 1960’s. It was during our long walks through the woods of New Hampshire that he encouraged me to write my first book on “Water and Aqueous Solutions,”

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and at the same time introduced me to the problem of hydrophobic interaction. In later years, Kauzmann staunchly supported and encouraged my work on both solvation and hydrophobic interaction.

I've got a lot of inspiration from his publications as well as his letters to me. Kauzmann is a gem of a scientist who continued to support my work even when we disagreed, or even when I published critical comments on his work. I feel that I will forever owe him a debt of gratitude.

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This work was partially done while I was at the National Institute of Standards and Technology (NIST). I also wish to thank my host Raymond Mountain for his hospitality while I was visiting NIST.

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LIST OF ABBREVIATIONS

BE:	Binding energy
CN:	Coordination number
FG:	Functional group
GPF:	Grand partition function
HS:	Hard sphere
HB:	Hydrogen bond
HR:	Hard rod
$H\phi I$:	Hydrophilic
$H\phi O$:	Hydrophobic
i.g.:	Ideal gas
KB:	Kirkwood-Buff
KBI:	Kirkwood Buff Integral
LJ:	Lennard Jones
MM:	Mixture model
MDF:	Molecular distribution function
1-D:	One-dimensional
2-D:	Two-dimensional
3-D:	Three-dimensional
PMHC:	Partial molar heat capacity
PF:	Partition function
PMF:	Potential of mean force
PMV:	Partial molar volume
PCF:	Pair correlation function
QCDF:	Quasi-component distribution function
RDF:	Radial distribution function
SPT:	Scaled particle theory
SOW:	Structure of water
SOOS:	Specific ordering of species
TSM:	Two-structure model
VP:	Voronoi polyhedron

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CHAPTER 1

Survey of the Properties of Water

Personal Introduction

My interest in the properties of water started while I was working on my PhD thesis in the early 1960s. My thesis focused on the outstanding properties of aqueous solutions of inert gases. It was clear then that the understanding of the properties of aqueous solutions hinged upon the understanding of the properties of liquid water.

I started to work on the theory of water only in my second year as a post-doctoral fellow at Bell-Labs with Frank Stillinger. For almost two years (1967–1968), I tried to construct a water-water pair potential. Most of the time was spent in determining the parameters of the potential function so that it would fit the experimental molecular properties such as dipole moment, second virial coefficient, and compressibility of ice (see Chapter 2).

I did not do any experimental work on pure water. All of the data reported in this chapter were either taken directly from the literature or derived from these data. Two relatively less known quantities are reported in Secs. 1.5 and 1.6. These quantities convey important local information derived from experimental data. The data that I used in my earlier book, published in 1974, were taken mainly from the Dorsey (1940) compilation. At that time, the book of Eisenberg and Kauzmann (1969) was also published. It summarized both the experimental and theoretical works on water. Fletcher's book (1970) summarized what

was known on the properties of ice. Most of the experimental data reported in this chapter were taken from NIST compilations.¹ The molecular interpretation of these properties will be discussed in Chapter 2.

1.1. Introduction and Some Historical Notes

In this chapter, we shall survey some of the most outstanding properties of liquid water. We shall begin with some historical notes on the earlier theories of water and aqueous solutions, and end this chapter with some notes on the relevance of the outstanding properties of water to life. To understand *liquid* water, it is necessary to be familiar with the properties of water in the gaseous phase, as well as in the solid phase. We shall briefly review these systems in Secs. 1.2 and 1.3. The outstanding properties of liquid water will be described in Secs. 1.4 through 1.6.

In anticipating the theoretical interpretation in Chapter 2, we can roughly divide the properties of water into two groups. The first includes properties such as the large heat capacity, the low solubility of inert solute, and hydrophobic interactions. At the molecular level, these were traditionally interpreted in terms of hydrogen bonds (*HBs*). This is basically true. However, the *HB*, *per se*, is not essential to the understanding of these properties. What is essential is the *strength* of the water-water interaction. Other liquids, with strong intermolecular interactions (whether by *HBs* or otherwise) will show similar behavior. As we shall see in Chapter 2, strong interactions or *HBs* by themselves do not reproduce any of the outstanding properties of water. Here, we emphasize that the strong interactions between water molecules are more fundamental than *HBs*.

¹Lemmon *et al.* (2007).

The second group consists of properties that are seemingly, as far as it is known, unique to liquid water.² Examples are the negative temperature dependence of the volume, the large negative entropy of solvation of inert solute, etc. These properties were traditionally interpreted at a molecular level in terms of the *tetrahedral structure* of ice — which also persists in liquid water. As we shall see throughout this book, the tetrahedral structure, though an important feature of water, is not essential to the understanding of water. What is essential is the unique correlation between low local density, and strong binding energy, as illustrated in the cover design and further elaborated on in Chapter 2.

The outstanding properties of liquid water were recognized long ago. A compilation of the properties of liquid water was first published in 1940 by Dorsey. Some of the outstanding properties of water were also discussed by Pauling (1940, 1960), Kavanau (1964), and Samoilov (1957) (the latter two are more concerned with the properties of aqueous solutions). The relevance of water to biology was discussed by Henderson (1913), Edsall and Wyman (1958), and Franks (2000). The modern era in the research on water started in the late 1960s with the publication of the Eisenberg and Kauzmann book in 1969. This was followed by a book on the molecular properties of liquid water (Ben-Naim, 1974). During the 1970s, a series of books were published by Franks (1973–1982) including chapters on specific topics written by specialized authors. A more recent book by Robinson *et al.* (1996) summarizes both the experimental and the theoretical advances in the field. An interesting, more descriptive book was also published by Ball (1999).

²For some exceptions, see Angell *et al.* (2000).

In this chapter, we shall survey some of the outstanding properties of pure water in the gaseous, liquid, and solid phases. We shall discuss only equilibrium thermodynamic quantities. Properties of aqueous solutions are deferred to Chapters 3 and 4.

1.2. Properties of Water in the Gaseous Phase

1.2.1. *The single water molecule*

In order to understand the properties of liquid water and its role in biological systems, one must be familiar with the basic properties of a single water molecule.

The notation H_2O for the water molecule shows the *composition* but not the geometry of the molecule. The structure of a single water molecule has long been established such that the nuclei of the oxygen atom and the two hydrogen atoms form an isosceles triangle (Fig. 1.1). The equilibrium³ O-H bond length is $0.957 \text{ \AA}$,⁴ and the H-O-H angle is equal to 104.52° .⁵ Note that this angle is smaller than the tetrahedral angle of 109.46° . The latter is an important quantity that we shall frequently encounter in this book (see also Appendix A).

This particular geometry has been established by a number of experiments utilizing a variety of methods as well as by theoretical calculations.⁶ For most of our studies of the properties of liquid water, we can assume that a water molecule has a *rigid* geometry with a fixed bond length and a fixed bond angle.

³Note that the two atoms O and H forming the bond O-H are not at a fixed distance. There are incessant vibrations that change the bond length. Therefore, we refer here to the equilibrium or the average bond length.

⁴One Ångström (Å) equals 10^{-8} cm.

⁵This is again an equilibrium or an average angle.

⁶For example, the heat capacity of water corresponds to three translational and three rotational degrees of freedom. Also from the dielectric constant of water vapor, one can determine the dipole moment of a single water molecule. These facts, as well as others, indicate that water is not a linear molecule.

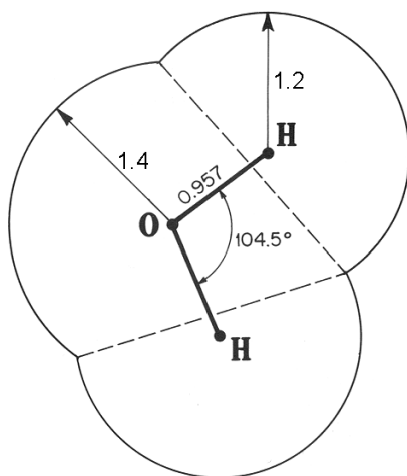


Fig. 1.1 The geometry of a single water molecule. The van der Waals radii of the hydrogen and oxygen atoms are indicated (in Å).

This simplified model is not sufficient for studying properties that are affected by the vibrations of a single water molecule, or by the dissociation of the molecule into charged ions H^+ and OH^- .

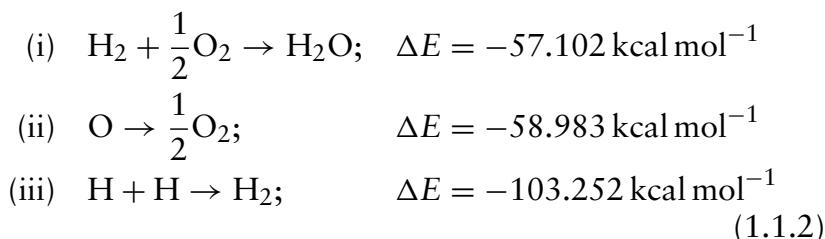
In this book we shall not discuss dissociation of a water molecule into either the ions H^+ or OH^- or to the neutral components hydrogen or oxygen. However, it is important to have an idea of the order of magnitude of the energies involved in the formation of a water molecule.

The energy of formation of a molecule H_2O is defined for the process



where H and O are the hydrogen and the oxygen atoms at the electronic ground state, and the water molecule is in the electronic, vibrational, rotational, and translational ground states, i.e. we carry out the hypothetical process (1.1.1) at absolute zero temperature. The energy associated with reaction (1.1.1) is

calculated from the energies of the following processes:



Thus, we have

$$\text{(i)} + \text{(ii)} + \text{(iii)} = (1.1.1); \quad \Delta E = -219.337 \text{ kcal mol}^{-1}
 \tag{1.1.3}$$

Note that the *electronic binding energy* is different from the energy of formation of the water molecule, the difference between the two being the zero point energy given in Table 1.1.

The motion of a water molecule may be described in terms of two components: (i) the motion of the center of mass of the entire molecule (this includes both translation and rotations) and (ii) the relative motions of the atoms within the molecule. The latter may be described in terms of three fundamental (“normal”) modes of vibration (see Fig. 1.2).

In Table 1.1, the frequencies ν_i ($i = 1, 2, 3$) correspond to the transition from the ground state (of all the vibrational modes) to the first vibrational level of the i th mode of vibration.⁷ The zero point energy of H₂O and of D₂O are also given in Table 1.1. For more details, see Eisenberg and Kauzmann (1969).

In Table 1.2 we present some data on the molecular properties of a single water molecule. All the values in the table pertain to the hypothetical “equilibrium state” of the molecule, i.e. a molecule that does not vibrate or rotate. Note also that the bond lengths and bond angles of H₂O and D₂O are nearly the same.

⁷It is easy to show that at room temperature less than 0.1% of the molecules are in any one of the excited vibrational states.

Table 1.1. The Vibrational Frequencies and Zero Point Energies of H₂O and D₂O^a

	H ₂ O	D ₂ O
ν_1 , symmetric stretching	3656.65	2671.46
ν_2 , asymmetric stretching	3755.79	2788.05
ν_3 , bending vibration	1594.59	1178.33
Zero point energy	4634.32	3388.67
	(13.2 kcal mol ⁻¹)	(9.8 kcal mol ⁻¹)

^aFrom Eisenberg and Kauzmann (1969), based on data from Benedict *et al.* (1956) and Herzberg (1950). Values of ν_1 , ν_2 , and ν_3 are in cm⁻¹. 1 cm⁻¹ corresponds to 2.859 cal mol⁻¹.

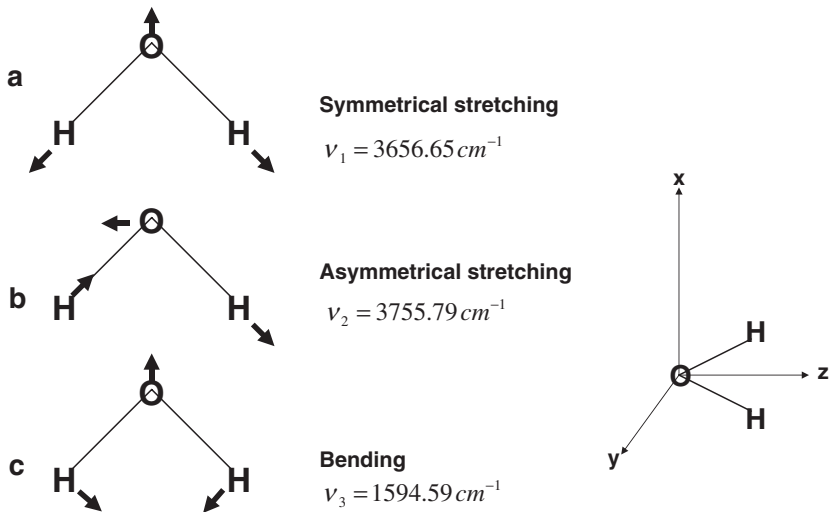


Fig. 1.2 The normal modes of vibration of a single water molecule. The first two vibrations (a) and (b) are referred to as the stretching vibrations with the corresponding frequencies ν_1 and ν_2 . The third (c) is referred to as the bending vibration, with frequency ν_3 .

In studying liquid water and aqueous solutions, most of the time we will be able to ignore both the internal motions (vibrations) of the atoms within molecules, and the dissociation of water molecules into their ionic components. This latter dissociation

Table 1.2. Molecular Properties of H₂O and D₂O^a

	H ₂ O	D ₂ O
Bond length $\times 10^8$ cm	0.9572	0.9575
Bond angle	104.523°	104.474°
Moment of inertia		
$I_x \times 10^{40}$ g cm ²	2.9376	5.6698
$I_y \times 10^{40}$ g cm ²	1.9187	3.8340
$I_z \times 10^{40}$ g cm ²	1.0220	1.8384

^aFrom Eisenberg and Kauzmann (1969) based on measurements by Benedict *et al.* (1956), all entries in this table refer to the equilibrium values. The x -axis passes through the center of mass of the molecule and is perpendicular to the plane of the molecule. The z -axis is a bisection of the bond angle, and the y -axis is perpendicular to x and z (Fig. 1.2).

phenomenon is important when we are interested in the acidity of aqueous solutions. Thus, our initial assumption is that a single water molecule has a fixed and rigid geometry. Since an oxygen atom is 16 times heavier than a hydrogen atom, the center of mass of the oxygen atom is approximately the same as the center of mass of the entire water molecule.

The geometry of a water molecule, as depicted in Fig. 1.1, takes into account only the *nuclei* of the three atoms. Of course, there are also electrons moving about these nuclei. This “cloud” of electrons gives rise to the notion of the “volume” of the water molecule. This molecular volume is not a well-defined concept; it is not like the concept of the volume of a (macroscopic) geometrical solid such as a sphere or a cube. Since the electrons are “spread” about the three nuclei, there exists no well-defined boundary to the water molecule. Nevertheless, we do assign an effective radius (hence volume) to each atom, referred to as the van der Waals radius of an atom, which is 1.4 Å for an oxygen atom and 1.2 Å for a hydrogen atom. With these van der Waals

radii, we can view the water molecule as though it has an *effective* solid structure. It is sometimes convenient to view a water molecule as a sphere of radius $1.41 \text{ \AA}$. (This radius is about half of the average distance between two closest water molecules as manifested by the first peak of the radial distribution function of water discussed in Sec. 1.4.5).

One more important property of the single water molecule that we need to define is the electric dipole moment. The nuclei and the electrons in each atom are charged particles — the positive nucleus and negative electrons. Since the total number of positive charges equals the total number of negative charges, the molecule as a whole is electrically neutral. However, the distribution of charges is not spherically symmetric; therefore, the water molecule as a whole is polar. The polarity of the molecule is a measure of the asymmetry in the distribution of the charged particles. This may be presented by a sum of electric multipoles,⁸ the first and the most important of which is the electric dipole moment.

The simplest example of a charge distribution would be two point charges of equal magnitude (e.g. $\pm q$), one positive and the other negative, separated by a distance d (Fig. 1.3). The strength of the dipole moment is $\mu = q \cdot d$, i.e. the charge multiplied by

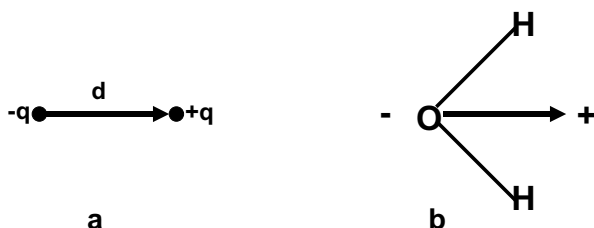


Fig. 1.3 (a) A dipole moment of two point charges at a distance d . (b) The direction of the dipole moment vector of a water molecule.

⁸For more details, see Bottcher (1952) and Jackson (1952).

the distance separating the two points. In a water molecule, the distribution charges are more complicated than this. One can assign dipole, quadrupole, octupole, etc. moments. The strength of the dipole moment denoted μ of a water molecule is 1.84×10^{-18} e.s.u. cm (electrostatic unit $\times$ centimeters) or 1.84 Debye.⁹ The dipole moment is a vector, the direction of which is usually designated from the negative to the positive charge.¹⁰ It has been established that the overall charge distribution of a water molecule produces a dipole moment that originates at the center of the oxygen atom and is directed along a line bisecting the angle H-O-H (see Fig. 1.3b). Values of higher multipoles are also known. For details, see Eisenberg and Kauzmann (1969) and Fletcher (1970).

1.2.2. *Interaction between two water molecules*

In the previous section, we presented the basic properties of a single water molecule. We now discuss the various ways two water molecules can interact. As we shall see in the following sections, knowledge of these interactions is essential to our understanding of the properties of liquid water and aqueous solutions.

What is a pair interaction? In the context of this book, the term “interaction” is an abbreviation for *interaction energy*.¹¹ In order to define the interaction energy between any two particles, we consider first two spherical atoms, e.g. two argon atoms. The interaction energy between two atoms at a distance R is defined as the difference in *energy* when we move the two atoms

⁹1 Debye = 10^{-18} e.s.u. cm.

¹⁰In chemistry, the dipole vector is defined from the positive to the negative charge.

¹¹In the literature, the term “interaction” is also used for what is referred to as the potential of mean force. This is discussed in Chapter 4.

from an infinite separation to a distance R . We denote this interaction energy by

$$U(R) = E(R) - E(\infty) \quad (1.2.1)$$

Note that we use here a “thought experiment” to define the interaction energy. We start with two atoms at rest (i.e. no kinetic energy) at infinite separation (∞), bring them to a distance R , and calculate the change of energy or the work done in this process. Clearly, such a process cannot be carried out in the laboratory. However, we can calculate the general form of the function $U(R)$ either by pure theoretical means, or from some experimental measurement that we can perform¹² (for instance, measuring deviations from ideal gas behavior, viscosity of gases, etc). From these calculations we get the general form of the function $U(R)$, which we call the pair potential or the pair-interaction energy. Figure 1.4 shows the qualitative form of this function for neon, argon, krypton, and xenon.

The curves for this illustration were obtained from the Lennard–Jones (LJ) function

$$U(R) = 4\varepsilon \left[\left(\frac{\sigma}{R} \right)^{12} - \left(\frac{\sigma}{R} \right)^6 \right] \quad (1.2.2)$$

with parameters given in Table 1.3.

The region of positive values of $U(R)$ is referred to as the repulsive part of the interaction. To reach this region, work must be done in order to push the two particles to a distance smaller than the effective diameter of the spherical atom, σ .¹³ On the other hand, energy is released when the two particles are brought to a distance greater than σ . As can be seen in Fig. 1.4,

¹²See, for example, Hirschfelder *et al.* (1954).

¹³In this preliminary discussion, we ignore the difference between σ , which is the location where $U(R = \sigma) = 0$, and the minimum of the function $U(R)$, which is at $\sqrt[6]{2}\sigma$.

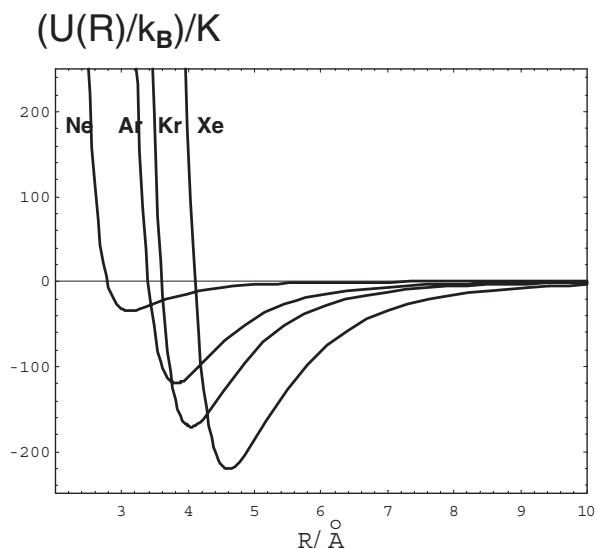


Fig. 1.4 The pair potential for neon, argon, krypton, and xenon.

Table 1.3. Values of σ and of ϵ/k_B for the Lennard–Jones Function Fitted to Obtain the Second Virial Coefficient of Inert Gases^a

Gas	$\sigma(\text{\AA})$	$\epsilon/k_B(K)$
Ne	2.78	34.9
Ar	3.40	119.8
Kr	3.60	171.0
Xe	4.10	221.0

^aFrom Hirschfelder *et al.* (1954).

the potential rises steeply for $R < \sigma$. We usually refer to σ as the van der Waals diameter of the particles. It is a “diameter” in the sense that two particles cannot penetrate into each other to a distance smaller than σ . Note also that a negative slope in the pair potential corresponds to a repulsive *force*, a positive slope corresponds to an attractive force between the two particles.

All we have said thus far is valid for spherical particles such as argon atoms for which the interaction energy is a function only of the distance R . Next, we describe a few simple interaction potentials. The interaction energy between two point charges, q_1 and q_2 , at a distance R , is given by Coulomb's law, i.e.¹⁴

$$U(R) = \frac{q_1 q_2}{R} \quad (1.2.3)$$

By extending Eq. (1.2.3), we can write the interaction energy between a point charge q_1 and a dipole (Fig. 1.5). It is clear that the interaction energy here depends on the orientation of the dipole moment. If we view the dipole as a combination of two-point charges (of charges $+q$ and $-q$ at distance d apart), then we can write the interaction energy between a charge q_1 and the dipole as simply the sum of two Coulombic interactions, namely (Fig. 1.5)

$$U(R_1, R_2) = \frac{q_1 q}{R_1} - \frac{q_1 q}{R_2} \quad (1.2.4)$$

Coulomb's law can be extended further for a *pair* of dipoles (see Fig. 1.6). Again, we can sum up all the Coulombic interactions between the four point charges (excluding here the two interactions between charges belonging to the same dipole). Thus, we write (Fig. 1.6)

$$U(R_1, R_2, R_3, R_4) = \frac{q^2}{R_1} + \frac{q^2}{R_2} - \frac{q^2}{R_3} - \frac{q^2}{R_4} \quad (1.2.5)$$

Note that we have assumed here that all point charges have the same magnitude q .

In most applications, we do not need Eq. (1.2.5) for the dipole-dipole interaction. Instead, we need only the interaction between two dipoles when the distances $R_i (i = 1, 2, 3, 4)$ are all

¹⁴Here, we show only the functional form of Coulomb's law; in order to fix the units, we would need to add a constant to the right-hand side of the equation.

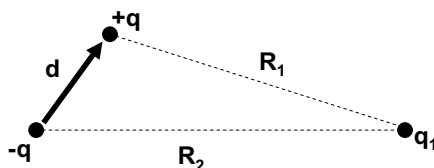


Fig. 1.5 The interaction between a point charge (q_1) and a dipole.

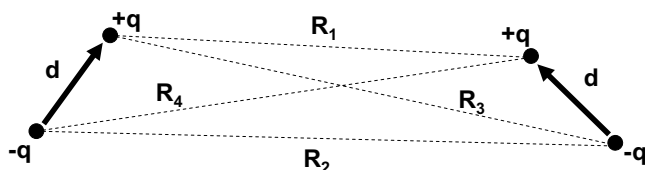


Fig. 1.6 The interaction between two dipoles is a result of the interactions between the four pairs of point charges.

very large compared to the distance d — in which case we say that we have two point-dipoles¹⁵ of strength $\mu = qd$, and the interaction between them is given by

$$U(R) = \alpha \frac{\mu^2}{R^3} \quad (1.2.6)$$

Here, R is the distance between the two point-dipoles, and α depends on (i) the orientation angles of the two dipoles, relative to the line connecting the two point-dipoles, and (ii) the dihedral angle of rotation between the dipoles (Fig. 1.7).

The most important aspect of the dipole-dipole interaction in Eq. (1.2.6) is that the interaction energy changes with distance as R^{-3} , whereas the Coulombic interaction between two charges changes with distance as R^{-1} . In general, the interaction energy

¹⁵A point-dipole is defined as the product of q and d when $q \rightarrow \infty$ and $d \rightarrow 0$, but the product $q \times d$ remains constant.

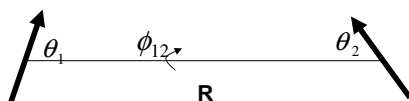


Fig. 1.7 The interaction energy between two dipoles depends on the distance R and the three angles θ_1 , θ_2 , and ϕ_{12} [Eq. (1.2.10)].

between two dipoles depends on four parameters: one distance and three angles.

The interaction energy between two water molecules is more complicated than the dipole-dipole interaction. Here, we shall describe some of the general features of this function.

As we indicated above, the pair potential between two water molecules is a complicated function of the distance R and the five orientation angles. The exact analytical form of this pair potential is not known.¹⁶ Earlier models of water were proposed by Bernal and Fowler (1933), Verwey (1941), Bjerrum (1951), Stockmyer (1941), Rowlinson (1951), and others. All these failed to reproduce the characteristic radial distribution of water (see Sec. 1.4.5). What one usually uses in the theory of water is not the true pair potential¹⁷ but an *effective* pair potential consisting of essentially three parts, which we write as

$$U(\mathbf{X}_1, \mathbf{X}_2) = U_{LJ}(R) + U_{DD} + U_{HB} \quad (1.2.7)$$

The first part, $U_{LJ}(R)$ is a Lennard–Jones (*LJ*) potential that has the general form as in Eq. (1.2.2), where ε and σ are parameters that approximately equal the parameters used to describe the pair potential between two neon atoms. $\varepsilon = 5.01 \times 10^{-15} \text{ erg} = 7.21 \times 10^{-3} \text{ kcal mol}^{-1}$, $\sigma = 2.82 \text{ \AA} = 2.82 \times 10^{-8} \text{ cm}$. Note that for $R = \sigma$, the pair potential is

¹⁶It is not clear that an exact analytical form of a pair potential exists.

¹⁷As we shall discuss in Chapter 2, the “true” pair potential in itself is not essential for understanding the behavior of water.

zero (see Fig. 1.4). On the other hand, the minimum of the LJ potential is obtained at $R_{\min} = \sqrt[6]{2}\sigma$, where the value of the potential is

$$U(R_{\min}) = -\varepsilon \quad (1.2.8)$$

Hence, σ measures the “size” of the particles, and ε the strength of the interaction energy between the particles.

The LJ part of the potential is used mainly to account for the repulsive interaction when the two molecules come to a very short distance $R \leq \sigma$. Sometimes, instead of an LJ potential of the form (1.2.2), one uses a hard-sphere (HS) potential, defined by (Fig. 1.8)

$$U_{HS}(R) = \begin{cases} \infty & \text{for } R \leq \sigma \\ 0 & \text{for } R > \sigma \end{cases} \quad (1.2.9)$$

The second part, U_{DD} , is the dipole-dipole interaction. For two point-dipoles μ_1 and μ_2 at locations $\mathbf{R}_1$ and $\mathbf{R}_2$, the

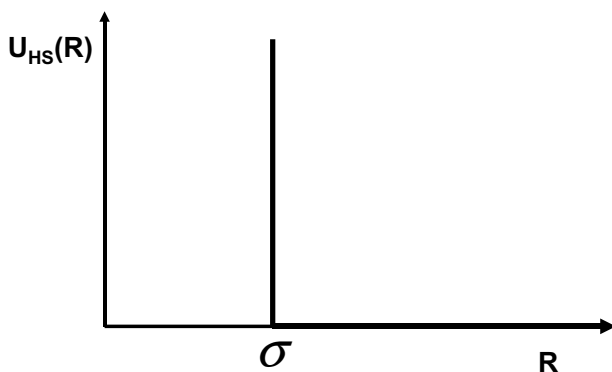


Fig. 1.8 The interaction potential function for a pair of hard spheres of diameter σ [Eq. (1.2.9)].

dipole-dipole interaction is

$$\begin{aligned}
 U_{DD}(\mathbf{R}_1, \boldsymbol{\Omega}_1, \mathbf{R}_2, \boldsymbol{\Omega}_2) &= \frac{(\boldsymbol{\mu}_1 \cdot \boldsymbol{\mu}_2) - 3(\boldsymbol{\mu}_1 \cdot \mathbf{u}_{12})(\boldsymbol{\mu}_2 \cdot \mathbf{u}_{12})}{|\mathbf{R}_1 - \mathbf{R}_2|^3} \\
 &= \frac{-\mu^2}{R^3} (2 \cos \theta_1 \cos \theta_2 - \sin \theta_1 \sin \theta_2 \cos \phi_{12}) \quad (1.2.10)
 \end{aligned}$$

where $\mu_i = |\boldsymbol{\mu}_i|$ is the dipole moment of the particle i and $\mathbf{u}_{12}$ is a unit vector along $\mathbf{R}_1 - \mathbf{R}_2$ and $R = |\mathbf{R}_1 - \mathbf{R}_2|$, is the distance between the two dipoles. The brackets on the right-hand side of (1.2.10) are the scalar products between the two vectors. The angles θ_1, θ_2 , and ϕ_{12} are shown in Fig. 1.7. In the second line of Eq. (1.2.10), we assume that $\mu = \mu_1 = \mu_2$.

This part of the pair potential is added mainly to account for the long-range interactions between the two molecules. It should be noted that the R^{-3} distance dependence of the dipole-dipole interaction is valid for fixed orientations of the dipoles. The *average* dipole-dipole interaction at large distance has an R^{-6} dependence.

The third contribution to the pair potential, U_{HB} , is the “hydrogen-bond” (*HB*) component of the interactions, which is more difficult to describe analytically. Qualitatively, U_{HB} should account for the *HB* interactions. We visualize a water molecule with four preferential directions, two along the O-H direction, and two along the “lone-pair” direction. These four preferential directions point to the four vertices of a regular tetrahedron (Fig. 1.9). Along the latter two (“lone-pair”) directions is a negative charge-concentration. When two water molecules are separated by a distance of about $R_{HB} \approx 2.76 \text{ \AA}$, and are oriented such that the O-H direction of one molecule is directed toward the lone-pair direction of the other, a hydrogen bond is formed (see the schematic description in Fig. 1.10). Fundamentally, a

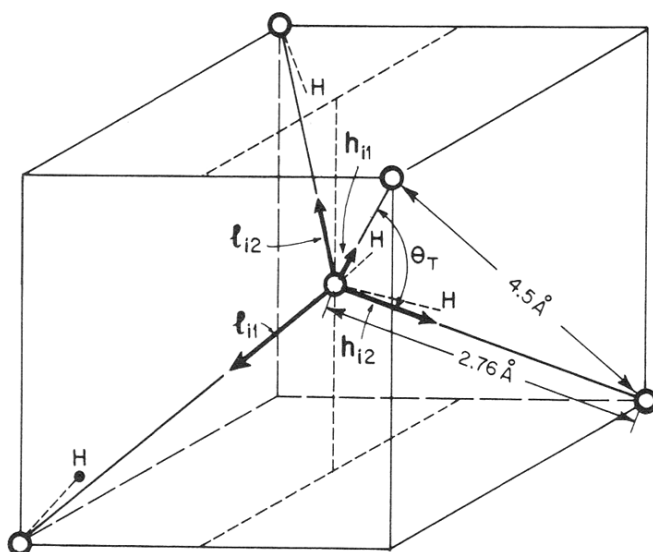


Fig. 1.9 Tetrahedral geometry (see the description in Sec. 1.2).

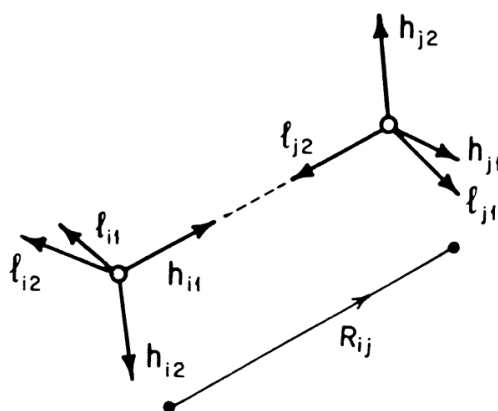


Fig. 1.10 A pair of water molecules in a configuration of a hydrogen bond.

hydrogen bond is a quantum-mechanical phenomenon,¹⁸ and our description of it here is only qualitative, but the important

¹⁸For an extensive discussion of hydrogen bonds, see Pauling (1959), Pimentel and McClellan (1960), or Marechal (2007).

thing to remember is that when two water molecules are oriented such that a hydrogen bond is formed; the interaction energy is quite large (of the order of $5\text{--}6\text{ kcal mol}^{-1}$).¹⁹ This interaction energy is an order of magnitude larger than that of a typical van der Waals interaction between two neon atoms, but an order of magnitude smaller than that of a typical covalent bond between two atoms within a molecule. (For instance, the O-H covalent bond energy is about 102 kcal mol^{-1} .)

It should be noted that tetrahedral geometry is not realized by a single water molecule. The ground state of an oxygen atom has the configuration $(1s)^2 (2s)^2 (2p)^4$. When forming a water molecule, the H-O-H angle is about 104.5° , slightly larger than the expected 90° from the perpendicular p-orbitals. This opening of the bond angle is ascribed to the repulsion between the two hydrogen atoms. The tetrahedral geometry is a result of the hybridization of the 2s and 2p orbital to form the sp^3 hybrid orbitals.

The “mechanism” for the formation of tetrahedral structures by water is similar to the formation of tetrahedral structures by carbon atoms. When a water molecule forms a hydrogen bond, the electron distribution around the oxygen atom changes. Four new orbitals are formed by the hybridization of the 2s and 2p orbitals of the oxygen atom. As a result of this hybridization, two lobes of charge are created by the unshared electron pairs (or lone-pair electrons), which are symmetrically located above and below the molecular plane. These two directions, together with the two O-H directions, give rise to the tetrahedral geometry, which is one of the most prominent structural features of the mode of packing of water molecules in the liquid and solid states.

¹⁹The linear configuration of the dimer as depicted in Fig. 1.10 has the lowest energy compared with other possible configurations of a dimer of water molecules.

It is convenient to introduce four unit vectors originating from the center of the oxygen atom and pointing toward the four corners of the regular tetrahedron (Fig. 1.9). Let $\mathbf{h}_{ik}$ ($k = 1, 2$) be the two unit vectors belonging to the i th molecule and pointing approximately along the two O-H directions. The remaining two vectors $\mathbf{l}_{ik}$ ($k = 1, 2$) are pointing along the directions of the lone pairs of electrons. Using the terminology of hydrogen-bond formation, we identify $\mathbf{h}_{ik}$ as the directions along which molecule i forms a hydrogen bond as a *donor* molecule, whereas $\mathbf{l}_{ik}$ is the direction along which the same molecule participates in a hydrogen bond as an *acceptor*. A simple geometrical consideration shows that the tetrahedral angle of $\theta_T = 109.46^\circ$ is obtained from the relation $\theta_T = \arccos(-1/3)$. For details, see Appendix A.

As mentioned above, because the pair potential for two water molecules [say, of the general form (1.2.7)] depends on six parameters, any calculation associated with the properties of water is extremely complex and time-consuming. For example, suppose we want to calculate an integral of the form

$$\int_a^b \{\exp[-\beta U(R)] - 1\} 4\pi R^2 dR \quad (1.2.11)$$

Here, $U(R)$ is a pair potential that depends only on distance R , β is a constant, $\beta = (k_B T)^{-1}$, and the integration extends from a to b . This kind of integral actually occurs in calculations of the pressure of a real gas. Here, we focus only on the technical aspect of the numerical calculation of this integral.

In order to perform a numerical integration, we divide the interval (a, b) into, say, 10 small intervals. We then calculate the area under the curve for each interval, as if it were a narrow rectangle, and then sum up all the areas obtained for each of these rectangles. As we increase the number of divisions of the interval a, b , we improve our estimation of the area under the curve.

Next, suppose we want to calculate an integral of the form (1.2.11), but with the pair potential for two water molecules. In this case, the potential function $U(R, \alpha_1, \alpha_2, \alpha_3, \alpha_4, \alpha_5)$ is a function of *six* parameters, one distance and five angles. We again choose only 10 points of divisions for each of the variables. This means that we have to evaluate the potential function at 10^6 points, instead of at only 10 points, as in the evaluation of the one-dimensional integral. This results in an exponential dependence of the computational time on the dimensionality of the pair potential and imposes a severe limitation on the accuracy of our calculations of the thermodynamic properties of water.

The pair potential is an important quantity that determines the deviations of the equation of state from the ideal gas equation of state. The equation of state of an ideal gas has the form

$$\rho = \frac{N}{V} = \frac{P}{RT} \quad (1.2.12)$$

where P is the pressure, R the gas constant, T the absolute temperature, and ρ the density of the gas.

The theoretical models of *ideal gases* presume the existence of non-interacting point particles. Such a system has an equation of state of the form (1.2.12). For *real gases* of interacting molecules, e.g. water, one can approximate the behavior of the system according to (1.2.12) provided that we take very low densities. How low? The answer depends on the specific molecules. The stronger the intermolecular forces, the lower the density is for which (1.2.12) holds true. For water, this low density ρ_w is much smaller than the low density ρ_A of argon. The reason is that, on average, two water molecules interact more strongly than two argon atoms. We must therefore take lower densities of water and hence, on average, larger intermolecular distances to obtain the ideal gas limiting behavior.

When we increase the density beyond the ideal gas limit, deviations from Eq. (1.2.12) are noticeable. In such cases one

can write correction terms to Eq. (1.2.12) that have the general form²⁰

$$\frac{P}{RT} = \rho + B_2(T)\rho^2 + B_3(T)\rho^3 + \dots \quad (1.2.13)$$

This equation gives the pressure of the gas as a function of the density. Clearly, when the density is very low, $\rho \rightarrow 0$, we have the limiting ideal gas behavior (1.2.12). At slightly higher densities, only the first correction to the ideal gas behavior should be taken into account, i.e. the equation of state at this density is

$$\frac{P}{RT} = \rho + B_2(T)\rho^2 \quad (1.2.14)$$

The coefficient $B_2(T)$ in the expansion (1.2.13) can be expressed as an integral over the pair potential. For spherical particles we have²¹

$$B_2(T) = -\frac{1}{2} \int_0^\infty \{\exp[-\beta U] - 1\} 4\pi R^2 dR \quad (1.2.15)$$

This result is one of the most remarkable achievements of statistical mechanics: it states that the first order deviations from an ideal gas behavior may be calculated from a system of exactly two molecules in a volume V and temperature T .

A similar expression may be written for more complicated pair-potential functions. A simpler form of the integral in Eq. (1.2.15) can be obtained for hard spheres of diameter σ , for which the potential function $U(R)$ is zero for $R \geq \sigma$, but infinite for $R < \sigma$ [see (1.2.9)]. Hence, the result of the integration is

$$B_2(T) = -\frac{1}{2} \int_0^\sigma (-1) 4\pi R^2 dR = \frac{2\pi\sigma^3}{3} = \frac{16\pi r_0^3}{3} \quad (1.2.16)$$

which is four times the volume of each hard sphere of radius r_0 .

²⁰The coefficients $B_2(T)$ and $B_3(T)$ depend on the temperature T , but not on the volume of the system.

²¹See, for example, Hill (1956).

The second virial coefficient for water may be written as²²

$$B_2(T) = -\frac{1}{2(8\pi^2)} \int d\mathbf{X}_2 f(\mathbf{X}_1, \mathbf{X}_2) \quad (1.2.17)$$

where f is defined by

$$f(\mathbf{X}_1, \mathbf{X}_2) = \exp[-\beta U(\mathbf{X}_1, \mathbf{X}_2)] - 1 \quad (1.2.18)$$

where $\mathbf{X}_i$ is the vector comprising the six coordinates that are used to describe the configuration of a water molecule.

Figure 1.11 shows the values of $B_2(T)$ for water and heavy water. The two curves are almost indistinguishable on the scale of Fig. 1.11a. Figure 1.11b is an amplification of a part of Fig. 1.11a, in the region of lower temperatures.

Note also that for any substance at very high temperatures, the function f must tend to -1 ; hence, the second virial coefficient will tend to the value of the volume as in (1.2.16). As can

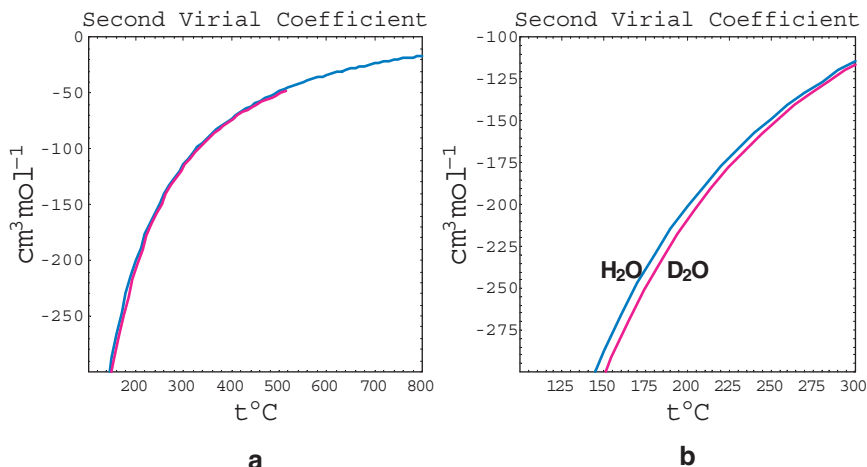


Fig. 1.11 Second virial coefficient for water and heavy water, based on data from Lemmon *et al.* (2007).

²²See, for example, Ben-Naim (1992).

be seen from Fig. 1.11, this limit is not reached at a temperature of 800°C.

The third virial coefficient $B_3(T)$ is more difficult to determine experimentally and far more difficult to compute. For a system with pairwise additive interactions, the third virial coefficient is expressed in terms of the pair potential as²³

$$B_3(T) = \frac{-1}{3(8\pi^2)^2} \int d\mathbf{X}_2 d\mathbf{X}_3 f(\mathbf{X}_1, \mathbf{X}_2) f(\mathbf{X}_1, \mathbf{X}_3) f(\mathbf{X}_2, \mathbf{X}_3) \quad (1.2.19)$$

Figure 1.12 shows the values of $B_3(T)$ for water and heavy water.

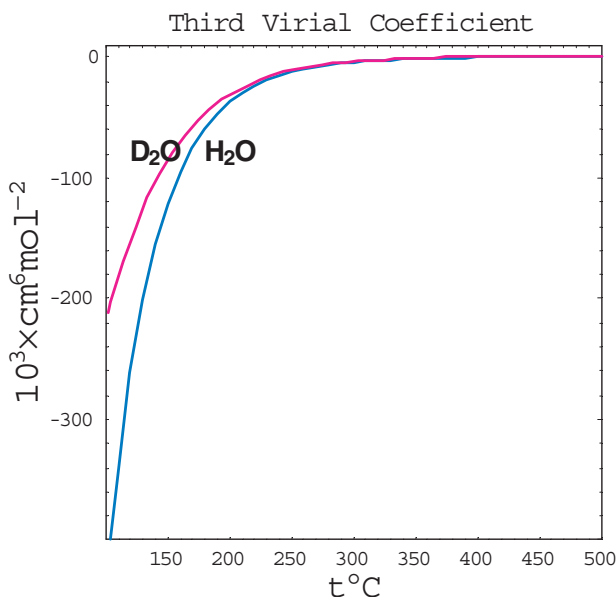


Fig. 1.12 Third virial coefficient for water and heavy water, based on data from Lemmon *et al.* (2007).

²³See, for example, Ben-Naim (1992).

Again, we note that in the high temperature limit,²⁴ $f \rightarrow -1$, and hence

$$B_3(T \rightarrow \infty) = \frac{1}{3} \left(\frac{4\pi\sigma^3}{3} \right)^2 \quad (1.2.20)$$

Before concluding this section it should be noted that in calculating the second virial coefficient, one needs the *true* pair potential for water. To study the properties of liquid water, or even the third virial coefficient, the *true* pair potential is not enough. The reason is that non-additive, higher order potentials are important in determining the properties of liquid water as well as of the third virial coefficient.

The extent of the non-additivity of the three-body potential is defined as the difference

$$\delta U_3 = U(\mathbf{X}_1, \mathbf{X}_2, \mathbf{X}_3) - U(\mathbf{X}_1, \mathbf{X}_2) - U(\mathbf{X}_1, \mathbf{X}_3) - U(\mathbf{X}_2, \mathbf{X}_3) \quad (1.2.21)$$

where $U(\mathbf{X}_i, \mathbf{X}_j)$ is the work done to bring two water molecules from infinite separation to the final configuration $\mathbf{X}_i, \mathbf{X}_j$. Similarly, $U(\mathbf{X}_1, \mathbf{X}_2, \mathbf{X}_3)$ is the work required to bring three water molecules to the final configuration $\mathbf{X}_1, \mathbf{X}_2, \mathbf{X}_3$.

A similar definition applies for four and higher order potential functions. For simple liquids, δU_3 is to a good approximation negligible. For water there is evidence that the additivity assumption of the higher order potentials is not justified.

The non-additivity of the *HB* was discussed qualitatively by Frank and Wen (1957),²⁵ and more quantitatively by Del Bene and Pople (1970) and Hankins *et al.* (1970). It was found that

²⁴Note that “high temperature” means high enough T such that $\beta U \rightarrow 0$ in regions where U is finite. For distances $R \leq \sigma$, $\beta U(R)$ is assumed to be infinity, or $\exp[-\beta U(R)] = 0$.

²⁵Frank and Wen use the term “cooperativity” of the hydrogen bonding to describe non-additivity.

the non-additivity of the hydrogen bonding is very significant.²⁶ We shall return to this question of non-additivity of the potential energy in Chapter 2.

1.3. Properties of Water in the Solid Phase

1.3.1. Ordinary ice

Ice can have at least nine different stable and well-characterized structures. The one referred to as “ordinary ice” is the one that we are all familiar with. This is obtained when water freezes at 0°C under ordinary atmospheric pressure. It is sometimes referred to as *hexagonal* ice and is denoted I_h .

The basic structure of ice was determined by Bragg in 1922 using the technique of X-ray crystallography. The “structure” of ice refers to the arrangement in space of the oxygen atoms. The structure of ordinary ice is shown in Fig. 1.13. The most important feature of the structure of ice is the *tetrahedral*

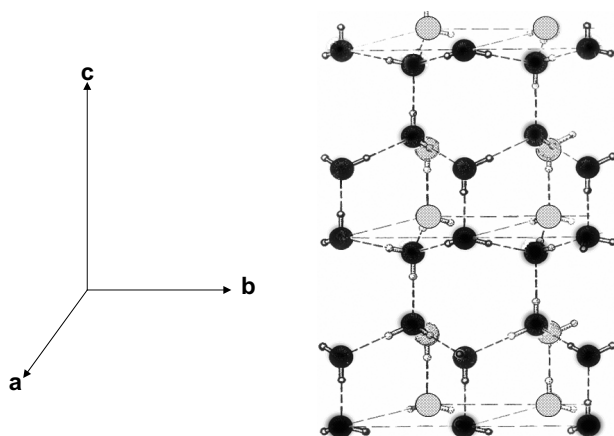


Fig. 1.13 The structure of ordinary ice I_h .

²⁶Hankins *et al.* (1970).

geometry: each oxygen atom is surrounded by four other oxygen atoms situated at the vertices of a regular tetrahedron, at a distance of $2.76 \text{ \AA}$ from the central oxygen atom (see Figs. 1.9 and 1.13). As far as the geometry is concerned, the structure of D_2O is almost exactly the same as that of H_2O .

Suppose we shrink ourselves and sit at the center of an oxygen atom. We see four other oxygen atoms in our immediate vicinity, each one at a distance of $2.76 \text{ \AA}$ and all four positioned in the four corners of a regular tetrahedron. This point of view does not reveal to us the entire three-dimensional structure of ice I_h . Take note that along the axis labeled c in Fig. 1.3, the oxygen atoms are arranged in a structural pattern that differs from the corresponding pattern of the oxygen atoms along the two axes perpendicular to c . The difference is shown in Fig. 1.14. If we look through an O-O nearest-neighbor bond along the c -axis, we see that all the other O-O bonds are “eclipsed,” i.e. on a 2-D drawing they would all be superimposed. On the other hand, if we look through an O-O bond along an axis (nearly) perpendicular to the c -axis, we see that three of the O-O bonds are rotated at an angle of 60° relative to the other three O-O bonds; this is the “staggered” configuration.

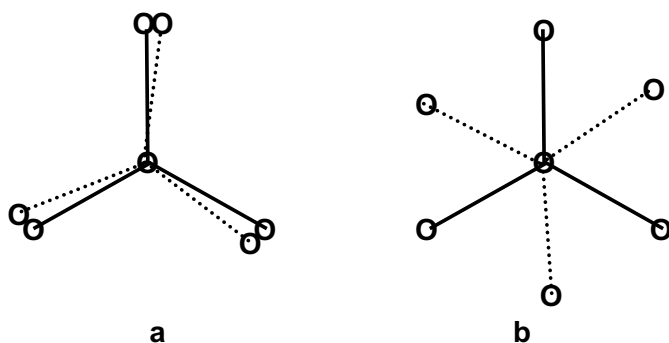


Fig. 1.14 Two views of the distribution of oxygens along the O-O axis: (a) eclipsed, and (b) staggered.

This difference in structure along different axes is revealed in the way the properties of ice differ according to the measurement along different axes. For example, the coefficient of linear expansion is $63 \times 10^{-6} \text{ } ^\circ\text{C}^{-1}$ along the c -axis but $46 \times 10^{-6} \text{ } ^\circ\text{C}^{-1}$ along an axis perpendicular to the c -axis (at -10°C). Similarly, the isothermal compressibility and the dielectric constant of ice are different along the different axes. For more details, see Eisenberg and Kauzmann (1969).

1.3.2. *The residual entropy of ice*

All the structural information discussed in the previous subsections is about the locations of oxygen atoms. Using X-ray crystallography, one cannot determine the locations of the hydrogen atoms.

In 1933, Bernal and Fowler concluded from the available experimental data that water molecules in ice maintain their molecular identity, and that the hydrogen atoms are located at the corners of a regular tetrahedron, the center of which is occupied by an oxygen atom. They formulated the so-called two ice conditions (see Fig. 1.15).

- (i) Each O-O line accommodates one and only one hydrogen atom.
- (ii) Each oxygen atom has two hydrogen atoms that are at a distance of about $1 \text{ \AA}$ and two hydrogen atoms at a distance of about $1.76 \text{ \AA}$.

These two ice conditions reflect the experimental findings that when ice is formed from either the gas or the liquid phase, water retains its identity as a single molecule, i.e. one can identify single water molecules in the ice lattice. In addition, each pair of nearest-neighbor water molecules form hydrogen bonds in such a way that only *one* hydrogen is situated along the O-O

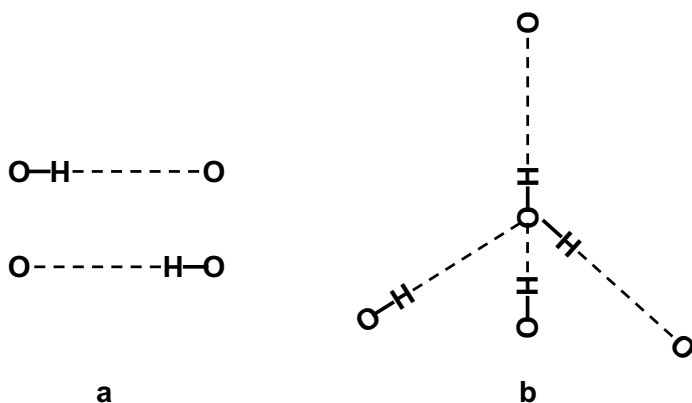


Fig. 1.15 The two ice conditions: (a) fulfilling condition (i), and (b) fulfilling condition (ii).

line (see Fig. 1.15). In this discussion of the structure of ice, we are disregarding the very small concentrations of ions such as OH^- and H_3O^+ . Such local defects do not conform to the ice conditions. Given the structural arrangement of the oxygen atoms, and assuming the validity of the two ice conditions, there is still a large number of possible arrangements for the hydrogen atoms.

In 1935, Pauling calculated the approximate number of possible configurations for the hydrogen atoms that are consistent with the ice conditions. This calculation is now considered a classical example of a successful prediction based on an elementary probabilistic argument. Because of its historical importance and its didactic simplicity, we present here Pauling's solution to this problem.

Consider a perfect ice structure containing N water molecules, i.e. N oxygen atoms are situated at N lattice points. The question is: How many ways can we arrange the $2N$ hydrogen atoms on this lattice such that the two ice conditions are fulfilled?

Since we are dealing with a macroscopic quantity of ice, N is of the order of the Avogadro number. Hence, we can neglect surface effects in our calculations.

For a very large crystal, N oxygen atoms produce $2N$, O-O nearest-neighbor bonds. We need to place the $2N$ hydrogen atoms in such a way that the two ice conditions are fulfilled. We first position the hydrogen atoms on the O-O bonds so that one hydrogen falls on each of the O-O bonds. Each O-O bond provides two locations for placing the hydrogen atom. These we denote $\text{O}-\text{H}\cdots\text{O}$ and $\text{O}\cdots\text{H}-\text{O}$. In the first placement, the H is near the oxygen on the left-hand side; in the second, it is near the oxygen on the right-hand side. See Fig. 1.15a.

Since each of the hydrogen atoms can be placed at one of the two locations on the O-O bond, there are a total of 2^{2N} configurations that fulfill condition (i). Clearly, not all of the 2^{2N} configurations fulfill condition (ii). In Fig. 1.16, we show a system of five oxygen atoms and all of the possible arrangements of hydrogens around the central oxygen atom. Most of these configurations are not consistent with condition (ii). The next question is: How many of the 2^{2N} configurations are consistent with the second ice condition?

If we focus on a single oxygen atom and its four oxygen neighbors, we can make the following list of configuration types

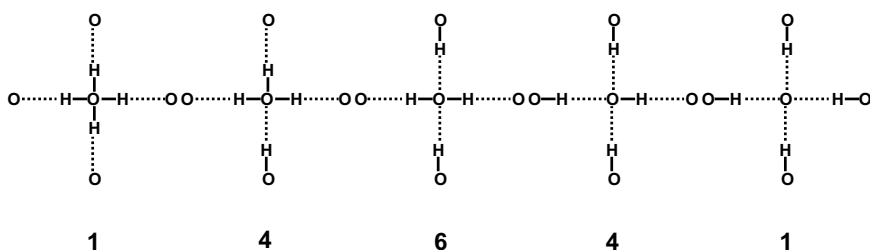


Fig. 1.16 The five possible arrangements of hydrogens around a given oxygen.

(see Fig. 1.16 from left to right):

- (1) One arrangement in which all hydrogens are close to the central oxygen.
- (2) Four arrangements in which three hydrogens are close to the central oxygen, while the other one is far away.
- (3) Six arrangements in which two hydrogens are close to the central oxygen, while the other two are far away.
- (4) Four arrangements in which one hydrogen is close to the central oxygen, while the other three are far away.
- (5) One arrangement in which all hydrogens are far away from the central oxygen.

Altogether, there are 16 different arrangements divided into five groups:

Group:	1	2	3	4	5
Number of arrangements:	1	4	6	4	1

Of these 16 arrangements, all of which are consistent with the first ice condition, only six arrangements (i.e. those in group 3) are also consistent with the second ice condition.

Pauling's reasoning is as follows: first assume that the fraction $6/16$ is also the *probability* of finding a single oxygen atom with the right configuration (i.e. one that fulfills the second ice condition),²⁷ and then assume that all oxygen atoms are

²⁷Note that this assumption is not exact. In the classical definition of probability, one calculates the probability of an event by taking the ratio of all configurations that are consistent with the event (here, 6), and dividing by the total number of configurations (here, 16). This method of calculating probability is valid only when all of the configurations are elementary events, i.e. when they all have an equal probability of occurring. It is not clear whether the 16 configurations in our case are elementary events.

independent.²⁸ The probability that all oxygen atoms have configurations that fulfill the second condition is therefore $(6/16)^N$. This is also the fraction of the total configurations that fulfill the two ice conditions. Hence, the number of the configurations that fulfill the two ice conditions is

$$\Omega = \left(\frac{6}{16}\right)^N 2^{2N} = \left(\frac{3}{2}\right)^N = 1.5^N \quad (1.3.1)$$

This result would not have been so remarkable had it not been related to the residual entropy of ice (see Appendix B).

The experimental value of the residual entropy of ice is known²⁹:

$$S_{\text{exp}} = 0.81 \text{ cal mol}^{-1} \text{K}^{-1} \quad (1.3.2)$$

Assuming that the residual entropy is determined by the number of configurations Ω in (1.3.1), we get the theoretical value of the residual entropy:

$$S_{\text{th}} = k_B \ln \Omega = k_B \ln (1.5)^N = R \ln 1.5 = 0.805 \text{ cal mol}^{-1} \text{K}^{-1} \quad (1.3.3)$$

The relation between S and Ω is the famous Boltzmann equation. It is engraved on Boltzmann's tombstone, which can be found in a Vienna cemetery. This is a very remarkable relation between a thermodynamic quantity (the entropy) on the one hand and the number of configurations of a system on the other. The larger the number of configurations (having equal probabilities), the larger the uncertainty, or the larger the missing information in the system. This is the essence of the

²⁸Again, from a mathematical point of view, independence exists only when the probability of occurrence of a particular configuration around a particular oxygen atom does not depend on the configuration around any other oxygen atom. It is not clear how valid this assumption is in the physical world of oxygen atoms in ice.

²⁹Giauque and Stout (1936). See also Di Marzio and Stillinger (1964) and Lebowitz (1968).

meaning of entropy. For more details, see Ben-Naim (2008). It is also a remarkable achievement that in spite of the drastic approximations made in calculating the number of configurations in (1.3.1), the experimental value of residual entropy of ice agrees quite well with the theoretical value based on Pauling's calculation.

Exercise 1.1. Calculate Ω by a different method. First, fulfilling condition (ii), then fulfilling condition (i).

The agreement between the experimental and the theoretical values of the residual entropy of ice clearly indicates that the distribution of hydrogen atoms within the ice lattice is not unique. There are many possible configurations that are consistent with the two ice conditions.

Note that to fulfill the second ice condition, we must maintain water molecules in ice as single entities, i.e. a pair of hydrogen atoms must “belong” to each oxygen atom. This does not mean that the structure of a single water molecule is the same as that of molecules in the gas phase. We recall that the H-O-H angle in a single water molecule in the gas phase is 104.5° . In a perfect ice crystal, the tetrahedral angle (a characteristic of a triplet of neighboring oxygen atoms O-O-O) is 109.5° , definitely larger than 104.5° .

1.3.3. *The phase diagram of water*

Figure 1.17 shows the phase diagram of water at low pressures. There are three regions denoted by: solid (I_h), liquid, and vapor. In each of these regions, one can change both the pressure P and the temperature T , and still observe only a single phase. For instance, suppose we start at point A in the figure, corresponding to a system of pure vapor. In this state, we have *two degrees of freedom*, i.e. we can change both the pressure P and the temperature T , and still observe a single pure phase. We can wander

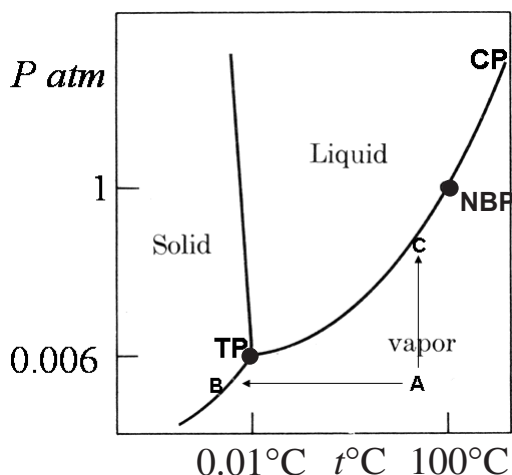


Fig. 1.17 The phase diagram of water at low pressures. The triple point (TP), the critical point (CP), and the normal boiling point (NBP) are indicated.

in each of these areas, i.e. changing independently both P and T , without encountering a new phase. However, when we reach one of the boundary lines, a new phase appears. For example, suppose we start at point A as above. As long as we make small changes in either P or T , we stay in the vapor area. If we keep the pressure fixed and decrease the temperature, we shall be moving along the line AB. As long as we do not hit the boundary line between vapor and solid, we have pure vapor. Once we reach point B, ice appears. The system now consists of two phases at equilibrium. The phase-rule of thermodynamics tells us that a system of two phases at equilibrium has only *one degree of freedom*. This means that we cannot change both P and T independently. Changing, for instance, the temperature, determines the pressure, i.e. we have the function $P = f_{VS}(T)$, which is the boundary curve between the vapor and the solid phases. Clearly, in this diagram, we have three such functions, one for the vapor-liquid boundary, one for the vapor-solid boundary, and one for

the liquid-solid boundary. Along each of these curves, there are two phases at equilibrium. As long as we change the temperature, as well as the pressure, in such a way that we “move” along one of these lines, we maintain the two phases at equilibrium.

Starting again at point A , keeping the temperature constant and increasing the pressure, we move along the AC line. As long as we do not hit point C , we observe one phase only, pure vapor. At point C , liquid appears and we observe two phases: liquid and vapor at equilibrium. Again, when we move along this line while maintaining the two phases, we must follow the corresponding function $P = f_{VL}(T)$, which describes the dependence between the two degrees of freedom P and T . Note that the three curves in this phase diagram are described by three different functions. We denote these functions by $f_{VL}(T)$, $f_{VS}(T)$, and $f_{SL}(T)$ for the vapor-liquid, vapor-solid, and solid-liquid phases, respectively.

Moving along any of the boundary lines, e.g. the vapor-solid line, we observe two phases at equilibrium. This is true until we reach a point, denoted TP in the diagram, at which a third phase appears. We now have three phases, vapor, liquid, and solid, at equilibrium. At this point, the phase-rule of thermodynamics tells us that there are *zero degrees of freedom*. In other words, we cannot “move” in the phase diagram while observing the three phases at equilibrium. The point at which the three phases exist at equilibrium is called the triple point (TP). This is a unique point in the phase diagram, and is characterized by $P = 0.006 \text{ atm}$ and $t = 0.01^\circ\text{C}$.³⁰

Note that since three phases are at equilibrium at the triple point, it must be the intersection of the three boundary lines. In other words, at the triple point, we have the equalities:

$$P_{TP} = f_{VL}(T_{TP}) = f_{VS}(T_{TP}) = f_{SL}(T_{TP}) \quad (1.3.4)$$

³⁰ $1 \text{ kbar} = 10^9 \text{ dyn cm}^{-2} = 986.9 \text{ atm}$.

In Fig. 1.17, we have noted one more unique point labeled *CP*. This is the vapor-liquid critical point. When we increase the temperature but follow the vapor-liquid boundary line, i.e. when we move along the curve $P = f_{VL}(T)$, we eventually reach a point where there is no distinction between the vapor and the liquid phases. The two phases become one. This point is characterized by the pressure $P_{CP} = 218 \text{ atm}$ and $T_{CP} = 374.15^\circ\text{C}$. The molar volume of the water at the critical point is $59.1 \text{ cm}^3 \text{ mol}^{-1}$.

Note that both the triple and critical points are uniquely defined in the phase diagram. They are fundamentally different kinds of points. The triple point, here of vapor-liquid-ice I_h , is characterized by the coexistence of three phases at equilibrium. On the other hand, when we approach the critical point along the vapor-liquid boundary line, the two phases become more and more similar — in the sense that the densities of the two phases become closer and closer. At the critical point, the densities of the vapor and the liquid phases become identical, and hence, we observe only a single phase. Beyond the critical point, i.e. increasing either the pressure, or the temperature, there exists only one phase which is referred to as a fluid. The fluid may be viewed as either a highly compressed gas or as an expanded liquid.³¹

If we move along the solid-liquid boundary, do we encounter a new critical point? The answer is no. We might encounter other triple points (see below) but never another critical point. The reason is that there exists a fundamental difference between a solid phase (any solid, not necessarily ice), and either a liquid or gaseous phase. Both the liquid and the gas phases are randomly disordered systems: the two phases differ in their densities. When we move along the vapor-liquid curve, the difference

³¹Recently, it was suggested that a “second critical point” might exist at temperatures below 0°C . See Stanley *et al.* (1998).

in the densities of the two phases become smaller and smaller until it disappears at the critical point. On the other hand, a solid is an ordered phase. When it is at equilibrium with either a gas or a liquid, there is a clear-cut distinction between the two phases. Order and disorder cannot gradually change until they are equal.

The slope of the two co-existing phases is obtained from the following considerations.

For two phases α and β at equilibrium, we have the equality of the chemical potentials of the two phases:

$$\mu_{\alpha}(T, P) = \mu_{\beta}(T, P) \quad (1.3.5)$$

Moving along the equilibrium line for two phases, the equality (1.3.5) must be maintained; hence

$$\begin{aligned} 0 = d\Delta\mu &= \left(\frac{\partial\Delta\mu}{\partial T}\right)_P dT + \left(\frac{\partial\Delta\mu}{\partial P}\right)_T dP \\ &= -\Delta S dT + \Delta V dP \end{aligned} \quad (1.3.6)$$

where $\Delta\mu = \mu_{\beta} - \mu_{\alpha}$. From (1.3.6), it follows that

$$\left(\frac{\partial P}{\partial T}\right)_{eq} = \frac{\Delta S}{\Delta V} \quad (1.3.7)$$

where $\Delta S = \bar{S}_{\beta} - \bar{S}_{\alpha}$ and $\Delta V = \bar{V}_{\beta} - \bar{V}_{\alpha}$ and the derivative is taken along the co-existing curve. This is the well-known Clapeyron equation. Since $\Delta\mu = \Delta H - T\Delta S = 0$, we can rewrite (1.3.7) as

$$\left(\frac{\partial P}{\partial T}\right)_{eq} = \frac{\Delta S}{\Delta V} = \frac{\Delta H}{T\Delta V} \quad (1.3.8)$$

Note that the slopes of the liquid-vapor and the solid-vapor are always positive. This is understandable; changing from a condensed phase (solid or liquid) to the vapor involves

an increase in entropy (or equivalently of enthalpy),³² and an increase in volume. Therefore, the right-hand side of (1.3.8) is always positive.

In most substances the solid-liquid curve has a positive slope too, for the same reason given above. Water is anomalous as can be seen from Fig. 1.17: the slope of the solid-liquid curve is negative. This means that ΔH and ΔV have *different* signs. This is an important observation. We shall discuss its molecular implications in the next chapter.

Most substances have a phase diagram similar to that of Fig. 1.17. They differ in their triple point and critical point locations, and of course in the location of the boundaries between phase pairs.

Water has at least eight well-defined solid phases. Figure 1.18 shows the phase diagram of water. There are some metastable forms not shown in the figure. Note that the entire phase diagram of Fig. 1.17 is not even seen in Fig. 1.18. The reason is simple. The triple point of water (i.e. ice I_h , liquid, and vapor) is at a pressure of less than 1 atm. Even the critical point has a pressure of 218 atm. The units of pressures in Fig. 1.18 are in kbars (about 1000 atm). This means one kbar is already far higher than the critical point of water. In the phase diagram of Fig. 1.18, the boundary lines are either between the liquid and one solid phase, or between two solids of different crystalline structures. Note that there are several triple points, each representing three phases at equilibrium. In this phase diagram we see seven triple points. Four of these include liquid water, and two solid forms, and three include only solid forms at equilibrium (the triple point of ice I_h , liquid-vapor, is not seen in this figure).

³²The increase in entropy is traditionally interpreted as an increase in *disorder*. However, one does not need to invoke *disorder* to explain $\Delta S > 0$. Since $\Delta H = T\Delta S$, one can interpret the positive change in entropy as a positive change in enthalpy, which is basically a change in energy.

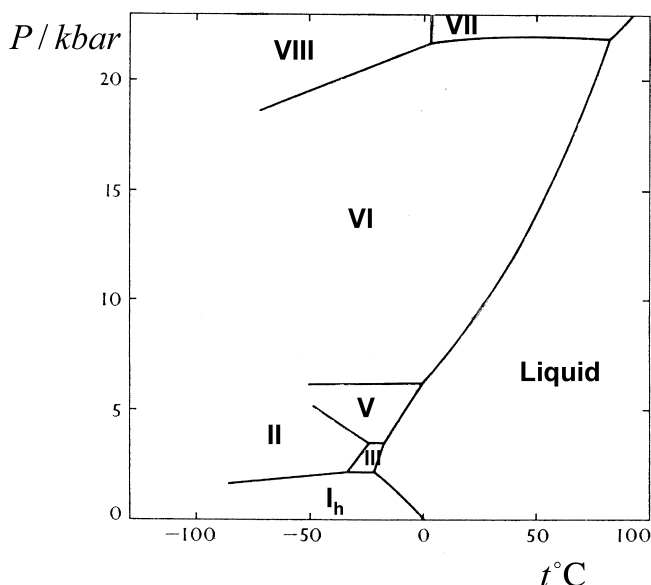


Fig. 1.18 The phase diagram of the various forms of ice.

Much work has been done to characterize the structure and properties of all the ice polymorphs. For the purpose of understanding liquid water and its role in biological systems, one does not need to know the details of the high pressure forms of ice. There is one property worth noting, however, which is relevant to the study of liquid water. This has to do with the densities and lattice energies of the high pressure ices.

When we cross the boundary line between ice I_h to ice II, the volume *decreases* by about $3.92 \text{ cm}^3 \text{ mol}^{-1}$ and the internal energy *increases* by 19 cal mol^{-1} . Furthermore, crossing the boundary between ice II and ice V, there is an additional *decrease* in volume of about $0.7 \text{ cm}^3 \text{ mol}^{-1}$, but an *increase* in internal energy of 347 cal mol^{-1} . Crossing from ice V to ice VI causes a further *decrease* in the volume of $0.7 \text{ cm}^3 \text{ mol}^{-1}$, and an *increase* in the internal energy of 101 cal mol^{-1} . Finally, crossing from ice VI to ice VII causes a *decrease* of about $1.05 \text{ cm}^3 \text{ mol}^{-1}$ in

volume, and an *increase* in energy of 550 cal mol^{-1} . Note that all these slopes are relatively small compared with transitions such as VII $\rightarrow$ VIII. Some of these changes involve a change in the ordering of hydrogen atoms. For more details, see Eisenberg and Kauzmann (1969).

At first glance these findings are puzzling. The high pressure polymorphs have a higher density (or lower molar volume). A higher density means that, on average, each water molecule is surrounded by a larger number of neighbors. Normally, a larger number of neighbors implies a stronger interaction energy between a molecule and its surroundings.³³ A stronger interaction energy should increase the (absolute) internal energy (i.e. make it more negative) of the entire solid. The actual finding in the ice polymorphs is that in some cases increasing the densities causes an increase in internal energy (i.e. makes the internal energy *less* negative) in spite of the fact that each water molecule interacts with a larger number of neighbors.

A variety of interesting properties are manifested by the high pressure polymorphs of ice. For details, see Fletcher (1970) and Eisenberg and Kauzmann (1969). For the purpose of the study of liquid water, it is useful to remember that a large number of structures can be formed around a water molecule in the solid state. In particular, we draw attention to the fact that both open and close-packed structures are possible. There is no doubt that the open structure of ice, I_h , is maintained because of strong directional forces (hydrogen bonds) operating along the directions of the four unit vectors, as depicted in Fig. 1.9. The high pressure polymorphs of ice are characterized by relatively higher densities. That is, each water molecule experiences a higher local

³³This is true as long as the pressure is not so high that the molecules are pushed into intermolecular distances shorter than their molecular diameters.

density than in ice I_h . In spite of the fact that the number of nearest neighbors is larger in some of these structures, their internal energies are higher than those of ice I_h , which indicates that the average binding energy of a water molecule in an open structure may be stronger than the binding energy of the same molecule in a more closely packed structure.³⁴ We will see later that the relation between local density and binding energy is the most important aspect of the mode of packing of water molecules in the liquid state. It is so important that I have chosen to depict this principle in the cover design for this book.

1.4. Properties of Water in the Liquid Phase

In this section, we shall survey some of the outstanding properties of liquid water. We shall discuss only equilibrium thermodynamic quantities. Sometimes these properties are referred to as *anomalous* properties or *unique* properties. We shall occasionally use these terms as well as the term *outstanding*, in describing those properties of liquid water that differ considerably from the values of the same properties in other liquids. To claim uniqueness is not always justified unless one examines the properties of *all* other liquids and find that water has indeed a unique property.³⁵ Recently, Angell *et al.* (2000) concluded that water's position "is not one of extreme anomaly as often supposed but rather one of intermediate status." It should be noted that supercooled water shows some anomalies, both experimentally and in simulation. It was also postulated that there exists a "second critical point" in the supercooled region (Stanley *et al.* 1998). For a review, see Lang and Ludermann (1982)

³⁴It should be noted that, in general, higher local density can be achieved by either more neighbors or by the same number of neighbors but at closer distances.

³⁵Recently, Agarwal *et al.* (2007) showed that beryllium difluoride exhibits some properties similar to liquid water.

and Angell *et al.* (2000). An interesting discussion of the various anomalies of liquid water was published very recently by de Oliveira *et al.* (2006).

1.4.1. *Some outstanding properties of water*

Consider the following series of substances: methane (CH_4), ammonia (NH_3), water (H_2O), hydrofluoric acid (HF), and neon (Ne). These substances are all isoelectronic, i.e. they all have 10 electrons (hence also 10 protons — since the molecules themselves are electro-neutral).

Table 1.4 shows the values of the melting point (in $^\circ\text{C}$), the boiling point (in $^\circ\text{C}$), and the heat of evaporation (in cal mol^{-1}) of each of these substances. Looking at each of these three columns we notice that the values first increase, then sharply decrease — and that the maximal value is attained by liquid water. The same information is also shown graphically in Fig. 1.19, where, in addition to the series of substances reported in Table 1.4, we have a series of compounds of the general formula RH_n , where R is a varying atom down a column of the periodic table of the elements and n is the number of hydrogens in the compound.

Consider the series of CH_4 , SiH_4 , GeH_4 , and SnH_4 . We see that in this homologous series, the properties change “regularly”

Table 1.4. Some Physical Properties of a Series of Isoelectronic Substances

Substance	Melting Point ($^\circ\text{C}$)	Boiling Point ($^\circ\text{C}$)	Molar Heat of Vaporization (cal mol^{-1})
CH_4	−184	−161.5	2200
NH_3	−78	−33.4	5550
H_2O	0	+100	9750
HF	−92	+19.4	7220
Ne	−249	−246	415

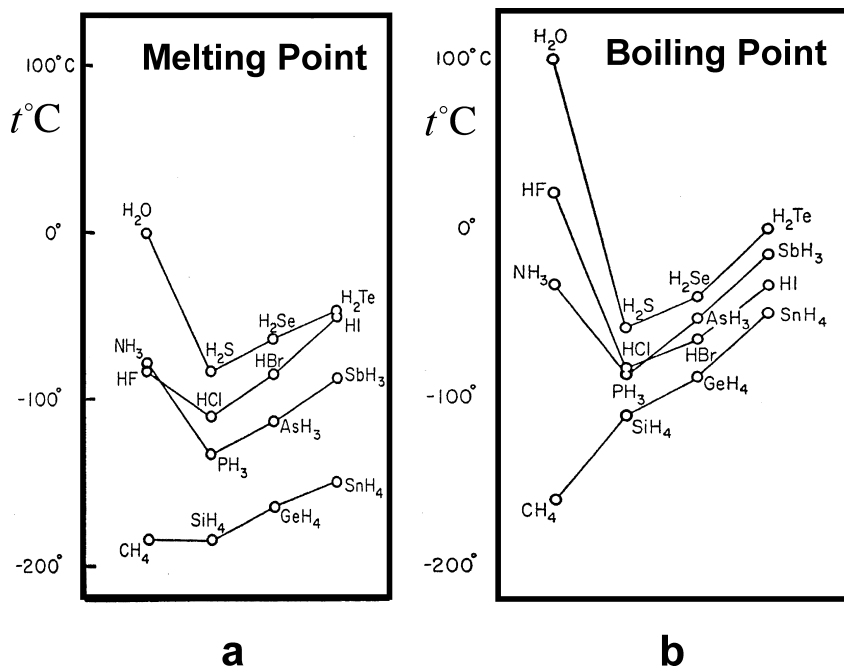


Fig. 1.19 (a) The melting points and (b) boiling points of isoelectronic sequences of hydride molecules [redrawn from Pauling (1960)].

with the molecular weight, or with the size of the molecule. Note that the ordinates in these figures report the numerical values of the melting points and the boiling points. The abscissa, on the other hand, indicates only the row in the periodic table from which the element R in RH_4 has been taken. From this series one can conclude that the larger the molecular weight of the substance, the higher the melting and boiling temperatures.

We see clearly that the properties of the substances HF , H_2O , and NH_3 have high values — far above the values that we would have derived if we extrapolated from the values of the same property of the homologous substance. This is most conspicuous for the homologous substances H_2O , H_2S , H_2Se , and H_2Te .

Although the last three compounds roughly form a straight line with increasing values from H_2S to H_2Se to H_2Te , the value of water is outstandingly high.

The high values of the melting points, the boiling points, and the heat of vaporizations of H_2O , NH_3 , and HF can all be explained by introducing the concept of hydrogen bonding. This was qualitatively explained by Pauling in his classic book, "The Nature of the Chemical Bond," first published in 1939. Basically, the hydrogen bond is not a chemical bond in the usual sense. Although a hydrogen atom can form only one pure covalent bond, a hydrogen *ion* H^+ — with its small radius — exerts a strong electrostatic force that attracts simultaneously two electro-negative atoms, such as oxygen atoms. Figure 1.20 shows how the small proton H^+ can bring two relatively large negative ions (denoted A_1^- and A_2^-) in close proximity. As can be seen in Fig. 1.20, a third ion (denoted A_3^-) approaching this pair cannot come close to the proton. Hence, effectively, the hydrogen ions act as a "glue" that binds no more than two negative ions together. This type of "saturation" is typical in a chemical bond and can be observed in all hydrogen bonds.

It has also been found that the greater the electro-negativity of the ions, the stronger the hydrogen bonds. Fluoride ions form

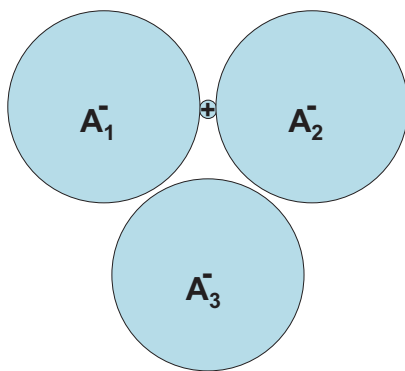


Fig. 1.20 Schematic description of the electrostatic interaction in hydrogen bonding.

very strong hydrogen bonds, oxygen forms somewhat weaker hydrogen bonds, nitrogen forms still weaker hydrogen bonds, and carbon almost does not form hydrogen bonds.

Note that although the strength of a single hydrogen bond increases from nitrogen to oxygen to fluoride, the effect of hydrogen bonding is more dramatic in water than in hydrofluoric acid. The reason is that in liquid water a water molecule can form up to *four* hydrogen bonds with its neighboring molecules.

Viewing the phenomenon of hydrogen bonding as a force of adhesion between water molecules in the liquid state, we can immediately understand the high values of the melting point, boiling point, and heat of vaporization. Since the forces that hold water molecules together are strong, a relatively high temperature is needed to melt ice. Note that we are comparing the melting point of pure water with the melting points of only those substances shown in Fig. 1.19. There are many other substances with much stronger binding forces, and hence higher melting points. Table 1.5 shows the values of melting points and boiling points of H_2O , D_2O , and T_2O . The larger values of both the melting points and the boiling points of D_2O and T_2O indicate stronger interaction energies among D_2O and T_2O molecules compared with H_2O .

Throughout the entire liquid range of temperatures; 0°C to 100°C , the average number of hydrogen bonds decreases as the temperature increases. However, even at the boiling point, there are many water molecules still engaged in hydrogen bonding.

Table 1.5. Melting and Boiling Points of Various Liquids

	Melting Point ($^\circ\text{C}$)	Boiling Point ($^\circ\text{C}$)
H_2O	0.00	100
D_2O	3.82	101.42
T_2O	4.49	101.51

Table 1.6. The Entropy of Vaporization Divided by the Gas Constant R for Various Liquids

Substance	$\Delta S_v/R$
Ar	9.0
Kr	9.1
Xe	9.2
CH ₄	8.8
H ₂ S	10.6
NH ₃	11.7
CH ₃ OH	12.6
CH ₃ CH ₂ OH	13.2
H ₂ O	13.1

To detach water molecules from the liquid and to send them into the gaseous phase, one needs more energy, which explains the relatively higher boiling temperature of water and high value of the heat of vaporization.

An empirical law known as Trouton's Law says that the entropy of vaporization is almost constant, about $20.3 \text{ cal mol}^{-1} \text{ K}^{-1}$. Water has an anomalously large entropy of vaporization of about $26 \text{ cal mol}^{-1} \text{ K}^{-1}$. Table 1.6 shows the entropy of vaporization divided by the gas constant R for different liquids. Note that the entropy of vaporization of ethanol is as large as that of water.

1.4.2. *Molar volume of water and its temperature dependence*

Among the other unusual properties of pure liquid water, one of the best known is the way water expands when it freezes.³⁶ Never put a bottle filled with water inside the freezer. It will

³⁶The molar volumes of water and ice at the normal freezing points are 18 and $19.6 \text{ cm}^3 \text{ mol}^{-1}$, respectively.

explode upon freezing. This is quite an unusual phenomenon (though not entirely unique to water; there are other substances that also have a larger molar volume in the solid state compared to the liquid state). The molecular reason for this phenomenon is clear. It is due to the “open” mode of packing water molecules in ordinary ice.

An even more unusual property, one which is unique to liquid water is the continual decrease of the molar volume of water upon increasing the temperature between 0°C to 4°C (for heavy water, D₂O, up to 11°C); see Fig. 1.21.

The expansivity of a substance is defined by

$$\alpha_p = \frac{1}{V} \left(\frac{\partial V}{\partial T} \right)_p \quad (1.4.1)$$

where V is the volume of the system, and the derivative is taken with respect to the temperature, keeping the pressure constant. Figure 1.21 shows the temperature dependence of the volume of water, heavy water and for comparison also for methanol and ethanol (Fig. 1.21c).

All known liquids expand upon increasing the temperature, whereas liquid water between 0°C and 4°C shows the opposite behavior. Note also that D₂O has a larger molar volume in the entire range of temperatures. The locations of the minimum volume are indicated in Fig. 1.21b. This phenomenon is also due to the mode of packing water molecules in such a way that low local density is correlated with strong binding energy. We shall discuss this principle in great detail in Chapter 2. We shall see that the understanding of this phenomenon at a molecular level is essential to the understanding of some of the outstanding properties of aqueous solutions.

Figure 1.22 shows that as we increase the pressure, the minimum of the volume is shifted to lower temperatures. At

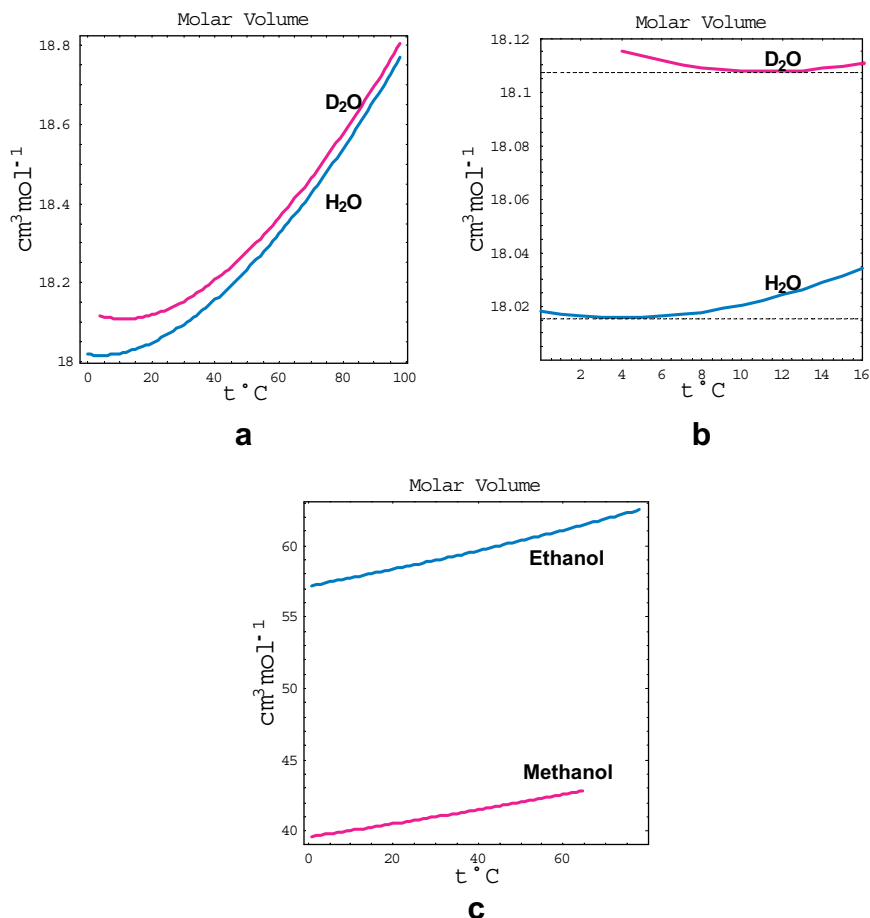


Fig. 1.21 The temperature dependence of the molar volume of (a) water and heavy water, (b) A magnified figure near the minimum of the volume, and (c) methanol and ethanol.

higher pressures the minimum disappears and water behaves as a normal liquid.

1.4.3. Heat capacity

The heat capacity is defined as the amount of heat required to raise the temperature of one mole of a substance by one degree.

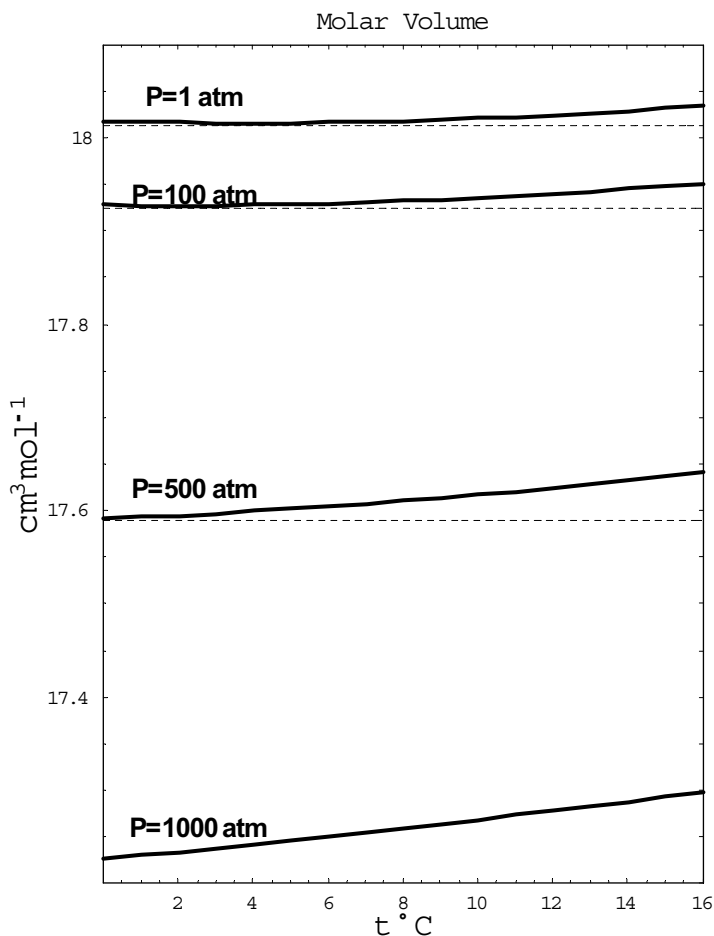


Fig. 1.22 The temperature dependence of a volume of water at different pressures.

The value of the heat capacity depends on the conditions in which the experiment is carried out. The most commonly used heat capacities are:

$$C_V = \left(\frac{\partial E}{\partial T} \right)_V, \quad C_p = \left(\frac{\partial H}{\partial T} \right)_p \quad (1.4.2)$$

where E is the internal energy of the system and H is the enthalpy of the system.

The heat capacity of water is much larger than that of other normal liquids. For example, the heat capacity of water at 25°C is about $1 \text{ cal g}^{-1} \text{ K}^{-1}$. For ethanol, it is $0.6 \text{ cal g}^{-1} \text{ K}^{-1}$, and for hexane, $0.6 \text{ cal g}^{-1} \text{ K}^{-1}$, but for ammonia, it is $1.23 \text{ cal g}^{-1} \text{ K}^{-1}$. When we say large, we mean larger than the value that is expected from a regular non-hydrogen bonded fluid. Note that in both the solid and the gaseous phases, the value of the heat capacity is “normal,” i.e. it is consistent with what one would calculate from statistical thermodynamics. In the liquid phase, however, the value of the heat capacity is almost three times larger than expected.

Figure 1.23 shows the values of the heat capacity C_P as a function of T for H_2O , D_2O , and for comparison also for ethanol and methanol. Figure 1.24 shows the heat capacity C_V for the same four liquids. Note that the curve of C_P for H_2O goes through a minimum at about 35°C . For D_2O there seems

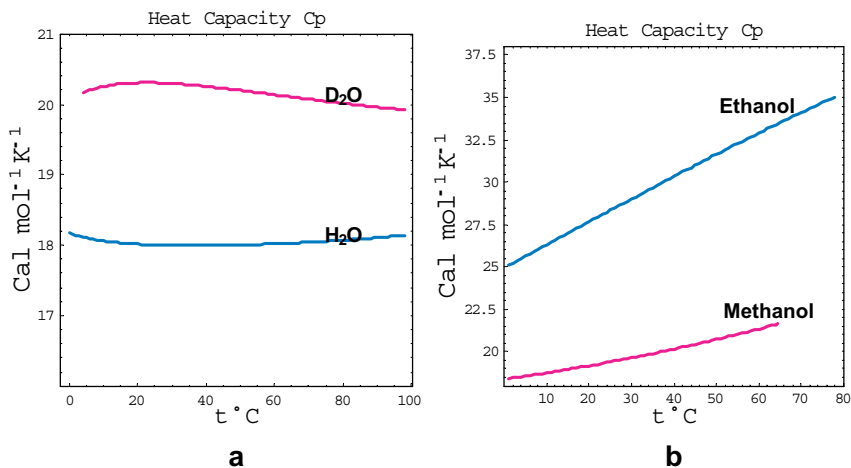


Fig. 1.23 Heat capacity C_P of (a) H_2O , D_2O , and (b) ethanol and methanol as a function of temperature T at $P = 1 \text{ atm}$.

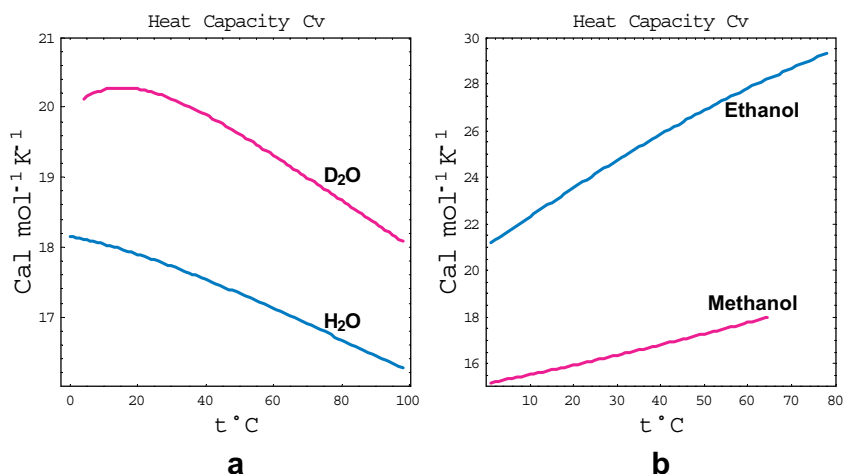


Fig. 1.24 Heat capacity C_V of (a) H_2O , D_2O , and (b) ethanol and methanol as a function of T at $P = 1 \text{ atm}$.

to be a maximum of both C_V and C_P around 20°C . Note that the high value of the heat capacity is not unique to liquid water. Other liquids such as ammonia also have high heat capacity. The molecular interpretation of these quantities will be discussed in Chapter 2.

Figure 1.25 shows that when we increase the pressure, the heat capacities become smaller and the minimum disappears; again, the behavior of a normal liquid.

1.4.4. Isothermal compressibility

The isothermal compressibility of water, denoted κ_T , is a measure of the response of the volume of a liquid to increasing the pressure.³⁷ This is defined by

$$\kappa_T = -\frac{1}{V} \left(\frac{\partial V}{\partial P} \right)_T = \left(\frac{\partial \ln \rho}{\partial P} \right)_T \quad (1.4.3)$$

³⁷Some refer to the isothermal compressibility as a “response function.” This is true, but it is true for any derivative with respect to P , T , or N .

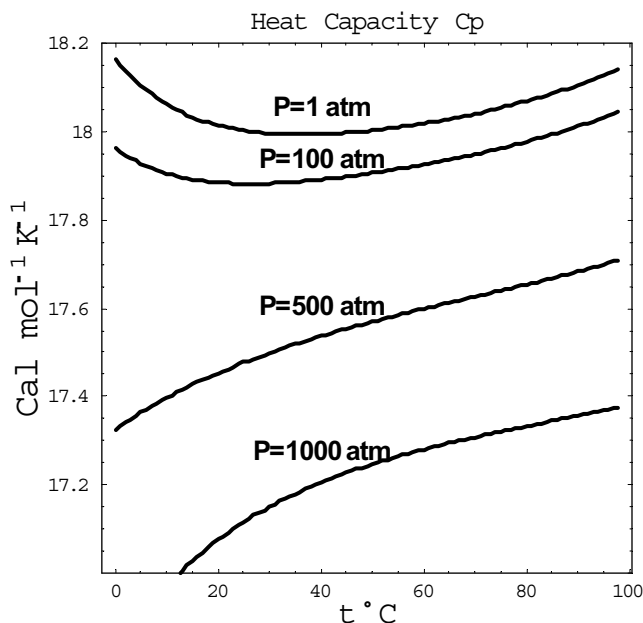


Fig. 1.25 The heat capacity C_p of water as a function of temperature at different pressures.

Normally, as the temperature of a liquid increases the average intermolecular distance between the particles of the liquid increases. This makes it easier to compress a liquid at a higher temperature. Thus, we expect the compressibility to increase as we increase the temperature. Water is anomalous in that it has a region below approximately 45°C, where κ_T actually decreases as the temperature increases (Fig. 1.26). At 45°C, the compressibility passes through a minimum, and thereafter it increases with T , as in the case of normal liquids.

Figure 1.27 shows the temperature dependence of the compressibility curves at different pressures. As can be seen from Fig. 1.27, when we increase the pressure, the minimum in the compressibility becomes less and less pronounced, but even at 3000 atm we still observe a shallow minimum.

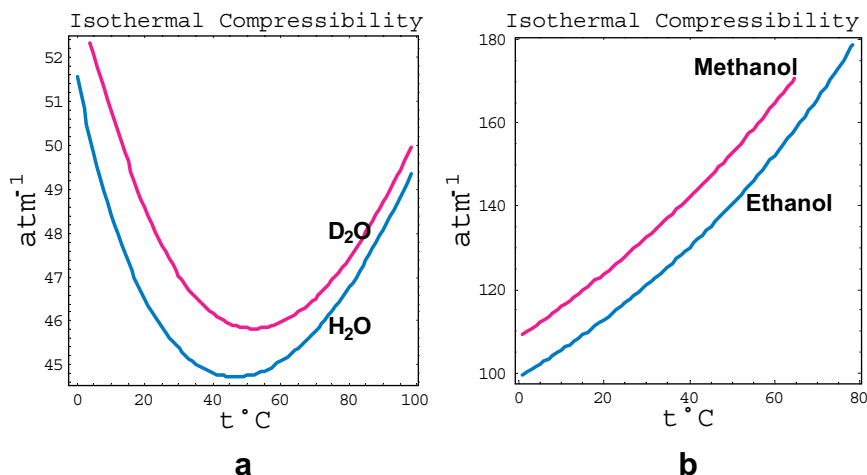


Fig. 1.26 The isothermal compressibility κ_T as a function of T for (a) H_2O , D_2O , and (b) ethanol and methanol as a function of T at $P = 1$ atm.

Table 1.7 shows the isothermal compressibilities of some liquids at $P = 1$ atm. Note that water has a relatively small value of compressibility. However, the isothermal compressibility of glycerol at 28°C is even smaller: $21.1 \times 10^{-6} \text{ atm}^{-1}$.

Liquid water has many other properties that exhibit anomalous values, e.g. dielectric constant, surface tension, diffusion coefficient, viscosity, etc. Aqueous solutions also exhibit unusual properties, some of which will be discussed in Chapter 3. In this introduction, we have mentioned only a few properties, the interpretation of which can be given by some simple theoretical arguments. We shall discuss these properties again in Chapter 2.

1.4.5. The radial distribution function of water

The most important experimental information on the mode of packing of water molecules in the liquid state is contained in the radial distribution function, which is obtained from X-ray

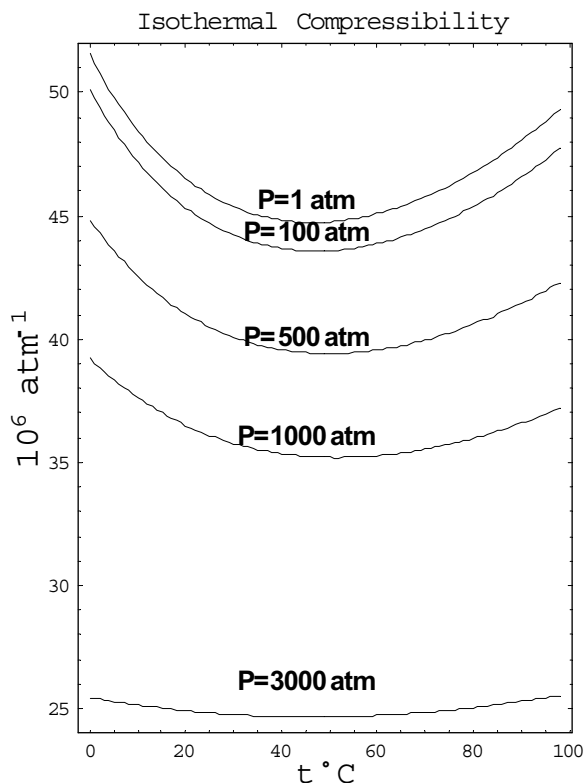


Fig. 1.27 The isothermal compressibility of water as a function of T for various pressures.

or neutron scattering data. A solid is characterized by a well-defined structure: the molecules are packed in some orderly fashion. The liquid phase, on the other hand, seems to be lacking any structure. Nevertheless, it is possible to detect some regularities in the packing mode of the molecules in the liquid phase.

If we could sit at the center of one of the particles and observe our surroundings, we would not see any regular pattern that we could call a “structure.” But if we counted the number of particle centers that appeared within a spherical shell of width dR at a distance R , we would find the following regularities.

Table 1.7. Isothermal Compressibilities of Water and Some Alcohols

	t ($^{\circ}\text{C}$)	$\kappa_T \times 10^6 \text{ atm}^{-1}$
H_2O	20	45.91
	25	45.52
Methanol	20	121.4
Ethanol	20	111.9
Acetone	20	126.2
Ethyl acetate	20	113.2
Ethylene glycol	20	36.4
Glycerol	28	21.1

Each spherical shell of width dR at a distance R has a volume $4\pi R^2 dR$. If the average (or macroscopic) density of the liquid is $\rho = N/V$, then we would expect to find, on average, $\rho 4\pi R^2 dR$ particle centers within this volume. However, because our vantage point is located at the center of a specific particle, we observe an average density that deviates from the expected density ρ . We define a function $g(R)$ in such a way that the actual average density at a distance R from the center of a specific particle is $\rho g(R)$. Equivalently, the average number of particles in each spherical shell is $\rho g(R) 4\pi R^2 dR$, not $\rho 4\pi R^2 dR$. Thus, $g(R)$ is a measure of the deviation of the actual count of the average number of particles around a given particle, relative to the average number of particles that we should expect to find in a spherical shell of radius R centered at a *random* point in the liquid. The function $g(R)$ is referred to as either the pair correlation function or as the radial distribution function (RDF).

Having this qualitative definition of $g(R)$, we now turn to describing some of its salient features for spherical particles:

- (i) If σ is the diameter of each particle in the system, then the probability of finding any other particle at a distance of less

than σ from a given particle is almost zero, i.e.

$$g(R) \approx 0 \quad \text{at } R \leq \sigma \quad (1.4.4)$$

The reason for this is that at distances $R \leq \sigma$, the two particles exert strong repulsive forces; hence, they are effectively impenetrable. (In fact, the diameter σ is *defined* as the distance below which the repulsive forces are so large that the two particles practically cannot approach each other to a distance shorter than σ .)

- (ii) At a very long distance $R \rightarrow \infty$, we expect that the average number of particles in the element of volume dV will not depend on the fact that we have placed a particle at the origin of our coordinate system. Therefore, we expect that the average number of particles in the spherical shell around the center of a specific particle to be the same as $\rho 4\pi R^2 dR$. We say that as R becomes very large, there exists no *correlation* between the particles. Clearly, in this case $g(R) \approx 1$, for $R \rightarrow \infty$. We have written $R \rightarrow \infty$ to signify that R is a very large distance. In practice, for regular liquids not close to their critical point, one finds that the correlation function is very close to unity (i.e. that there is no correlation) when R is approximately five or six times the molecular diameter of the particles (see Fig. 1.28).
- (iii) At distances $\sigma \lesssim R \lesssim 4\sigma$, we find (both experimentally and from theoretical calculations) that $g(R)$ has, in general, successive maxima and minima, as is shown in Fig. 1.28. Note that the first maximum occurs at about $R \approx \sigma$, the second maximum at $R \approx 2\sigma$, and the third at $R \approx 3\sigma$. Each time we increase R , the value of the maximum decreases from $g(R \approx \sigma)$ to $g(R \approx 2\sigma)$, to $g(R \approx 3\sigma)$. For $R \approx 4\sigma$ or $R \approx 5\sigma$, the value of $g(R)$ becomes practically unity, i.e. there is almost no correlation beyond, say, $R \approx 5\sigma$.

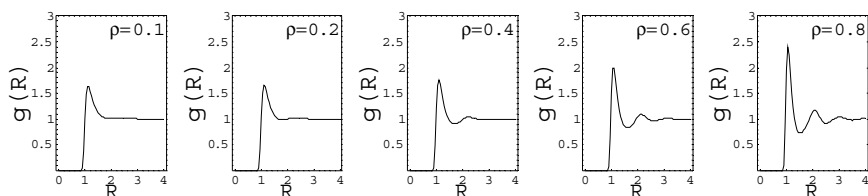


Fig. 1.28 Dependence of $g(R)$ on the density of the system. The corresponding (number) densities are indicated in each figure. The functions $g(R)$ for these illustrations were computed using a numerical solution to the Percus–Yevick equation for Lennard–Jones particles with parameters $\sigma = 1.0$ and $\varepsilon/k_B T = 0.5$.

- (iv) In Fig. 1.28, we see that more maxima and minima appear as the density of the liquid increases. At very low densities, there is only one maximum (left-hand curve in Fig. 1.28). This is the limit of $g(R)$ as $\rho \rightarrow 0$. At this limit, $g(R)$ is determined only by the pair potential. The relation between the two is: $g(R) = \exp[-\beta U(R)]$. Note that $\rho \rightarrow 0$ is the low density limit of a *real* liquid. A *theoretical* ideal gas is a system containing only non-interacting particles. For such particles, $g(R) \approx 1$, i.e. whatever the distances and densities in the system, correlations between the particles are never present.

The typical concentric and approximately equidistant peaks observed in $g(R)$ are a result of the spherical-symmetrical interaction between the particles. This information provided by $g(R)$ is sometimes called the “structure” of the liquid, but when applied to liquid water $g(R)$ is not a good measure of structure.

Figure 1.29b shows the first two distances σ and 2σ , where one can expect to find a peak in the pair correlation function for spherical molecules. For non-spherical molecules such as water, the pair correlation function is a function of both the distance and the relative orientation of the pair of molecules.

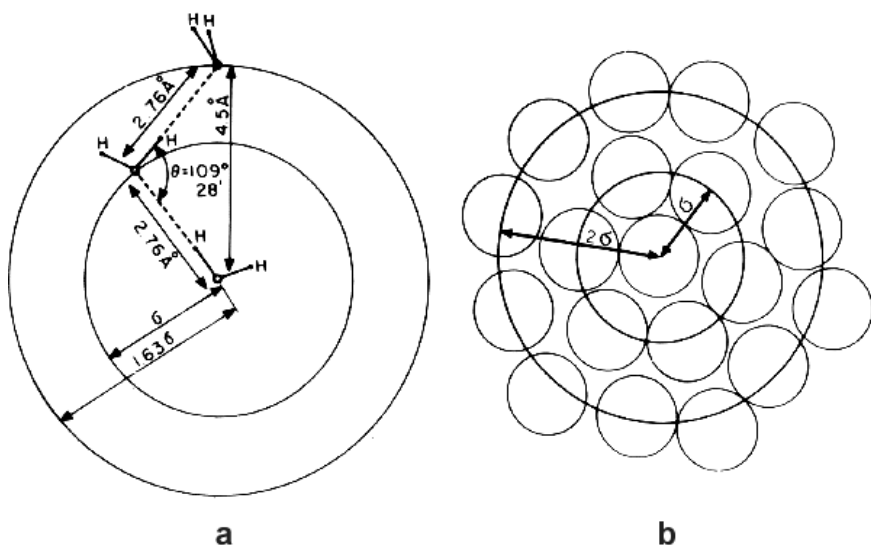


Fig. 1.29 The distribution of first and second neighbors in (a) water, and (b) a simple liquid.

Figure 1.29a shows the distances at which we can expect relatively higher densities around a central water molecule.

The full orientation-dependent pair correlation function cannot be obtained from experiments. Instead, only information on the *spatial* correlation function is obtainable. The spatial correlation function is defined as

$$g(\mathbf{R}_1, \mathbf{R}_2) = \frac{1}{(8\pi^2)^2} \iint d\Omega_1 d\Omega_2 g(\mathbf{R}_1, \Omega_1, \mathbf{R}_2, \Omega_2) \quad (1.4.5)$$

where the function $g(\mathbf{R}_1, \mathbf{R}_2)$ is a function of the scalar distance $R = |\mathbf{R}_2 - \mathbf{R}_1|$.

Water, as a hetero-atomic liquid, produces a diffraction pattern that reflects the combined effects of O-O, O-H, and H-H correlations. Thus, in principle, we have three distinct atom-atom pair correlation functions: $g_{OO}(R)$, $g_{OH}(R)$, and $g_{HH}(R)$. Earlier experimental data based on X-ray scattering could not be

resolved to obtain these three functions separately. Therefore, the only information obtained is a weighted average of these three functions. In all our future references to the experimental radial distribution function, we shall always refer to $g_{OO}(R)$, or simply $g(R)$. Recently, neutron scattering experiments have provided more detailed information on $g_{OO}(R)$, $g_{OH}(R)$, and $g_{HH}(R)$. We shall not need this additional information for the present book. For details, see Narten and Levy (1971), Soper (1996), Soper (2000), and Tromp *et al.* (1994).

Recently, Sorenson *et al.* (2000) reported new results for the oxygen-oxygen pair correlation function based on Advanced Light Source (ALS) X-ray scattering on pure liquid water. They found that their results at the second and third peak are nearly the same as the results reported by Narten and Levy (1971) and Soper *et al.* (1997). On the other hand, the location and the width of their results at the first peak differ considerably from the older results.

Figure 1.30 shows the *RDF* for water at 25°C obtained by X-ray (Narten and Levy, 1971) and by neutron scattering (Soper, 1997). As can be seen from the figure, the agreement between the two curves is quite good.³⁸

Figure 1.31 shows $g(R)$ for water and for argon, not as a function of R but as a function of the *reduced* distance $R^* = R/\sigma$. The reason we plot the *RDF* as a function of R/σ is to facilitate the comparison between the two functions. As we have seen, the first peak of $g(R)$ appears at the distance $R \approx \sigma$. Therefore, plotting $g(R^*)$ gives the first peaks of *RDF* of both argon and water at $R^* \approx 1$. First, we note that the curves for both argon and water are practically zero for $R^* \leq 1$. Second, the first peaks of the two curves are at about $R^* \approx 1$, and the

³⁸For more details, see Soper (1996), Soper (2000), Tromp *et al.* (1994), Soper and Philips (1986), Soper *et al.* (1997), Hura *et al.* (2003), and Sorenson *et al.* (2000).

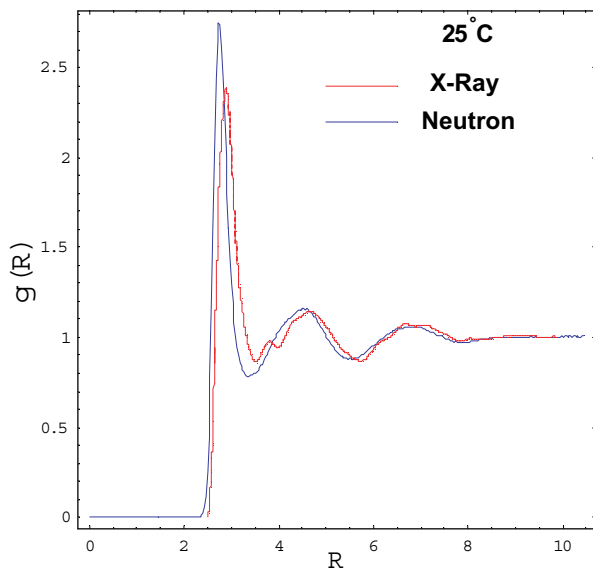


Fig. 1.30 The radial distribution function for water obtained from X-rays and neutron scattering [based on data from Narten and Levy (1971) and Soper (2000)].

two curves tend to unity for $R^* \geq 4$, i.e. beyond 4σ there is no more correlation.

The two curves in Fig. 1.31 differ in several aspects that are important for the understanding of liquid water. First, the curve of the water-*RDF* at about $R^* \approx 1$ is narrower, and its maximum value is lower than that of the argon-*RDF*. This is quite surprising. In general, one would have expected the first peak to be higher, the stronger the interaction. This is certainly true if we are in the gaseous phase, in which case the *RDF* is given by $g(R) \approx \exp[-\beta U(R)]$. Hence, the stronger the pair interaction, the higher the peak. However, in liquid water there is a unique mode of packing of the water molecules such that a strong binding energy is correlated with low local density (here, binding is simply the total interaction energy of a molecule with its surrounding molecules). We shall further discuss this peculiar correlation in Chapter 2.

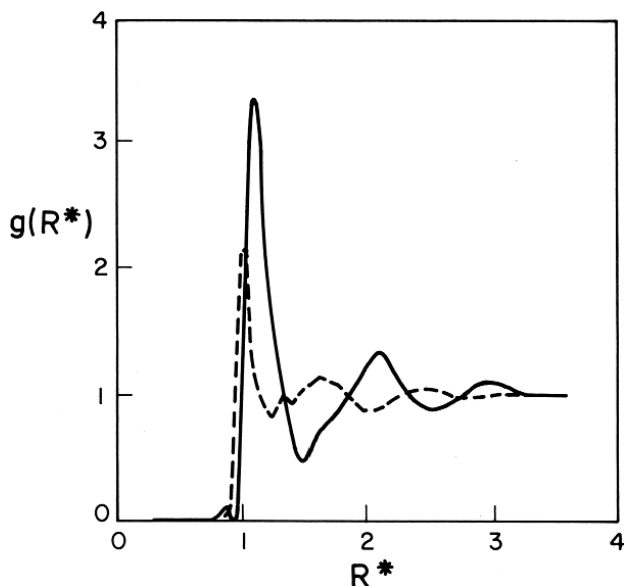


Fig. 1.31 Radial distribution function $g(R^*)$ for water (dashed line) at 4°C and 1 atm, and for argon (solid line) at 84.25 K and 0.71 atm, as a function of the reduced distance $R^* = R/\sigma$. (From Ben-Naim (1974) based on data for argon courtesy of N. S. Gingrich, and for water courtesy of A. H. Narten.)

Second, the area under the curve around the first peak is related to the differences in the local density or the coordination number in the two liquids. The coordination number is defined using the following procedure. We first choose a radius R_M ; then we determine the average number of particles contained within a sphere of radius R_M centered at any given particle in the system. Since $\rho g(R)4\pi R^2 dR$ is the average number of particles in a spherical shell of width dR and radius R , the average number of particles in the *entire sphere* of radius R_M is simply the sum of the average numbers of particles in all the spherical shells between $R = 0$ to $R = R_M$. This sum is the integral

$$\text{CN}(R_M) = \rho \int_0^{R_M} g(R)4\pi R^2 dR \quad (1.4.6)$$

Clearly, once we have $g(R)$, we can calculate $CN(R_M)$. In particular, we can define the first coordination number as the quantity $CN(R_M)$, for a choice of R_M , as the location of the first minimum of $g(R)$, following the first maximum. We shall denote the first coordination number as n_{CN} . The first coordination number for water at 4°C and 1 atm was estimated to be around 4.4. On the other hand, for liquid argon at 84.25°K and 0.7 bar the first coordination number is about 10. The latter value is typical of a close-packed liquid having a coordination number in the range of 10 to 12. On the other hand, the value of 4.4 for water is unusual for a liquid and is strongly reminiscent of the exact coordination number of the solid hexagonal ice I_h . It suggests that the “local structure” of water is very similar to the local structure of ice. No similar resemblance in local structure is observed in argon or in any other simple liquid. It is also of interest to note that the first coordination number of a simple liquid normally decreases with an increase in temperature. The opposite is true for liquid water. Since the location of the first minimum of the *RDF* changes with temperature, we have plotted in Fig. 1.32 the function $CN(R_M)$ for R_M between 3.3 Å to 3.7 Å. As can be seen from the figure if we choose $R_M \approx 3.3$ Å, we see that if we increase the temperature, the *CN* initially *increases*, but at higher temperatures it decreases with the increase in temperature. As the figure shows, the temperature dependence of the *CN* depends on the choice of R_M . Figure 1.33 shows for comparison the *RDF*, the coordination number as a function of R_M , and n_{CN} calculated for $R_M = 1.5$ and as a function of T for Lennard–Jones particles.³⁹

The third difference between the two *RDF* curves in Fig. 1.31 is the location of the second peak in the *RDF*. We have noted

³⁹These curves were calculated by Raymond Mountain using the molecular dynamics method.

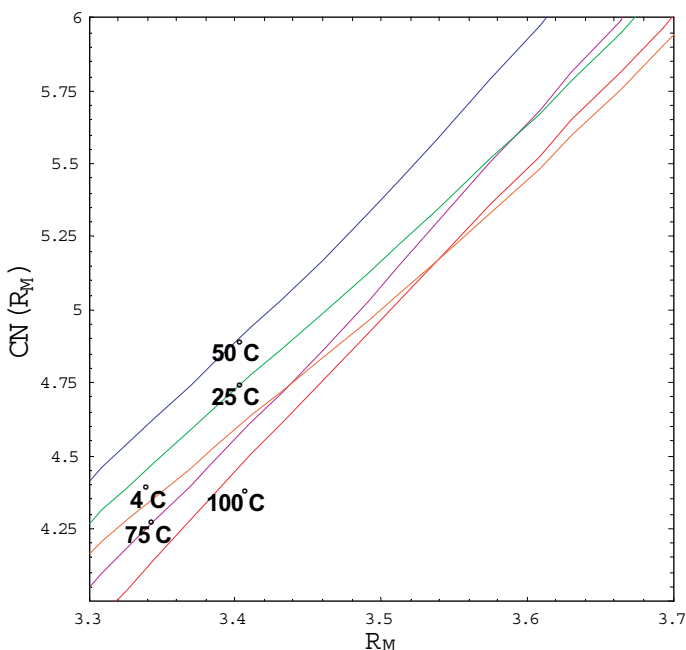


Fig. 1.32 Coordination number and its temperature dependence for water as a function of R_M [see Eq. (1.4.6)].

that for a simple liquid such as argon, a large correlation can be expected at about $R^* \approx 2$ (i.e. at a distance of $R = 2\sigma$). Indeed, we see that the *RDF* of argon has a peak at about $R^* \approx 2$. This is “normal” behavior, as we have explained before. In contrast, the *RDF* of water shows a second peak at an “abnormal” location at about $R^* \approx 1.6$, i.e. at a distance of $R = 1.6\sigma$. If we take $\sigma \approx 2.8 \text{ \AA}$ as the effective diameter of water, we have the second peak at $R = 4.5 \text{ \AA}$. What does this distance mean in terms of the packing mode of water molecules?

We recall that in the structure of ordinary ice (see Sec. 1.3) the O-O distance is $2.76 \text{ \AA}$. A simple calculation shows that the second-nearest neighbor distance between oxygens is $2 \times 2.76 \sin(\theta_T/2) = 4.5 \text{ \AA}$. This is the “ideal” O-O distance

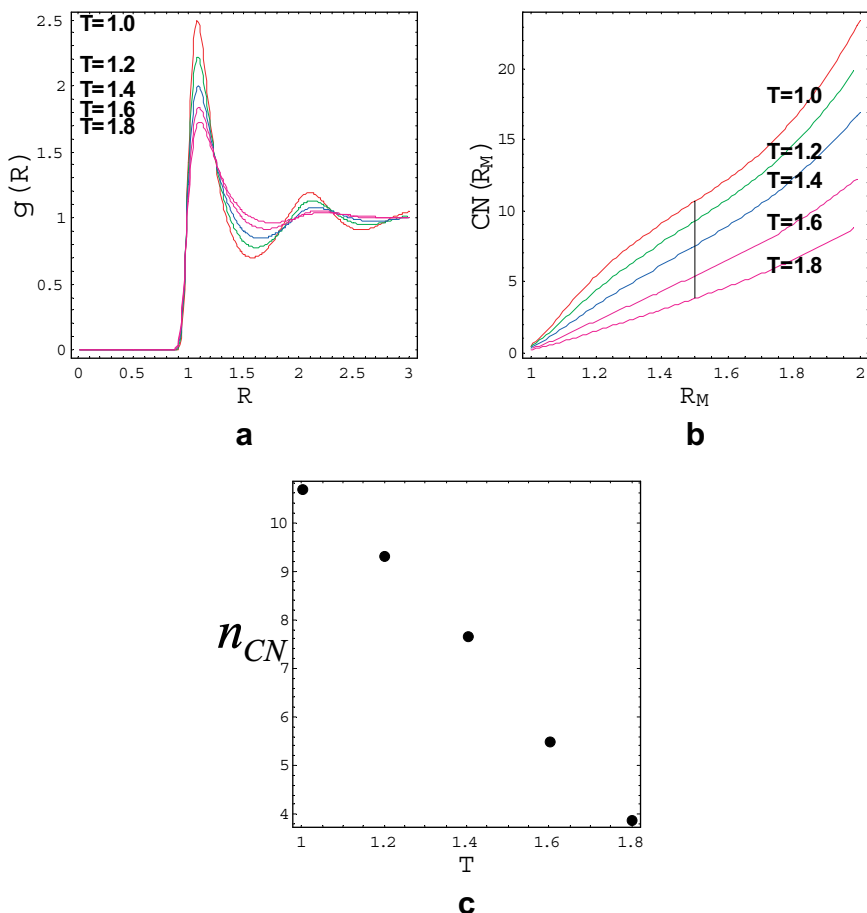


Fig. 1.33 (a) Radial distribution functions for Lennard–Jones particles at different temperatures, (b) coordination number as a function of R_M , and (c) coordination number as a function of T , for Lennard–Jones particles. All the calculations were performed by molecular dynamics in the T, P, N ensemble for LJ particles with $\sigma = 1$ and $\varepsilon/k_B = 1$. (The data was provided by Raymond Mountain.)

for second-nearest neighbor oxygens in ice. The fact that the second peak in the *RDF* of water is also found at $4.5 \text{ \AA}$ means that the probability of finding second-nearest neighbors in liquid water is greatest at $4.5 \text{ \AA}$ (see Fig. 1.29a). This, together

Table 1.8. First Coordination Numbers in Solid and Liquids^a

Substance	n_{CN} in solid	n_{CN} in liquid
Li	14	9.8
Na	14	9.3
K	14	8
Ar	12	10.2–10.9
Xe	12	8.5
Ga	7	7.8
Ge	4	8

^aFrom Samoilov (1957).

with the coordination number of water, is a strong indication that the local structure around a water molecule is very similar to the local structure around a water molecule in ice I_h .

Some authors consider the value of $g(R = 4.5 \text{ \AA})$ as a signature of the structure of water. This is basically correct.⁴⁰ However, in principle, a high peak at $R = 4.5 \text{ \AA}$ could also be a result of a large concentration of triplets of water molecules in the configuration as in Fig. 1.29a, not necessarily having the local structure of ice.

At this point in our discussion, it is clear that the *RDF* of water, $g(R)$, does reveal some qualitative information about the structure of liquid water. Thus far, we have not defined the

⁴⁰Note that some authors *define* the structure of a liquid in terms of the correlation functions. For instance, Fletcher (1970) writes: “From a statistical point of view, the structure of a liquid water is defined by a set of correlation functions; $g_n(R_1; R_2, \dots, R_n)$ which specify the probability that an atom can be found at the position R_1 , given that there are atoms at positions $R_2, \dots, R_n$.” In my opinion, this cannot serve as a definition of the structure of water. First, because these probabilities are defined for any liquid and there is no direct relationship between the values of these probabilities and the extent of *structure* as commonly understood. Second, one cannot use a whole *function* as a measure of structure. One needs a *number* that expresses the extent of structure which is typical of liquid water. We shall further discuss this topic in Chapter 2.

concept of water structure. In Chapter 2, we shall see that a single number that measures the degree of structure of water is needed for the understanding of both water and aqueous solutions.

These three features of the radial distribution function lead to the following conclusion. The basic geometry around a single molecule in water is, to a large extent, similar to that of ice. This is to say that, on average, each molecule has a coordination number of about four, and furthermore, there is a high probability that triplets of molecules will be found with nearly the same geometry as triplets of molecules at successive lattice points in ice. This conclusion pertains only to the *local* environment of a water molecule; no information whatsoever is furnished by $g(R)$ about the structure of the extended layer of molecules. In other words, if one were to sit at the center of a water molecule and observe the local geometry in a sphere of radius, say, $5 \text{ \AA}$, one would see most of the time a picture very similar to the one seen from an ice molecule, with frequent distortions caused by thermal agitation typical of the liquid state. These facts were recognized long ago by Bernal and Fowler and by Pauling. Beyond that radius (of about $5 \text{ \AA}$), the structure will not be recognized as that of ice.

Figure 1.34 shows the pair correlation function for H_2O and D_2O . It is clear that the two functions are almost identical. On the scale of this figure, the two curves cannot be distinguished. As we shall see in Chapter 2, this fact is consistent with the fact that the geometry of water and of the hydrogen bonds are nearly the same for the two liquids. However, the *structures* of the two liquids are not the same as could be erroneously deduced by comparing the *RDFs* of H_2O and D_2O .

The temperature dependence of $g(R)$ for water is shown in Fig. 1.35. There is a gradual shift in the location of the first peak from $2.84 \text{ \AA}$ at 4°C to about $2.94 \text{ \AA}$ at 100°C . A more characteristic feature is the rapid decay of the second peak, which

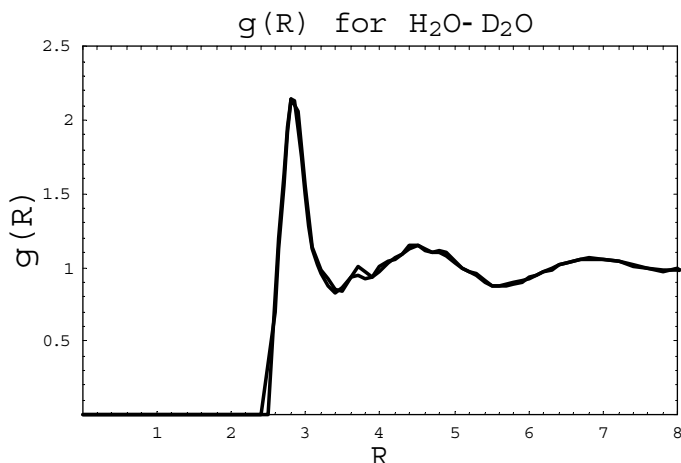


Fig. 1.34 The radial distribution function of water and heavy water at 4°C.

is almost unrecognizable at 100°C. Narten and Levy (1971) also reported the *RDF* at 150°C and 200°C. It is not clear at which pressures these results were obtained. In Fig. 1.36, we compare the *RDF* at 100°C and 150°C. As can be seen, there is almost no change in the curve around the first peak while beyond the first peak there is not much of a structure at either temperature.

1.5. The Kirkwood–Buff Integral

Recently, a new way of studying, analyzing, and interpreting liquid mixtures has been suggested.⁴¹ The traditional approach to mixtures is based on the study of the excess thermodynamic quantities such as excess free energy, excess entropy, and enthalpy volume.⁴² These quantities convey macroscopic

⁴¹Ben-Naim (2006, 2008d).

⁴²Prigogine (1957), Van Ness and Abbott (1982), and Rowlinson and Swinton (1982).

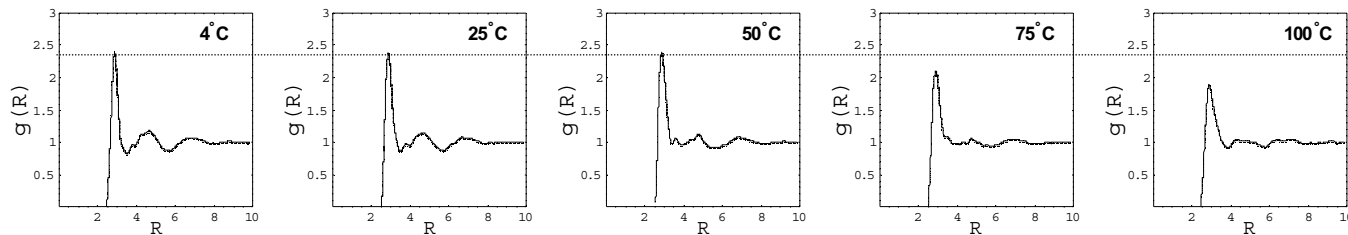


Fig. 1.35 The temperature dependence of $g(R)$ of water [based on data from Narten and Levy (1971)].

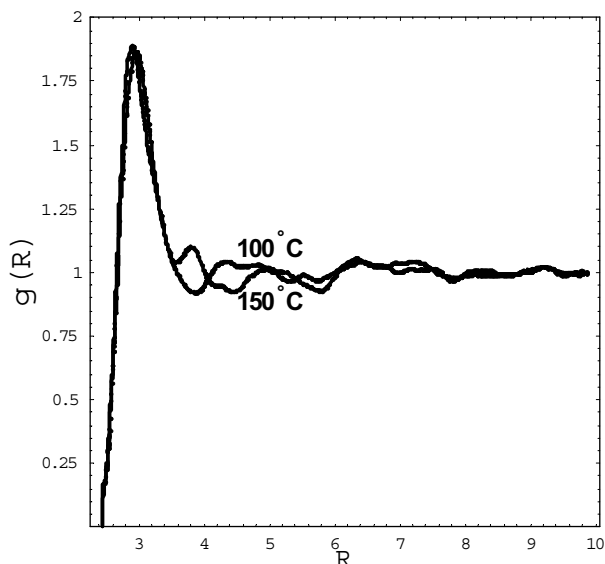


Fig. 1.36 The radial distribution function for water at 100°C and 150°C [based on data from Narten and Levy (1971)].

information and were thus referred to as *global* properties of the mixtures. The new approach is based on the so-called Kirkwood–Buff integrals (*KBI*). These quantities probe into the immediate surroundings of the molecules, and therefore are referred to as the *local* properties of the mixtures. For mixtures, the *KBI*s provide rich and interesting information on the local densities, local composition, and preferential solvation around a single molecule in the mixtures. In addition, the solvation thermodynamic quantities provide information on the strength of the interaction of a molecule with its environment, the effect of a molecule on the “structure” of the solvent, and so on (see Sec. 1.6).

Nowadays, it is common to refer to the quantities

$$G_{\alpha\beta} = \int_V [g_{\alpha\beta}(R) - 1] d\mathbf{R} \quad (1.5.1)$$

as the Kirkwood–Buff integrals. They were used in the original “Kirkwood–Buff theory of solutions” published in 1951.⁴³ However, the same integrals were introduced much earlier by Ornstein and Zernike⁴⁴ in connection with the fluctuation in the number of particles in an open system of *one* component. In this section, we report on some values of the *KBIs* for one-component systems.

The Kirkwood–Buff integral (*KBIs*) for a one-component system is defined by

$$G_O = \int_V [g_O(R) - 1] d\mathbf{R} \quad (1.5.2)$$

where $g_O(R)$ is the pair correlation function, or the radial distribution function defined in an open system (or in the grand canonical ensemble); the integration is extended over the entire macroscopic volume of the system V . Note that R in $g(R)$ is the intermolecular distance, whereas $d\mathbf{R}$ is an element of volume $dx dy dz$.

The *KBI* is related to two macroscopic quantities by the equations⁴⁵

$$\frac{\langle N^2 \rangle - \langle N \rangle^2}{\langle N \rangle} - 1 = \rho G_O = k_B T \rho \kappa_T - 1 \quad (1.5.3)$$

where k_B is the Boltzmann constant, T is the absolute temperature, ρ is the average number density N/V in the system, and κ_T is the isothermal compressibility of the system.

On the left-hand side of (1.5.3), we have the fluctuations in the number of particles in the open system. On the right-hand side, we have a connection with macroscopic measurable

⁴³Kirkwood and Buff (1951).

⁴⁴Ornstein and Zernike (1914).

⁴⁵Hill (1956), Münster (1969), and Hansen and McDonald (2006).

quantities. This side of the equation is known as the compressibility equation.⁴⁵

It should be emphasized that Eq. (1.5.3) is valid only when G_O is defined as in (1.5.2) in an *open* system (hence the subscript O). Failing to recognize this fact has been a notorious pitfall. To see this we first write the *KBI*, defined in the same way as in (1.5.2), but in a *closed* system (hence the subscript C).

$$G_C = \int_V [g_C(R) - 1] d\mathbf{R} \quad (1.5.4)$$

The two quantities G_O and G_C look deceptively similar (and identical if we remove the subscripts C and O) but, in fact, they are quite different. The difference between the two can be demonstrated even for an ideal gas (see Appendix C). For any liquid, and at any density, the closure condition, i.e. the fixed number of particles in the system, imposes the normalization condition on G_C :

$$G_C = \int_V [g_C(R) - 1] d\mathbf{R} = -1/\rho \quad (1.5.5)$$

Clearly, this condition arises from the fact that the total number of particles N in the system is conserved, i.e.

$$N = \rho \int_V d\mathbf{R} = \rho \int_V g_C(R) d\mathbf{R} + 1 \quad (1.5.6)$$

On the right-hand side of (1.5.6), the counting of the total number of particles is done in two steps; first, count the number of particles around a selected particle, then add the selected particle to get N . As was pointed out by Münster (1969), if one uses the same notation for $g_C(R)$ and $g_O(R)$, and substitute the integral in (1.5.6) into the compressibility equation (1.5.3), one gets the *absurd* result $\kappa_T = 0$. Clearly, this result can be avoided

by using different notations for the pair correlation functions in the closed and open systems.

We know from both experimental data on the pair correlation functions and from theoretical calculation that the pair correlation function is significantly larger than unity only in a small region about the center of a given molecule. In other words, there exists a correlation length R_{CORR} such that for $R \geq R_{CORR}$, $g(R)$ is practically unity. This fact allows us to deduce *local* information from G_O (but not from G_C). To see this, it is convenient to rewrite the KBI as

$$\int_V [g(R) - 1] d\mathbf{R} = \int_{V_{CORR}} + \int_{V - V_{CORR}} \quad (1.5.7)$$

where $V_{CORR} = 4\pi R_{CORR}^3/3$ is the correlation volume, which is essentially a *microscopic* volume, and $V - V_{CORR}$ is the *macroscopic* volume V of the system minus V_{CORR} . It is well known that the pair correlation function in the region $V - V_{CORR}$ is different in open and closed systems, i.e.

$$g_O(R \geq R_{CORR}) \cong 1 \quad (1.5.8)$$

$$g_C(R \geq R_{CORR}) \cong 1 - \frac{k_B T \rho \kappa_T}{N} \quad (1.5.9)$$

From (1.5.8) and (1.5.7) it follows that the second integral on the right-hand side of (1.5.7) can be neglected in G_O , but not in G_C . Hence, we have

$$\begin{aligned} G_O &= \int_V [g_O(R) - 1] d\mathbf{R} \\ &= \int_0^\infty [g_O(R) - 1] 4\pi R^2 dR \\ &\approx \int_0^{R_{CORR}} [g_O(R) - 1] 4\pi R^2 dR \end{aligned} \quad (1.5.10)$$

$$G_C = \int_0^{R_{CORR}} [g_C(R) - 1] 4\pi R^2 dR - \frac{k_B T \rho \kappa_T}{\rho'} \quad (1.5.11)$$

where $\rho = N/V$ and $\rho' = N/(V - V_{\text{CORR}})$. Thus, because of (1.5.10), G_O itself provides *local* information around a molecule. Furthermore, since in the correlation region ($R \leq R_{\text{CORR}}$) the values of $g_C(R)$ and $g_O(R)$ are nearly the same, the same local information is also contained in the integral of (1.5.11). However, in this case this integral is not equal to G_C . Therefore, we cannot identify the local information contained in G_O with G_C . Another way of viewing the different behaviors of open and closed systems is shown schematically in Fig. 1.37. In a closed system with *fixed* density $\rho = N/V$, placing one particle at the center of a sphere of radius R_{CORR} will change the density in the region $R_{\text{CORR}} \leq R \leq R_M$, where R_M is the radius of the macroscopic system, from $\rho = N/V$ to $\rho^* = \rho(1 - \frac{k_B T \rho \kappa_T}{N})$. The same process in an open system does not change the density ρ .

Thus, for an open system one can replace the integral over the entire region V by an integral over the correlation region. This makes the KBI, G_O , useful for studying local quantities, such as local density, local composition, and local preferential solvation (Ben-Naim, 2006). The same is not true for G_C , for

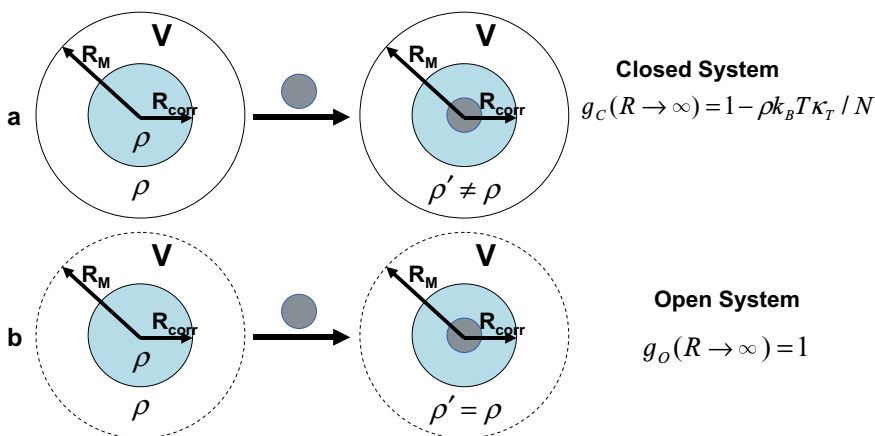


Fig. 1.37 The effect of placing a particle (dark disk) at the center of the correlation sphere (blue disk) in (a) closed, and (b) open systems.

which the second integral on the right-hand side of (1.5.7) is finite.

The *local* meaning of the KBI (G_O , but not G_C) is the following: $\rho 4\pi R^2 dR$ is the average number of particles in a spherical shell of radius R and width dR . $\rho g_O(R) 4\pi R^2 dR$ is the average number of particles in the same spherical shell, but in the center of which a particle is placed. Therefore, $\int_0^{R_{CORR}} \rho [g_O(R) - 1] 4\pi R^2 dR$ is the *change* in the average number of particles in the sphere of radius R_{CORR} , caused by placing a particle at the center of the sphere. Because of the property (1.5.8) in the open system, one can replace the upper limit R_{CORR} by infinity to obtain the same interpretation for the KBI (G_O but not G_C).

Another useful relation between the KBI and the partial molar volume at a fixed position is (Ben-Naim, 2006)

$$G_O = -V^* \quad (1.5.12)$$

Note that the molar volume V_M is the change in the volume of the system caused by adding one mole (or one molecule, depending on the context) of particles to the system at constant T and P . The quantity V^* is the change in the volume of the system caused by placing a particle at a *fixed position* in the system, keeping T and P constant. The relation between the two volumes (per particle) is

$$V_M = V^* + k_B T \kappa_T \quad (1.5.13)$$

From (1.5.12) it follows that

$$\rho G_O = \Delta N(R_{CORR}) = -\rho V^* \quad (1.5.14)$$

Thus, the change in the average number of particles in the correlation volume $\Delta N(R_{CORR})$ caused by placing a particle at the center of the correlation volume is equal to minus the

average number of particles occupying the volume V^* in the liquid having the density ρ .

It is sometimes convenient to reinterpret the *KBI* as follows (we drop the subscript O in the rest of this section since we shall always refer to G_O and not to G_C):

$$\begin{aligned}
 G &= \int_V [g(R) - 1] d\mathbf{R} \\
 &= \int_{V^{EX}} + \int_{V - V^{EX}} \\
 &= -V^{EX} + \int_{V - V^{EX}} [g(R) - 1] d\mathbf{R} \\
 &= -V^{EX} + L
 \end{aligned} \tag{1.5.15}$$

where V^{EX} is the excluded volume. This is defined as the region around the center of the particle for which $g(R) \cong 0$; hence, the integration over this region produces the negative quantity $-V^{EX}$. For spherical particles with hard-core diameter σ , this volume is simply

$$V^{EX} = \frac{4\pi\sigma^3}{3} \tag{1.5.16}$$

Thus, in general, G has two contributions: $-V^{EX}$, which is always negative, and L , which may be either positive or negative depending on the strength of the correlation function in the region $V_{CORR} - V^{EX}$.

We now present a few examples of the *KBI*s.

1.5.1. *Ideal gas*

Ideal gas behavior can be realized by either systems of hypothetical, *strictly-non-interacting* particles, or by real particles but at the limit of low densities $\rho \rightarrow 0$. Both of these give the same

equation of state

$$P = \rho k_B T \quad (1.5.17)$$

However, the two systems produce different *KBIs*. For the hypothetical ideal gas, all intermolecular interactions are zero, and hence, the pair correlation function is unity, and therefore

$$G(\text{hypothetical i.g.}) = 0. \quad (1.5.18)$$

Note that this equality is not true for the *KBI* defined in a closed system (see Appendix C).

For the *real* ideal gas, i.e. a system of interacting particles at $\rho \rightarrow 0$, we have the limiting value of the *KBI*:

$$G(\text{real i.g.}) = \lim_{\rho \rightarrow 0} G = \int_V \{\exp[-\beta U(R)] - 1\} d\mathbf{R} \quad (1.5.19)$$

This limit follows from the well-known expression for the pair correlation function at $\rho \rightarrow 0$, namely⁴⁶

$$g(R) \xrightarrow{\rho \rightarrow 0} \exp[-\beta U(R)] \quad (1.5.20)$$

where $U(R)$ is the pair potential.

The simplest interacting particles are hard spheres for which

$$U_{HS}(R) = \begin{cases} \infty & \text{for } R \leq \sigma \\ 0 & \text{for } R > \sigma \end{cases} \quad (1.5.21)$$

Hence,

$$G(\text{hard spheres}, \rho \rightarrow 0) = -\frac{4\pi\sigma^3}{3} \quad (1.5.22)$$

This is simply the excluded volume for the hard-sphere particles.

⁴⁶Hill (1956), Münster (1969), and Ben-Naim (2006).

For a *real* ideal gas, we can write

$$G(\text{real i.g.}) = \frac{-4\pi\sigma^3}{3} + \int_{V-V_{EX}} \{\exp[-\beta U(R) - 1]\} d\mathbf{R} \quad (1.5.23)$$

where σ is the *effective* hard-core diameter. For Lennard–Jones (*LJ*) particles, the effective hard-core diameter can be chosen as the parameter σ in the Lennard–Jones potential (see Sec. 1.2 and Table 1.3). For such a system, G consists of two terms: one negative due to the excluded volume and one positive due to the positive correlation (i.e. $g(R) \geq 1$ in the region $R \geq \sigma$). The two corresponding regions of the integrand in (1.5.19) are shown in Fig. 1.38. Here, we have a clear-cut separation between the positive and negative contributions to G .⁴⁷

1.5.2. *Inert gases represented as Lennard–Jones particles*

Lennard–Jones (*LJ*) particles are defined through the pair potential

$$U_{LJ}(R) = 4\epsilon \left[\left(\frac{\sigma}{R} \right)^{12} - \left(\frac{\sigma}{R} \right)^6 \right] \quad (1.5.24)$$

Figure 1.39 shows the functions $g(R)$ and $G(R_M)$ for the Lennard–Jones parameters corresponding to neon, argon, krypton, and xenon. All the plots are based on equations (1.5.24) and calculated for $T = 273$ K

$$G(R_M) = \int_0^{R_M} [g(R) - 1] 4\pi R^2 dR \quad (1.5.25)$$

⁴⁷We neglect the region between σ and $\sqrt[6]{2}\sigma$, where the potential is repulsive but $g(R)$ is smaller than unity.

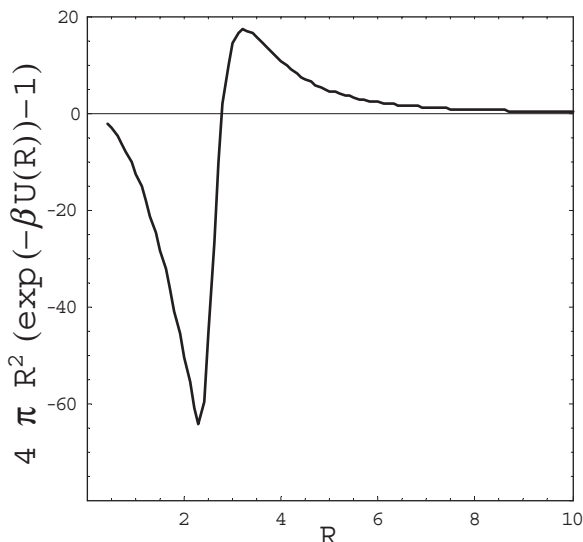


Fig. 1.38 The integrand $\{\exp[-\beta U(R)] - 1\}4\pi R^2$ as a function of R for LJ particles with parameters $\sigma = 2.78 \text{ \AA}$, $\varepsilon/k_B = 34.9 \text{ K}$ and at $T = 273 \text{ K}$. The negative and the positive regions contribute negative and positive values to the integral G in (1.5.19), respectively.

where

$$g(R) = \exp[-\beta U(R)] \quad (1.5.26)$$

with parameters given in Table 1.3. As can be seen from Fig. 1.39, for neon at very low densities, the excluded volume term V^{EX} in (1.5.15) is the dominant contribution to G , making the value of G negative. In all other cases, the values of G are positive, indicating that the attractive part of the potential dominates in (1.5.15) and the resulting values of G are all positive.

1.5.3. Water, methanol, and ethanol

Figure 1.40 shows the KBI for a series of linear alcohols having the formula $\text{CH}_3(\text{CH}_2)_{n-1}\text{OH}$ as a function of the number of carbon atoms. It is seen that the values are all negative and

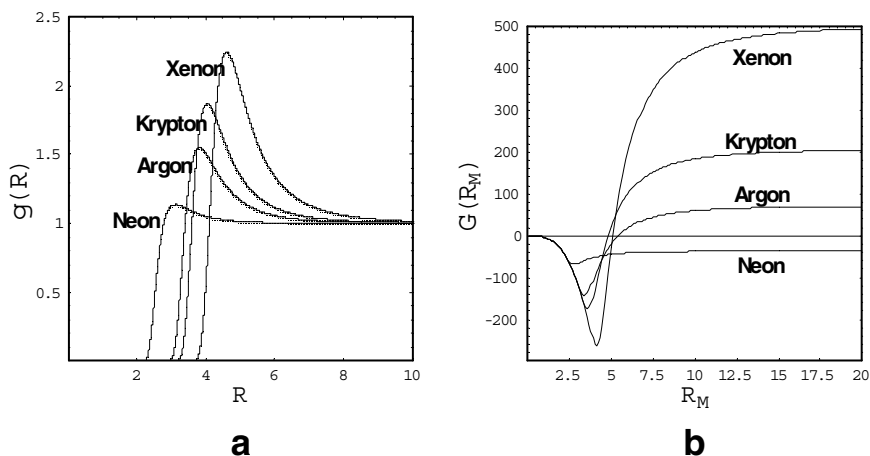


Fig. 1.39 Values of $g(R)$ and $G(R_M)$ for inert gases at low densities ($\rho \rightarrow 0$) with parameters given in Table 1.3 and $T = 273$ K.

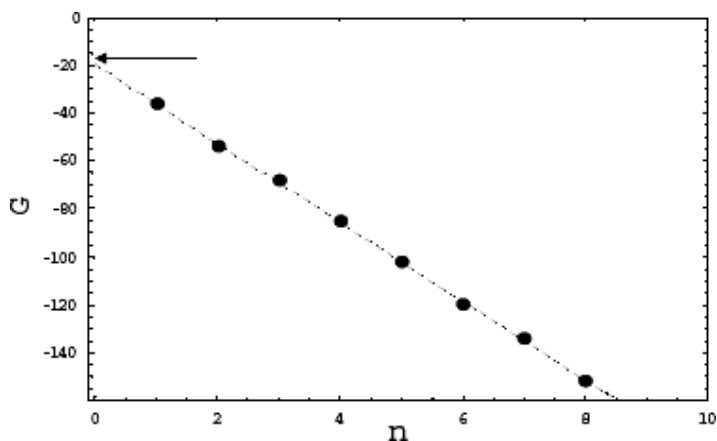


Fig. 1.40 Values of G for pure linear alcohols at 1 atm and 25°C . The extrapolated value at $n = 0$ is indicated by the arrow.

decrease with n . Clearly, the larger the chain, the larger the contribution from the hard-core repulsion, and hence, the more negative the value of the *KBI*. If we extrapolate from these values to $n = 0$, we get the value of G for the *hypothetical* alcohol

with no carbon atoms. Interestingly, the value of the *KBI* for water almost coincides with the extrapolated value from the series of alcohols. This finding is quite puzzling for the following reasons. As can be seen from Eq. (1.5.3), the *KBI* is determined by both the molar volume and the compressibility of water. These two properties show anomalous behavior as a function of temperature, yet the combination of the two produces a quantity that seems to behave “normally.”

Figure 1.41 shows the values of *G* for water as a function of temperature at 1 atm. From what we know about water, we would have expected for a small molecule such as water, with an effective diameter similar to that of neon and with such strong interactions (hydrogen bonding), that the positive contribution to the *KBI* would dominate the value of *G*. Yet the values of the *KBI* of liquid water are all negative over the entire range of temperatures. On the other hand, the *KBI* for low density steam has large and positive values (see Fig. 1.41c). The reason is that in the gaseous phase at low density, the pair interaction determines the pair correlation function [Eq. (1.5.26)]. Hence, strong interactions (hydrogen bonding) should contribute large positive values to the *KBI*. In the liquid state, the pair correlation function is determined not only by the pair interactions but also by higher order, non-additive potentials. The net effect of these interactions is to produce a relatively narrow first peak of the pair correlation function of water. This is equivalent to small coordination numbers. Hence, in this case the effect of the strong attractive forces is reduced and the value of *G* becomes negative.

Note that the values of *G* for D_2O are systematically lower than the corresponding values of H_2O . This curve goes through a maximum value at about $6^\circ C$ (not corresponding to either the minimum of the volume or the compressibility of D_2O).

Since H_2O and D_2O have almost the same effective diameters, one cannot explain the larger negative values of *G* of D_2O

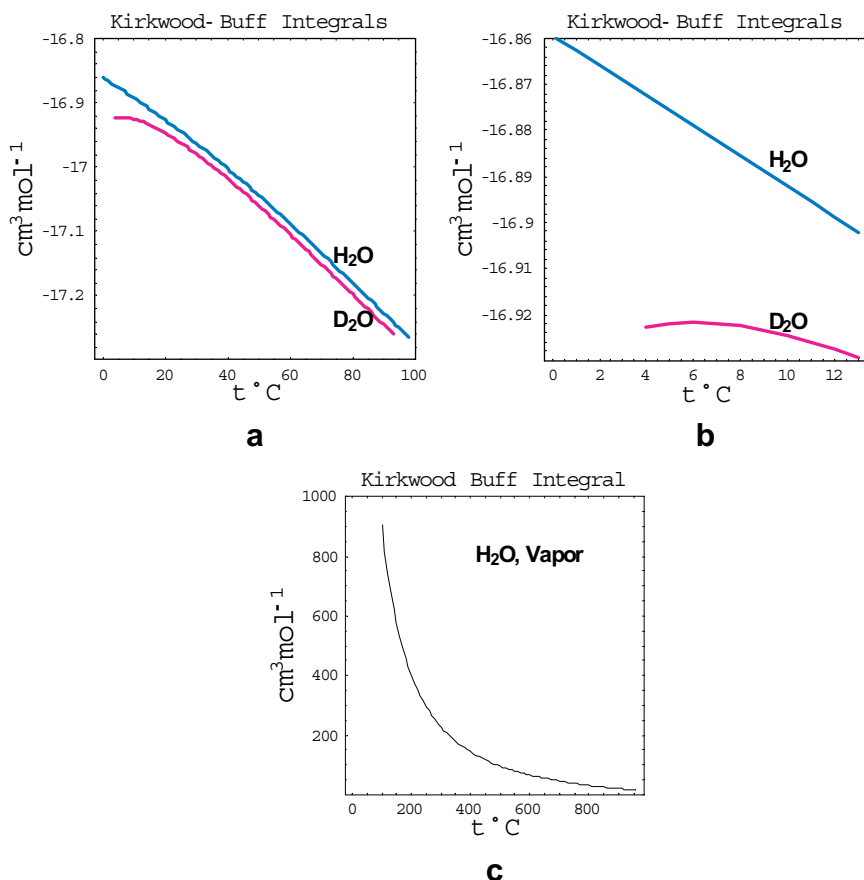


Fig. 1.41 (a) Values of G for H_2O and D_2O as a function of temperature at 1 atm, (b) details at low temperatures, and (c) the KBI for water vapor.

due to a larger excluded volume. Hence, Eq. (1.5.15) is of no help in this regard. On the other hand, looking at the compressibility equation, we notice that the term $k_B T \kappa_T$ is much smaller than the molar volume V_M . We can interpret the difference in the KBIs of H_2O and D_2O in terms of the molar volumes. The molar volumes in turn may be interpreted in terms of the “relative degree of structure” of the two liquids. The strength of

the hydrogen-bond (*HB*) energy of D_2O is known to be larger than that of H_2O . Therefore, it is reasonable to expect that, on average, more molecules are being engaged in hydrogen bonding in D_2O . This leads to a larger concentration of the open structure component, and hence, to a larger negative *KBI*. We shall further discuss the structures of H_2O and D_2O in Chapter 2.

The pressure dependence of the *KBI* for H_2O and D_2O at 25°C is shown in Fig. 1.42. The two curves are almost linear and almost parallel to each other. Again, we see that D_2O has the larger (negative) values of the *KBI* in the entire range of pressures.

Figure 1.43 shows the *KBI* for some hydrocarbons and for methanol and ethanol as a function of temperature at 1 atm. Since in each group the overall attractive part of the intermolecular interactions have similar magnitude, the relative difference in the *KBI*s is expected to depend on the size of the molecules.

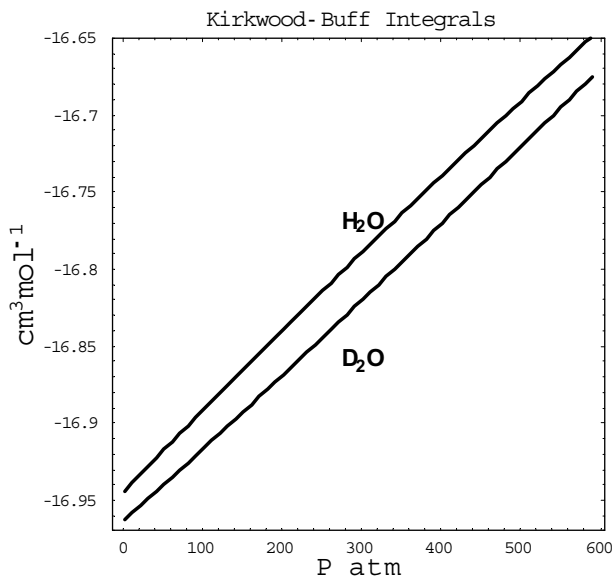


Fig. 1.42 The pressure dependence of G for H_2O and D_2O at 25°C .

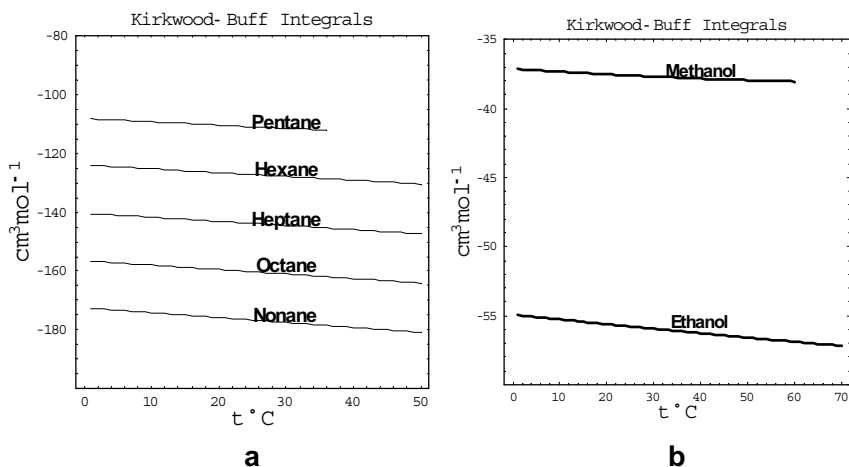


Fig. 1.43 Values of G for (a) some linear hydrocarbons, and (b) methanol and ethanol as a function of temperature at 1 atm.

In this figure, all the $KBIs$ are negative and the temperature dependence is also negative.

1.6. Solvation of Water in Water

Another set of quantities which also convey information of *local* character are the solvation thermodynamic quantities.

We shall discuss at length solvation quantities in Chapter 3. Here, we present some values of the thermodynamics of solvation of water in pure water. It should be noted that in the traditional approach to solvation, only solvation of one component in very dilute solution in a solvent can be defined and measured. In the definition used here, the concept of solvation can be applied to any molecule in any liquid at any concentration.⁴⁸

We define the solvation process as the transfer of a molecule from a fixed position in an ideal gas phase to a fixed position

⁴⁸For details, see Ben-Naim (2006).

in the liquid. The statistical mechanical expression for the solvation Gibbs energy follows directly from the definition of the solvation process. We define the pseudo-chemical potential in the liquid by

$$\mu_w^{*l} = -k_B T \ln \frac{\Delta^l(T, P, N + 1, \mathbf{R}_0)}{\Delta^l(T, P, N)} \quad (1.6.1)$$

where $\Delta^l(T, P, N)$ is the T, P, N partition function (PF) of pure water at T, P, N . $\Delta^l(T, P, N + 1, \mathbf{R}_0)$ is the PF for a system at the same T and P but with an additional water molecule placed at some fixed position in the liquid.

Likewise, we define the pseudo-chemical potential of water in an ideal gas phase as

$$\mu_w^{*ig} = -k_B T \ln \frac{\Delta^{ig}(T, P, N + 1, \mathbf{R}_0)}{\Delta^{ig}(T, P, N)} \quad (1.6.2)$$

where Δ^{ig} are the corresponding PF s, in the ideal gas phase.

The solvation Gibbs energy is now defined by

$$\Delta G_w^* = \mu_w^{*l} - \mu_w^{*ig} \quad (1.6.3)$$

It is easy to show that if we assume that the internal degrees of freedom of the solvated molecules are not affected by the solvation process, then we have the expression⁴⁹

$$\Delta G_w^* = -k_B T \ln \langle \exp[-\beta B_w] \rangle_0 \quad (1.6.4)$$

where B_w is the total interaction energy of the added molecule with all the particles in the liquid, and the average $\langle \cdot \rangle_0$ is over all the configurations of the N molecules (excluding the added molecule) and all possible volumes of the system at given T, P, N .

⁴⁹ See Ben-Naim (2006).

Equation (1.6.4) is important for the theoretical interpretation of the solvation quantities (see Chapters 2 and 3). Here, we are interested in the method of calculating the quantity ΔG_w^* from experimental data. This is obtained as follows. We write the chemical potentials of w in the liquid and in the gaseous phases at equilibrium

$$\mu_w^l = \mu_w^{*l} + k_B T \ln \rho_w^l = \mu_w^g = \mu_w^{*g} + k_B T \ln \rho_w^g \quad (1.6.5)$$

From (1.6.5) it follows that

$$\mu_w^{*l} - \mu_w^{*g} = k_B T \ln (\rho_w^g / \rho_w^l)_{eq} \quad (1.6.6)$$

Note that, in general, this quantity is different from the quantity defined in (1.6.3). Equation (1.6.6) is more general than (1.6.3) since it applies to any phase g , not necessarily an ideal gas phase. If we can assume that the vapor in equilibrium with the liquid is an ideal gas, then (1.6.6) becomes the solvation Gibbs energy as defined in (1.6.3). In the more general case, (1.6.6) is the *difference* in the solvation Gibbs energies in the two phases, i.e.

$$\begin{aligned} \Delta G_w^{*l} - \Delta G_w^{*g} &= \mu_w^{*l} - \mu_w^{*ig} - (\mu_w^{*g} - \mu_w^{*ig}) \\ &= \mu_w^{*l} - \mu_w^{*g} \end{aligned} \quad (1.6.7)$$

Figure 1.44 shows the values of $\Delta G_s^{*l} - \Delta G_s^{*g}$ (s can be either H_2O or D_2O) for water and heavy water in the entire range of the liquid state. Note that the values for D_2O are systematically lower than those for H_2O . As we increase the temperature along the liquid-vapor equilibrium line, the densities of the two phases become closer and closer. The values of $\Delta G_w^{*l} - \Delta G_w^{*g}$ become smaller and smaller, and at the critical point they should approach zero.

In the range of temperatures between 0°C to 100°C , we can assume that the vapor above the liquid is nearly ideal

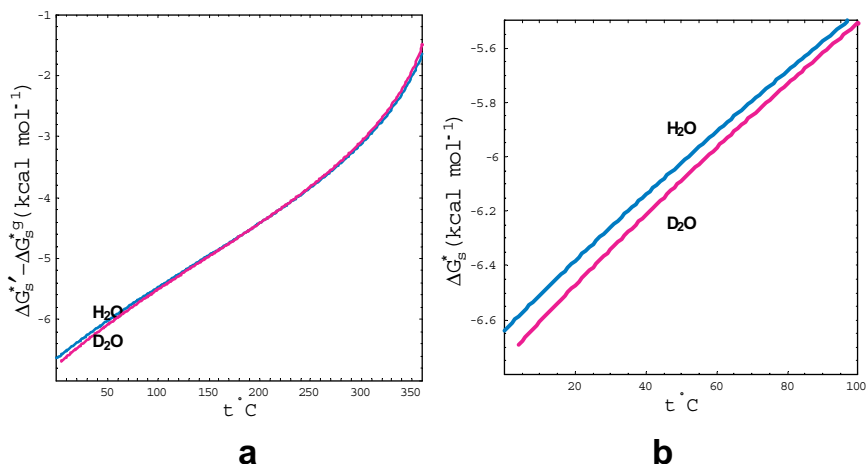


Fig. 1.44 (a) The difference in the solvation Gibbs energy between two phases for H_2O and D_2O as a function of temperature along the vapor-liquid equilibrium line. (b) Solvation Gibbs energies at lower temperatures.

gas. In this case, the values of $\Delta G_w^{*l} - \Delta G_w^{*g}$ in Fig. 1.44b are approximately equal to the solvation Gibbs energies in the liquid phase.

If the density of the vapor can be assumed to be an ideal gas, then

$$\frac{P_s}{k_B T} = \rho_s^{*ig} \quad (1.6.8)$$

where P_s is the vapor pressure of the pure liquid s . In this case, the solvation Gibbs energy of s in pure liquid s can be calculated from:

$$\Delta G_s^{*l} = k_B T \ln \left(\frac{\rho_s^{ig}}{\rho_s^l} \right)_{eq} = k_B T \ln \left(\frac{\rho_s}{k_B T \rho_s^l} \right)_{eq} \quad (1.6.9)$$

When evaluating other thermodynamic quantities of solvation from data along the equilibrium line, care must be exercised to distinguish between derivatives at *constant pressure* and

derivatives *along the equilibrium line*. The connection between the two is

$$\left(\frac{d\Delta G_s^{*l}}{dT}\right)_{eq} = \left(\frac{\partial\Delta G_s^{*l}}{\partial T}\right)_P + \left(\frac{\partial\Delta G_s^{*l}}{\partial P}\right)_T \left(\frac{dP}{dT}\right)_{eq} \quad (1.6.10)$$

Here, we used straight derivatives to indicate differentiation along the equilibrium line. The two derivatives of ΔG_s^* on the right-hand side of (1.6.10) are identified as the solvation entropy and the solvation volume, respectively, i.e.

$$\left(\frac{d\Delta G_s^{*l}}{dT}\right)_{eq} = -\Delta S_s^{*l} + \Delta V_s^{*l} \left(\frac{dP}{dT}\right)_{eq} \quad (1.6.11)$$

Usually, data are available to evaluate both of the straight derivatives in Eq. (1.6.11). This is not sufficient, however, to compute both ΔS_s^{*l} and ΔV_s^{*l} . Fortunately, ΔV_s^{*l} may be obtained directly from data on molar volume and compressibility of the pure liquid.

The relationship between the molar volume and the pseudo molar volume is⁵⁰

$$\overline{V}_s^l = \left(\frac{\partial\mu_s^l}{\partial P}\right)_T = V_s^{*l} + k_B T \kappa_T^l \quad (1.6.12)$$

where κ_T^l is the isothermal compressibility of the pure s .

Fortunately, the term $k_B T \kappa_T^l$ in liquids is small compared with the values of V_s^{*l} . Furthermore, the term $\Delta V_s^{*l} \left(\frac{dP}{dT}\right)_{eq}$ in (1.6.11) is also small compared with ΔS_s^{*l} . These facts may be used to calculate approximate values of both ΔV_s^{*l} and ΔS_s^{*l} from data on the densities of s at equilibrium between the gas and the liquid phases.

⁵⁰The pseudo molar volume is the pressure derivative of the pseudo-chemical potential (Ben-Naim, 2006).

The solvation volume is defined as

$$\Delta V_s^{*l} = V_s^{*l} - V_s^{*g}. \quad (1.6.13)$$

With ΔV_s^{*l} and $(\partial P/\partial T)_{eq}$, we can solve (1.6.11) for ΔS_s^{*l} , and from ΔS_s^{*l} we also get

$$\Delta H_s^{*l} = \Delta G_s^{*l} + T\Delta S_s^{*l} \quad (1.6.14)$$

$$\Delta E_s^{*l} = \Delta H_s^{*l} - P\Delta V_s^{*l} \quad (1.6.15)$$

and the heat capacity of solvation

$$\Delta C_{P,s}^{*l} = \left(\frac{\partial \Delta H_s^{*l}}{\partial T} \right)_P$$

Figure 1.45 shows the values of ΔG_s^{*l} , ΔS_s^{*l} , and ΔH_s^{*l} . Figure 1.46 shows values of ΔV_s^{*l} and $\Delta C_{P,s}^{*l}$. In Figs. 1.47 and 1.48 we present some values for the solvation quantities for methanol and ethanol.

1.7. The Importance of Water in Biological Systems

It is hardly necessary to emphasize the importance of water to life. Water in the blood not only runs through our bodies, but also runs our bodies. We need to constantly supply our body with water in order to keep it going. Water, as a solvent, helps distribute various chemicals needed in the different parts of the body, and at the same time it helps to discharge other waste chemicals that are not needed, or those that are even harmful. But water does much more than merely transport chemicals around the body. It affects in specific ways a multitude of biochemical processes taking place in each of our cells. It has long been speculated that life as we know it on this planet could not have started without water. Although this is merely speculation, it is a reasonable one. Strictly speaking of course, we

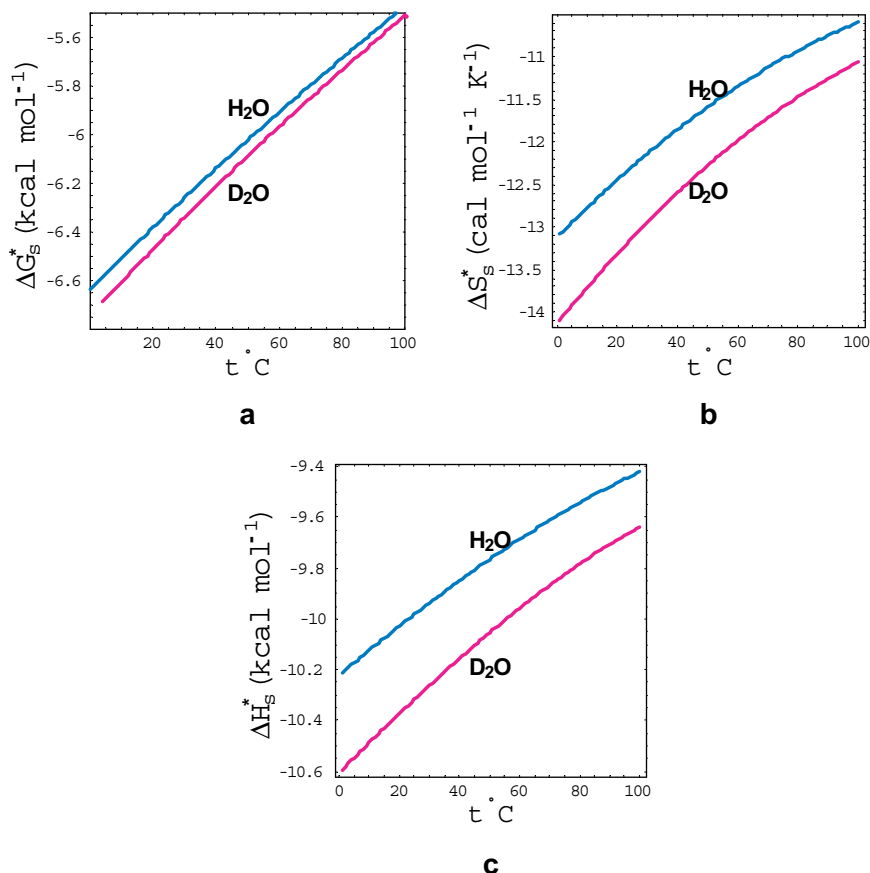


Fig. 1.45 (a) Solvation Gibbs energy, (b) entropy of solvation, and (c) enthalpy of solvation of water in water as a function of temperature.

cannot preclude the possibility of the existence of some other kind of life-form based on some other liquid.

As we have noted, the molar volume of ice is larger than that of liquid water. Everyone is familiar with the phenomenon of ice floating on top of water. If the molar volume of ice were *not* larger than that of water, ice formed on the surface of the ocean would sink to the bottom and then be insulated by the water covering it (water is a good thermal insulator). Over time, more

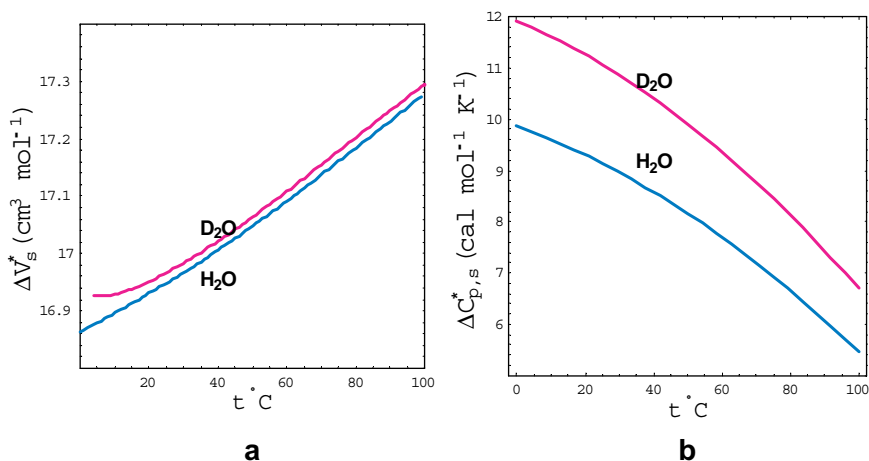


Fig. 1.46 (a) Solvation volumes, and (b) partial molar heat capacities of solvation of H₂O and D₂O.

and more layers of ice would accumulate on the bottom in a process that would gradually freeze nearly the entire ocean.

The fact that ice floats on top of the water helps to maintain the relatively high temperature of liquid water underneath — this in turn helps to maintain life in water in spite of lower temperatures above the surface. Clearly, when the temperature of the atmosphere increases, it is the ice on the surface that melts first — this too contributes to the maintenance of the water temperature underneath.

The fact that ice has a larger volume than liquid water can also be harmful to living organisms. When a living cell containing water freezes, the expanding ice can break the cell's membrane, possibly killing the cell. Some marine creatures that live in extremely cold environments possess a special “antifreeze” protein that lowers the freezing temperature and delays the process of ice formation.

The high value of the heat capacity of water is of primary importance in regulating the temperature of a living system. In

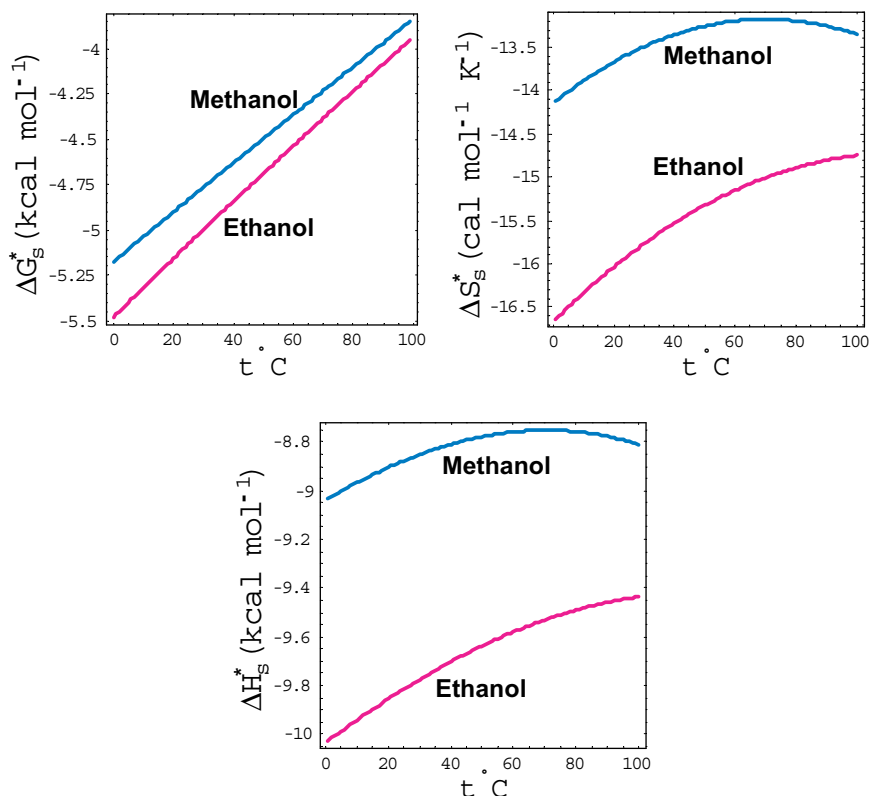


Fig. 1.47 Solvation quantities for methanol and ethanol.

each living cell, hundreds of chemical reactions take place. Some of these chemical reactions are exothermic, i.e. they release heat into the cell's surroundings. If this heat is not absorbed by some mechanism, the temperature will rise to a dangerous level. The large heat capacity of water means that for a given amount of heat absorbed by one unit volume of water, the temperature increase is smaller than it would be in a normal liquid. Thus, most of the heat released in chemical reactions is absorbed by the water — with a minimal increase in its temperature. This is also the reason why laboratories use water in a thermostat-bath when a constant temperature must be maintained. Because of its

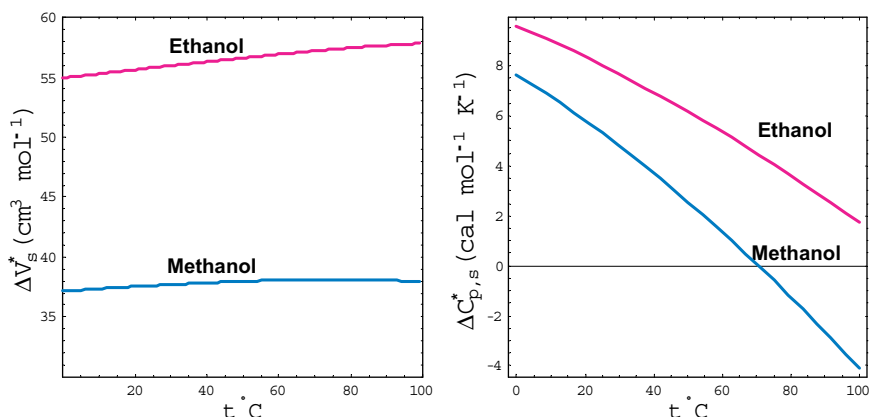


Fig. 1.48 (a) Solvation volumes, and (b) partial molar heat capacity of solvation of methanol and ethanol.

large heat capacity, the temperature does not change so rapidly as a result of heat flowing inside or outside the thermostat.

Another property of water that helps regulate body temperature is its large heat of vaporization. When the atmospheric temperature is high, both animals and plants evaporate some of their water content. This is the familiar phenomenon of sweating. Because the heat of vaporization of water is large, only a small quantity of water needs to be evaporated to maintain the temperature of the body. Note that the actual amount of sweat visible on the skin in hot weather or after exercising is not an indication of the amount of water that is evaporating. The evaporating sweat is released into the air as a gas and is not conspicuous. Sweat becomes visible only when liquid is released by the body more rapidly than the rate of evaporation. The rate of evaporation is affected by the relative humidity of the air. When the relative humidity is low, water evaporates quickly from the skin. When it is high, water evaporates slowly from the skin because the air has a lowered capacity to absorb additional water, and temperature regulation by sweating becomes

inefficient. This is the reason one feels more comfortable in the dry atmosphere of, say, Jerusalem than in the humid atmosphere of, say, Tel Aviv.

The large heat of vaporization helps to regulate not only the bodies of living organisms, but also the Earth's natural environment. Most of the radiant energy from the sun that reaches the Earth is absorbed by evaporating ocean water. The fact that the heat of evaporation of water is large, partially explains why this evaporation effectively prevents an increase in the Earth's temperature. If the seas were filled with some other liquid, e.g. alcohol, the Earth's temperature would sharply increase. Such an increase would probably kill all living creatures (assuming they had developed and were surviving in an "alcoholic" environment, which is doubtful).

We have mentioned the large amount of heat that is absorbed when ice melts, and the damaging effect of any water freezing within a living cell. If the temperature of pure water or any aqueous solution falls below the freezing point (which is normally lower for aqueous solutions than for pure water), ice begins to form and a large amount of heat is released. This release of heat decelerates the rate of any further ice formation, preventing or at least delaying the conversion of all the water in the body into ice.

In concluding this section, we mention two more properties of water that are important in biological systems. The first is a critical factor affecting the ability of plants to absorb water. This property is surface tension. Compared to "normal" liquids (e.g. alcohols, simple paraffins, and benzene), water has a very high surface tension. The surface tension of water at 20°C is about 72.75 (in ergs cm^{-2}), compared with acetone at 23.7, ethanol at 22.3, and n-hexane at 18.4, for the same temperature. This is significant because surface tension is the primary force that draws fluids up through capillaries. The higher the surface tension of a liquid, the higher the liquid can rise in capillaries.

This explains why water can rise in the interior of tall trees, even up to the highest leaves where it is needed in photosynthesis and temperature regulation.

The second property of water important for biological systems is the dielectric constant. The dielectric constant of water exceeds that of many liquids (for instance, hexane: 1.87; chloroform: 5.05; ethanol: 24; methanol: 33; water: 80; but hydrogen cyanide: 116). The dielectric constant of water is important for its capability of dissolving a great variety of molecules, from simple salts such as NaCl to very large molecules such as proteins. A more extensive discussion of the relevance of the properties of water to life may be found in Henderson (1913), Edsall and Wyman (1958), and Franks (2000).

The fact that the properties of water are “fine-tuned” to support life has been viewed as evidence of the existence of an Intelligent Designer. This is essentially the same argument as the so-called Anthropic Principle invoked by creationists in favor of the existence of an Intelligent Designer. If the Universe is so finely tuned to support life, the argument goes, there must be a “fine-tuner” who designed the Universe. In other words, an intelligent being has *designed* the Universe in such a way as to support life.

This type of argument is very appealing to those who believe that life as we know it on our planet is the only possible form of life. Still, one cannot exclude the possibility that other forms of life based on other liquids or even on different “fine-tuned” laws of physics could have evolved in some remote part of the Universe, or perhaps in other universes.

In Henderson’s (1913) book, “The Fitness of the Environment,” he discusses the reciprocity of Darwin’s fitness ideas and the fitness of water to life. He asks the question: “Water is indeed a wonderful substance which fills its place in nature most

satisfactorily, but would not another substance do as well? Is not ammonia, for example, a possible substitute?" Henderson concludes the chapter on water by the words: "In truth Darwinian features are a perfectly reciprocal relationship. In the world of modern science a fit organism inhabits a fit environment."

CHAPTER 2

Theoretical Approaches to the Study of Liquid Water

Personal Introduction

Although my interest in the theory of water started before and during my work for my PhD, I actually worked on water only in my second year of my post-doc. When I first visited Frank Stillinger in 1966, I suggested working on water. At that time the mixture-model approach prevailed in the literature. This model was considered an ad hoc approximation, with neither experimental nor theoretical support. Our approach was different: start with a single water molecule, construct a pair potential, and see which theoretical methods could be applied to a system of such molecules. That task was extremely difficult; in fact, almost impossible. No one has done any theoretical work on such a system of complex molecules. At that time, it was not clear at all that an effective pair potential could be designed so as to be successful in reproducing the properties of water. It took almost two years just to construct the pair potential. By the time it was ready for use, I had to return to Israel. In the next few years, Frank Stillinger in collaboration with Aneesur Rahman carried out extensive molecular dynamic simulations on the water-like particles we had designed earlier. This potential was initially referred to as the BNS potential. Later, it was renamed the ST2 potential, and the BNS potential was forgotten.

Back in Israel, I tried to use the BNS potential in solving numerically the Percus–Yevick equation. This effort was only partially successful and the computational time was enormous. Therefore, I designed a new 3-D pair potential that would be easier to use for analytical work on water (Sec. 2.7). For some time, I tried to do some analytical work with that potential, but all my efforts were fruitless. I also tried a 2-D version of the same potential (see Sec. 2.6), and later a 1-D version of it (see Sec. 2.5).

At the same time, I was also trying to “legitimize” the application of the mixture-model (MM) approach to water. I was familiar with the MM theories of both water and aqueous solutions (see Secs. 2.2 and 2.3), but these were considered to be ad hoc models. Many scientists had expressed serious reservations about this approach on the grounds that there existed no experimental evidence for the existence of two or more species in water. I myself was fascinated with the success of the MM in the interpretation of so many properties of water as well as of aqueous solutions. I was also convinced that the MM approach was basically correct. It needed only to be firmly anchored within the framework of a statistical mechanical theory. That was exactly what I did. Once the general MM approach was established on solid grounds, for any liquid and not only for water, the exact and most powerful Kirkwood–Buff theory of solution could be applied to the pure liquid, viewed as a mixture. This has not only legitimized the general MM approach, but also showed that all the existing MM theories can be viewed as approximations to an exact MM.¹ One does not need any experimental evidence for the adoption of the MM approach. We shall see, in this and the next chapter, that the MM approach is just a different view of the system, a view that has proved to be very useful for the interpretation of the outstanding properties of water and

¹The term *mixture model* is somewhat misleading when applied to the *exact* mixture-model approach to liquids (see Sec. 2.3).

aqueous solutions. One example of the equivalence between the one-component and the MM approach is shown in Appendix D.

Studying the MM approach based on a quasi-component distribution function had led to the formulation of what I shall refer to as the principal molecular property of water, or for short, the principle. While the importance of the structure of water and the underlying hydrogen bonds were recognized long ago, the new and more fundamental aspect of the intermolecular interactions which can explain both the structure and the outstanding properties of water were recognized much later.

This principal feature of the water-water interaction was deemed so fundamental that I have used it for the cover design of this book. In short, it states that the most important aspect of molecular interactions between water molecules is the specific correlation between local density and binding energy. We shall encounter this principle in several places throughout this book. By invoking this principle, one can explain many properties of liquid water without ever using the concept of the structure of water.

One stringent test of this principle was to apply it to a one-dimensional model of water-like particles and see if one can obtain the anomalous properties of water while bypassing the concept of structure. Indeed, the model described in Sec. 2.5 utilizes nothing but the principle. To my astonishment, it has worked very well in one- and two-dimensional systems.

The success of these implementations (discussed in Secs. 2.5 and 2.6) firmed up my conviction that this principle is indeed an essential feature of the water-water interaction in producing the characteristic and outstanding properties of water. The concept of the structure of water is still useful, not as a fundamental principle but as an emergent property of the principle. A qualitative usage of the concept of the structure of water abounds in the literature. In Sec. 2.7, I shall discuss a possible definition of the structure of water based on the water-water pair potential. Also,

an approximate measure of the structure of water is provided for both liquid water and aqueous solutions of simple solutes. In the last section in this chapter, I shall briefly discuss some results obtained by simulations of a system of water-like particles. The results of the simulations have contributed to the understanding of the structure of water, but not much to understanding the properties of water.

2.1. Introduction

This chapter is not organized according to the chronological sequence of the published theories, nor is it organized according to the extent of resemblance of the models to real liquid water, but rather in what I believe is the order of *their* interpretive power. Therefore, I will start with the mixture-model (MM) approach (which happens to be the older approach), then proceed with the 1-D models for water, which though very far from real water is the most useful one for understanding the properties of water. I will follow with the 2-D and 3-D models in subsequent sections.

In Sec. 2.2, I will present the general theoretical framework for the study of water where the difficulties and the approximations of any theoretical approach will be discussed.

In Secs. 2.3 and 2.4, we turn to a thorough discussion of the MM approach to water. We shall start with some historical notes, present an example of a successful two-structure model, then proceed to the exact MM approach and some of its applications.

In Sec. 2.5, we discuss the simplest imaginable “model” of water referred to as the primitive 1-D model of water. We shall describe two equivalent views of the same model and also a modified model first published in 1969 by Lovett and Ben-Naim (1969). The latter will be shown to be particularly suitable in the study of aqueous solutions of non-polar solutes

(Chapters 3 and 4). In Sec. 2.6, we discuss a 2-D model of water-like particles first constructed in 1971 and 1972, and later extended to the study of aqueous solutions of both ionic and non-ionic solutes.

Section 2.7 is devoted to what may be viewed superficially as the more realistic 3-D models for water. It is realistic in the sense that real water molecules “live” in the real 3-D world. However, the 3-D models used are as far from reality as the 2-D and 1-D models described earlier. We shall discuss the main features of the pair potential, the long, short and intermediate ranges of the pair potential, and most importantly the features of the potentials that are crucial to the success of a model to describe the behavior of water. Some results obtained by simulations are also described in this section.

Until the early 1960s, most or all of the theoretical approaches to liquid water were based on a mixture-model approach. A sharp turning point in the theoretical study of water began with the publication of the first ever successful effective pair potential for water. Whereas old theories incorporated hydrogen bonding within the definition of the species (ice-like, clathrate-like or flickering clusters of water molecules), the new approach was based on mimicking the effect of *HB*ing by an effective pair potential, the primary feature of which was the propensity of molecules to prefer tetrahedral low-density packing.

From then on, pair potentials proliferated at a rate that is difficult to follow. Fortunately, these were reviewed by several authors. We shall discuss these very briefly at the end of Sec. 2.2.

2.2. The General Theoretical Framework

In this section, we present a general outline of a theoretical approach to water and point out some basic assumptions that are made in most theories.

The most fundamental starting point for any theoretical approach is the quantum mechanical partition function (PF), and the fundamental connection between the partition function and the corresponding thermodynamic potential. Once we have a PF , either exact or approximate, we can derive all the thermodynamic quantities by using standard relationships. Statistical mechanics is a general and very powerful tool to connect between microscopic properties of atoms and molecules, such as mass, dipole moment, polarizability, and intermolecular interaction energy, on the one hand, and macroscopic properties of the bulk matter, such as the energy, entropy, heat capacity, and compressibility, on the other.

The general quantum mechanical partition function of the system is²

$$Q(T, V, N) = \sum_i \exp[-\beta E_i] \quad (2.1)$$

where E_i is the energy of the i th state, $\beta = (k_B T)^{-1}$ and the sum is over all states of the system.

However, since the canonical PF requires the knowledge of all energy levels of a system, and this is impossible to calculate at present (except for highly simplified models), we resort to the classical analog of the canonical partition function Q_{class} . In making this transition from the quantum mechanical to the classical PF , we actually make a few assumptions and approximations.

The classical limit for the translational degrees of freedom is attained when $\rho \Lambda^3 \ll 1$, where ρ is the number density and Λ^3 is the momentum PF , or the de Broglie thermal wavelength.³ This

²In most of the book, we shall use the canonical PF . However, for special cases or special model systems, other partition functions might be more convenient.

³ Λ is a length of the order of magnitude of the de Broglie wavelength h/mv , where v is the velocity of the particle, and the kinetic energy is of the order of $k_B T$ (Hill, 1960).

approximation is valid at room temperature and atmospheric pressures, and for molecules of the size of water molecules. Specifically for water at, say, 25°C the number density is $\rho = 3.34 \times 10^{22}$ particles per cm^3 and with $h = 6.6261 \times 10^{-34}$ Js, $k_B = 1.3807 \times 10^{-23}$ JK $^{-1}$ we can calculate the momentum PF :

$$\Lambda^3 = \left(\frac{h}{\sqrt{2\pi m k_B T}} \right)^3 \quad (2.2)$$

Hence, we have

$$\rho \Lambda^3 \approx 0.00038 \ll 1 \quad (2.3)$$

The second approximation is the *separability* of the internal partition function from the configurational PF . Liquid water can be viewed as a mixture of hydrogens and oxygens; these can be chosen either as charged or as neutral atoms. In any case, it is very difficult to include interactions among all atoms in an explicit form in writing the classical analog of the partition functions:

$$\begin{aligned} Q_{class} = & \frac{1}{N_O! N_H!} \int \cdots \int d\mathbf{p}^{N_O} d\mathbf{p}^{N_H} d\mathbf{R}^{N_O} d\mathbf{R}^{N_H} \\ & \times \exp[-\beta H(\mathbf{p}^{N_O}, \mathbf{R}^{N_O}, \mathbf{p}^{N_H}, \mathbf{R}^{N_H})] \end{aligned} \quad (2.4)$$

Here, we view liquid water as a mixture of N_O oxygen atoms and $N_H = 2N_O$ hydrogen atoms. $\mathbf{R}^{N_O}$ stands for the locations of all oxygen atoms and $\mathbf{p}^{N_O}$ for all the momenta of the oxygen atoms, and similarly for the hydrogen atoms, we use the notation $\mathbf{R}^{N_H}$ and $\mathbf{p}^{N_H}$, respectively. $\beta = (k_B T)^{-1}$, and H is the Hamiltonian function for a system of N_w water molecules ($N_O = N_w$ and $N_H = 2N_w$) viewed as a mixture of oxygen and hydrogen atoms. The integration is carried out over all possible locations within the volume V and all possible momenta.

Fortunately, most of the outstanding properties of liquid water can be understood by viewing the water molecule as a

single molecular entity with very infrequent dissociation into atoms (either neutral H and O, or charged ions H^+ and O^-). This fact was long since established by Bernal and Fowler (1933) and was further corroborated by the findings that simulations based on this view provided results that conform with experimental data on water.

Of course, if one is interested in some special properties of water such as acidity, chemical reactivity, etc., one should take into account dissociation of water molecules into atoms, or ions. For most of the properties discussed in this book, it will suffice to view a water molecule as a single molecular entity.

We denote by q_w the internal partition function of a single water molecule. This includes the contributions due to the rotational, vibrational, and electronic degrees of freedom of a single water molecule. Although we recognize that all of these degrees of freedom might be affected by the interaction among water molecules, it is customary to ignore this effect. The internal PF , q_w may be calculated from the available molecular data, and is assumed to be *independent* of the interactions among the molecules.⁴ This independence allows us to factorize the classical partition function as

$$Q_{class} = \frac{q_w^{N_w} Z_{N_w}}{(8\pi^2)^{N_w} \Lambda^{3N_w}} \quad (2.5)$$

where Z_{N_w} is the configurational partition function of N_w water molecules. The factor $8\pi^2$ arises from the integration over all orientations of a single water molecule, namely⁵

$$\int_0^{2\pi} d\phi \int_0^\pi \sin\theta d\theta \int_0^{2\pi} d\psi = 8\pi^2 \quad (2.6)$$

⁴ Another assumption we usually make is that internal degrees of freedom are independent, hence the internal PF , q_w may be factored into rotational, vibrational, and electronic PF s.

⁵ The angles ϕ , θ , and ψ are conveniently chosen as the Euler angles. See, for example, Goldstein (1950).

Once we include all internal (rotational, vibrational, electronic) degrees of freedom in q_w , we can rewrite the partition function Q in the form

$$Q_{class} = \frac{q_w^{N_w}}{(8\pi^2)^{N_w} \Lambda^{3N_w}} \int d\mathbf{X}^{N_w} \exp[-\beta U(\mathbf{X}_1, \dots, \mathbf{X}_{N_w})] \quad (2.7)$$

where we have separated the internal partition function from the configurational partition function and integrated over all the translational momenta to obtain the momentum $PF \Lambda^3$ for each of the N_w water molecules. The configurational partition function is

$$Z_{N_w} = \int d\mathbf{X}^{N_w} \exp[-\beta U(\mathbf{X}_1, \dots, \mathbf{X}_{N_w})] \quad (2.8)$$

where the integration is over all locations and all orientations of the N_w water molecules viewed as rigid particles.

The next step is to simplify the total interaction energy $U(\mathbf{X}_1, \dots, \mathbf{X}_{N_w})$. This involves the approximation that the total interaction energy is pairwise additive, i.e. we write

$$U(\mathbf{X}^{N_w}) = \sum_{i < j} U(\mathbf{X}_i, \mathbf{X}_j) \quad (2.9)$$

where the sum is over all *different* pairs of water molecules, and $U(\mathbf{X}_i, \mathbf{X}_j)$ is the pair potential between two water molecules.

It is widely believed that such an assumption is a good approximation for simple non-polar fluids such as liquid argon.⁶ In a formal manner, one may write the total potential energy $U(\mathbf{X}^{N_w})$ as a sum of contributions due to pairs, triplets, quadruplets, etc. of particles:

$$\begin{aligned} U(\mathbf{X}^{N_w}) = & \sum_{i < j} U(\mathbf{X}_i, \mathbf{X}_j) + \sum_{i < j < k} U^{(3)}(\mathbf{X}_i, \mathbf{X}_j, \mathbf{X}_k) \\ & + \dots + U^{(N_w)}(\mathbf{X}_1, \dots, \mathbf{X}_{N_w}) \end{aligned} \quad (2.10)$$

⁶It is exact only for hard-sphere particles.

where $U^{(n)}(\mathbf{X}_1, \mathbf{X}_2, \dots, \mathbf{X}_n)$ is referred to as the n th-order potential.

Consider as a simple example a system of three particles. The total potential energy of the system at a given configuration can be written as

$$U_3(\mathbf{X}_1, \mathbf{X}_2, \mathbf{X}_3) = U(\mathbf{X}_1, \mathbf{X}_2) + U(\mathbf{X}_1, \mathbf{X}_3) + U(\mathbf{X}_2, \mathbf{X}_3) + U^{(3)}(\mathbf{X}_1, \mathbf{X}_2, \mathbf{X}_3) \quad (2.11)$$

Recent quantum mechanical computations for a triplet of water molecules have shown that deviations from the additivity assumption for such a system are quite appreciable. We shall further discuss this aspect of the interactions in Sec. 2.7.

Similarly, it is also expected that higher-order potentials may contribute to a significant extent to the potential energy. Higher-order potentials also exist for simple liquids such as argon. In water, the non-additivity of the potential energy of interaction is described as the cooperativity of the hydrogen bonding. A water molecule engaged in a hydrogen bond (*HB*) with a second water molecule also polarizes the second molecule in such a way as to enhance its capability of forming an *HB* with a third molecule. In other words, the energy involved in the formation of two *HB*s between a triplet of water molecules at some specific configuration can be larger (or smaller) than the energy involved in the formation of two separate *HB*s. In a formal way, one can account for most of the non-additivity effects by introducing the idea of an *effective* pair potential, i.e. one assumes that the total energy can be written as

$$U(\mathbf{X}^{N_w}) = \sum_{i < j} U_{\text{eff}}(\mathbf{X}_i, \mathbf{X}_j) \quad (2.12)$$

Thus, the main challenge of this approximation consists of the choice of the *effective* pair potential. Since U_{eff} includes contributions from higher-order potentials, it will in general depend

on T and ρ . As I have mentioned earlier, there is, in principle, no guarantee that an effective pair potential which reproduces the properties of water exists. It is possible that some aspects of the higher-order potential might not be captured by an effective pair potential. Also, the role of quantum effects in the properties of water is still not fully understood [see, for instance, Guillot and Guissani (1998), Paesani *et al.* (2006, 2007), and Luchi *et al.* (2007)]. Pair potentials have been constructed essentially from two sources: from quantum mechanical calculations of the energy of a pair of water molecules at some selected configurations, and by assuming some empirical model potential function, the parameters of which are determined by fitting the results to some experimental data. This is currently an active and changing field of research. We shall describe very briefly the essential features of such a pair potential function for water in Sec. 2.7.

Once we have chosen an effective pair potential, we have in fact committed ourselves to the study of a system of *model particles*. This is exactly the same procedure that one employs when studying Lennard–Jones or hard-sphere particles.

With these assumptions, we can rewrite the classical PF of N water molecules in the final form as

$$Q_{class} = \frac{q_w^N}{(8\pi^2)^N \Lambda^{3N}} \int \cdots \int d\mathbf{X}^N \exp \left[-\beta \sum_{i < j} U(\mathbf{X}_i, \mathbf{X}_j) \right] \quad (2.13)$$

At this stage, we have a solid starting point for any theoretical work. The internal PF can be calculated from the available data on the single water molecule. Unfortunately, the configurational integral is an extremely complicated function. To evaluate this, we need to make further approximations. In fact, even for simple liquids such as argon, there is no way of writing the

configurational partition function in a simple closed form. This is *a fortiori* true for liquid water, for which the pair potential is a function of six variables: three positions and three angles of orientation.

Facing such a formidable multi-dimensional integral on the one hand, and the urgent necessity of understanding the behavior of liquid water on the other, has forced scientists to make further drastic approximations. The choice of approximation is not an easy task either. How do we know when an approximation is indeed a good one? The answer is that we usually do not know. It is only by trial and error that one can make progress in solving this problem.

The theory of liquid water and aqueous solutions has been developed along several quite different routes. Each has some merits on the one hand, and involves serious approximations, on the other. The older approach, recognizing from the outset the immense difficulties involved in treating a system consisting of strongly interacting molecules, has focused on aggregates of water molecules, or clusters. All the strong interactions (hydrogen bonds) are included within the clusters. In this way, a one-component system is converted into a mixture of clusters, the interaction between which is relatively weaker than the typical hydrogen bond interaction. All hydrogen bonding within the cluster is therefore viewed as part of the internal degrees of freedom of a single cluster. Many such models have been described in the literature. We shall discuss one representative of this approach within the framework of the mixture-model theory of liquids in Sec. 2.3 and an exact version of this approach in Secs. 2.3 and 2.5.

For many years, the only approach to the molecular theory of water was the so-called mixture-model (MM) approach. We discuss further the origin and the historical development of the MM to liquid water in Sec. 2.3. Here, we note that in choosing the MM approach, one has to make a decision about the type of

components to include in the mixture. Furthermore, an additional assumption is usually made, namely that the mixture forms a symmetrical ideal solution. This assumption, though inevitable for pursuing the MM approach, cannot be justified. We shall discuss this in Sec. 2.3.2.

The second route that does not involve the MM approach is to apply some analytical theories that were originally developed for simple fluid to liquid water. This approach was only partially successful. We shall describe some of these theories in Sec. 2.7.

The third route has been the dominant approach since it started in the early 1970s. This route consists of simulation techniques, notably Monte Carlo and molecular dynamics.

In Sec. 2.7, we shall briefly review some of the results obtained by simulation methods. A few extensive reviews are now available; I shall mention only three. The first review was published by Beveridge *et al.* (1983) and entitled: "Monte Carlo Computer Studies of the Equilibrium Properties and Structure of Liquid Water." The authors critically examined some 10 models for water that were published at that time.

A quotation from their introduction is revealing:

"The extensive use of liquid water as a solvent and reagent in chemical reactions, the widespread occurrence of water on the planet Earth, and the unique role of water as a biological life-support system combine to make an understanding of the properties of liquid water in terms of structure a matter of central importance to chemistry, the earth sciences and biology. The focus of this chapter is to review recent research studies of the structure of water at ordinary temperature and pressure, and to present an opinion on the state of knowledge about this system considered both as a structural problem in physical chemistry and as a methodological problem in computer simulation of the liquid state."

Note that the term “structure” appears three times in this quotation: the “structure” of water is the *problem* in physical chemistry, the *main subject* of the review, and the key feature of water that *needs to be understood*. Indeed, the *structure* of water has been the focus of most investigations of water and aqueous solutions. It is so central a concept that it appears in the title of Eisenberg and Kauzmann’s book: “Structure and Properties of Water.” Clearly, the structure of water is an important feature of water. However, as we shall see throughout this book, the structure itself is not *essential* to the understanding of liquid water and aqueous solutions.

Beveridge *et al.* also compared some of the results obtained by the different pair potentials with the corresponding experimental values. They concluded:

“The quantitative agreement between calculated and observed results is sensitive to the details of the potential function, and no single potential is found to give uniformly good agreement for all properties.”

This conclusion is still valid today and probably will be valid for the foreseeable future. As I noted earlier, there is no guarantee that an effective pair potential that will reproduce all the properties of water exists. Therefore, it is likely that no single pair potential will ever be found that will “give uniformly good agreement for all properties.”

A more extensive review was published by Wallqvist and Mountain (1999) entitled: “Molecular Models of Water: Derivation and Description.” This is a highly technical review of the merits and achievements of the various potentials. Three quotations from this review are worthwhile noting:

- (i) *“Because all models have some limitations, various modifications of water-water interactions have also been introduced at an alarming rate.”*

- (ii) *“The development of a water potential is not a search for the ultimate potential to end all other potentials. Indeed, we have no simple set of criteria by which a potential model can be termed ‘good’ or ‘bad’.”*
- (iii) *“The proliferation of different water models amply shows the many possible ways of describing water interactions. Indeed, one must ask whether any significant differences among these models exist, and if so, what features make a water potential suitable for molecular studies. Because each water potential gives essentially the same results — a strongly hydrogen-bonded liquid arranged in a loose tetrahedral network — why have so many potentials been proposed?”*

I fully concur with the ideas of Wallqvist and Mountain. They make a clear-cut distinction between the “pre-computer era” models and the “computer era” models. In my opinion, a more appropriate demarcation line should be *before* and *after* the publication of the BNS potential. This publication was a turning point in the theoretical approach to liquid water. It was not the “computer era” that changed the course of studying water, but the publication of the BNS potential, along with its multiple offspring, that brought about the use of computers in the study of water.

The third and most recent review which I mentioned in the preface is by Guillot (2002), entitled: “A Re-appraisal of What We Have Learnt During the Decades of Computer Simulations on Water.” This review focuses less on the technical issues of the models and more on what has been achieved. In the introduction of this review, Guillot writes:

“In view of the continuous flow of theoretical literature published nowadays on water and aqueous solution

(about 1 paper/day) it seems worthwhile to step back in order to appraise what has been accomplished during the last three decades and what deserves to be improved."

Guillot lists over 40 models suggested for water and reflects on the "philosophy which underlies the models and their ability to yield useful results." He concludes his review with the following sobering statement:

"Despite many efforts to improve this situation, very few significant progress can be asserted."

Again, I fully concur with Guillot's conclusion. I would add, however, that even if some further improvement might be achieved, I doubt that the effort to achieve that is justified.

Once a choice of a pair potential is made, the rest of the procedure is akin more to an experimental approach rather than a theoretical one. It is an experiment carried out on a computer where one can see through a "magnifying glass" what is happening on a molecular scale, a sight that cannot be seen by a conventional experimental apparatus. These microscopic experiments cannot *explain* the outstanding properties of the *real* liquid water, much as any real experiment cannot explain its results. Furthermore, the results obtained by such "experiments" are relevant to a system of water-like particles. The relevance to real liquid water is not always clear. Even if one can get excellent agreement between calculated properties based on a model of water-like particles and experimentally measurable quantities, one cannot conclude anything about the reality of the model used as input in the simulation.

My personal opinion regarding the proliferation of simulated works on water can be summarized as follows. When we perform simulation of a simple liquid, the extent of the agreement between the calculated and the experimental result is a

good measure of the accuracy, or the reality, of the input pair potential; a better agreement indicates that the pair potential used is more accurate. More accurate does not necessarily mean that the specific functional *form* of the potential is accurate, only that the qualitative form of the potential is more realistic. This is not the case for water. Even a perfect agreement between the calculated and the experimental results cannot be used to assess the accuracy of the potential function. All one can conclude from such an agreement is that from some features of the model potential one can obtain some properties of water. In other words, the success of a model tells us that some water-like particles behave in a similar fashion to real water. It does not tell us anything about the accuracy of the pair potential used nor does it explain any property of real water.

Conversely, even if we had an exact pair potential, i.e. the interaction energy between two water molecules as a function of the distance and relative orientations of the molecules, it is doubtful that such a potential could be successful in reproducing the properties of liquid water. The reason is simple. The properties of water are determined not only by the pair potential, but also by higher-order potentials.

Therefore, I do not believe that the goal of achieving the best agreement between computed and experimental results justifies the immense effort invested in “improving” pair potentials. For this reason, most of the discussion in this and the following chapters will focus on theoretical works that do not explicitly use a pair potential, and if we do use a pair potential, it will be the simplest possible one.

There is one very important reason for performing simulations of water-like particles. This is when we study some problems of aqueous solutions that are not accessible to experiments. Examples are the hydrophobic or hydrophilic interactions discussed in Chapter 4, or the understanding of the role of water in biological systems.

Thus, although the model pair potential might not be realistic, it can still be useful in application to complex systems. Sometimes, the water-like particles are non-realistic from the outset (such as 1-D or 2-D models; see Secs. 2.4 and 2.5). Nevertheless, the study of such systems can teach us what features of the molecular model are essential for the manifestation of some macroscopic properties of the system. From such studies, one can draw similar conclusions about the features of the models in 3-D that account for the specific and outstanding macroscopic properties of real liquid water.

2.3. The Mixture-Model Approach to Liquid Water

This section presents various aspects of the mixture-model approach to the theory of water. We start with some historical notes in Sec. 2.3.1, and then proceed with one very simple representative of the *MM* approach due to Wada (1961). Although this model was successful in reproducing some of the anomalies of liquid water, it suffers from two serious drawbacks. One is the question of the validity of the specific *MM* approach used in the theory, and the second is the validity of the assumption of the ideality of the mixture. We shall discuss these problems in Sec. 2.3.3, where an exact *MM* is developed. We show that the assumption of ideality, though inconsistent with the requirement of a successful *MM*, is not essential to the interpretation of the properties of water.

2.3.1. *The origin of the mixture-model theory of water*

The idea that liquid water can be viewed as a mixture of a few different components is quite old. This is called the

mixture-model (*MM*) approach to water, and it has been used ever since people recognized that liquid water is a *structured* liquid (the concept of the structure of water will be further discussed in Sec. 2.7). The oldest document that refers to water as a mixture of two components is by Röntgen (the German physicist who discovered the very short electromagnetic waves that he called X-rays, known also as Röntgen rays). Röntgen (1892), in an attempt to explain the unusual properties of water, postulated that liquid water consists of two kinds of molecules: one referred to as ice molecules; the other as the more regular close-packed molecules. It should be noted that Röntgen himself admitted that the idea of the *MM* has been known for a long time; some believe that the first to suggest this model was the French philosopher-mathematician René Descartes.

Perhaps the most extensive use of the idea of a mixture model for water and aqueous solutions was published by Bernal and Fowler (1933). They assumed that water consists of three different “intermolecular arrangements,” meaning three different structures or different components: ice-tridymite-like at low temperatures, quartz-like at higher temperatures, and ammonia-like at temperatures higher than 200°C. This was the first mixture model where the *structures* of the components were explicitly described.

We shall present here two puzzling experimental facts that were hard to understand but were successfully interpreted by using the *MM* approach to water [for a review on this, see Chadwell (1927)]:

(i) The compressibility of some aqueous solutions

It was known for a long time that the addition of some solutes, such as ethyl ether $(\text{CH}_3\text{CH}_2)_2\text{O}$ or methyl acetate $(\text{CH}_3\text{COOCH}_3)$, to water causes a *decrease* in the compressibility of the system, in spite of the fact that the

compressibility of the pure solute is about three times *larger* than the compressibility of pure water. In order to appreciate this puzzling finding we do not need to know what compressibility is. It will be sufficient to think of the compressibility as one of the properties of the liquid, such as the color, the viscosity, the sweetness, or the degree of transparency of the liquid. Let us call this property P . Now suppose we know that the property P of pure water, denoted P_w , is smaller than the value of P of ethyl ether, denoted P_e , i.e. $P_e > P_w$. Naturally, when we add ether to pure water we should expect that the value of the property P will *increase* by the addition of the ether. The puzzling fact is that the value of P actually *decreases*.

How can we explain the fact that the addition of a substance that has a higher compressibility caused a decrease in the compressibility of the system? This finding can be explained by the MM approach to water. The explanation as it appeared in the earlier literature is as follows.

We view water as consisting of two components: one, ice-like with a relatively smaller compressibility, and a second, close-packed with a relatively larger compressibility. We also *assume* that adding ether to pure water causes a shift in the equilibrium concentration of the two components in favor of the ice-like component, giving rise to a net decrease in the compressibility of the system. This is the qualitative explanation of the observed phenomena. As we shall later see, this explanation is not entirely correct. Also, we have assumed that adding ether shifts the concentration of the two components in favor of the ice-like one. This in itself is an interesting phenomenon that, though correct, needs further explanation. We shall return to discuss this phenomenon in Chapter 3.

In Sec. 2.3.5, we shall see that a central concept in the theories of water is that of the “structure of water” (SOW). We shall devote Sec. 2.7.4 to discussing this concept. Here, we only point out that one way of defining the “structure of water,” is to use the mixture-model approach. The idea is very simple. We assume⁷ that liquid water may be viewed as a mixture of two components, say, an ice-like component and a close-packed one. We then identify the ice-like component with the more “structured” component, and hence, the degree of the structure can be measured simply by the concentration of this component.

- (ii) Partial molar volume of water in water-ethanol mixtures
The second well-known property of aqueous solution is the partial molar volume (PMV) of water in dilute solutions of ethanol in water.

Consider first the molar volume of the pure substance, say, pure water, denoted by $V_w = V/N_w$. This is simply defined by the ratio of the actual (macroscopic) volume V of the system divided by the number of moles of water N_w . Note that the molar volume is different from the actual sum of the molecular volumes in the system. For pure water at room temperature and atmospheric pressure, the molar volume is about $18 \text{ cm}^3 \text{ mol}^{-1}$.

The *partial* molar volume (PMV) of water in a *mixture* of water and ethanol is defined as

$$\bar{V}_w = \left(\frac{\partial V}{\partial N_w} \right)_{T,P,N_e}$$

i.e. the partial derivative of the volume with respect to N_w at constant T , P , and N_e . This is equivalent to the change of volume upon adding an infinitesimal quantity of water to a

⁷Here, we *assume* that water can be viewed as a mixture. In Sec. 2.3.3, it will be shown that any fluid, including water, can be viewed as a mixture of two or more components.

mixture at a given T , P , and composition x . For different mixtures of water-ethanol, we find different values of the PMV of water. The plot of the PMV of water as a function of the mole fraction of ethanol is shown in Fig. 2.1 [x is defined as $N_{ethanol}/(N_{water} + N_{ethanol})$].

We see that for most of the mixtures the PMV of water is *smaller* than the molar volume of pure water. However, in the region of dilute alcohol in water, we observe that the PMV of water is *larger* than that of pure water. This means that by adding one mole of pure water, the volume changes more than V_w . How could that happen?

To explain this we invoke once again the same two-structure model for water, and *assume* as before that the addition of a small amount of alcohol to water causes a shift in the equilibrium concentrations of the two components. (Note that “small amount” is important. This assumption is not valid for large amounts of alcohol.) The interpretation of this phenomenon is now simple. Take one mole of water; this has a molar volume of about $18\text{ cm}^3\text{ mol}^{-1}$. Add it to the mixture. Since the relative concentrations of the two water components now favor the ice-like structure, which is the

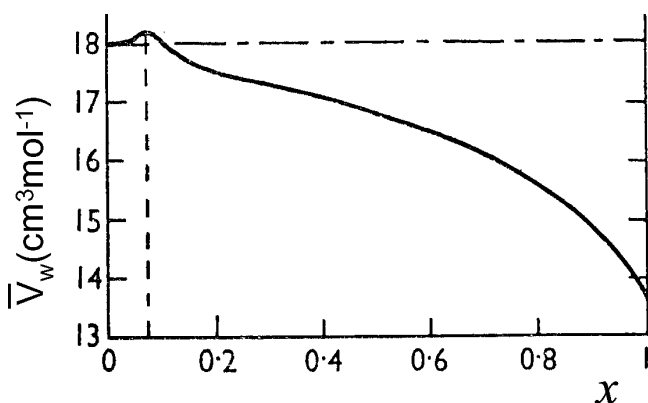


Fig. 2.1 The partial molar volumes of water in mixtures of water and ethanol as a function of the mole fraction of ethanol x .

component with the larger molar volume, the contribution of this one mole of pure water to the total volume of water will be larger than $18 \text{ cm}^3 \text{ mol}^{-1}$.

These two qualitative explanations of well-known phenomena added much confidence to the *MM* approach. However, for a long time, people questioned the validity of this approach. The main objection to the *MM* was raised on the grounds that there was no experimental evidence for the existence of different species in water. All the evidence was indirect. This question was settled later when it was shown that an *MM* approach can be developed for any liquid, not only for water, and that this approach does not require any experimental support. The only question is its usefulness. We shall further discuss this in Sec. 2.3.4. As we have noted earlier in Sec. 2.3.1, there has been an ongoing debate regarding the validity of the *MM* approach. Kauzmann (1976) has analyzed several properties of water based on a simple two-structure model of water where the more structured component was assumed to be an aggregate of n water molecules. Using this model, he found that in order to explain some properties, one needs a large value of n , whereas for other properties, one needs smaller aggregate.

Surprisingly, Kauzmann concluded that the *MM* approach is basically inadequate. This conclusion is unfortunate. It is not the *MM* approach that is inadequate, but the specific choice of the two components, together with the assumption of ideality of the mixture that are the culprits for the failure of the model.

2.3.2. *Wada's two-structure model for water: The success and the limitation of the MM approach*

We describe here a simple two-structure model (*TSM*) for water which was published by Wada in 1961. This model is

a representative one: a large number of similar models were published before and after Wada's publication.⁸ This mixture-model approach to water was suggested before the theoretical foundations of the *MM* approach were established.⁹ The assumptions of the model are the following:

- (i) Water consists of two components denoted by $(\text{H}_2\text{O})_{icy}$ and $(\text{H}_2\text{O})_{packed}$ in chemical equilibrium.
- (ii) The first component is presumed to have properties similar to ice; this is the open structure, or the low density component.
- (iii) The "packed" component is the close-packed one, or the high density component.
- (iv) The two components form symmetrical ideal solutions.

In this section we shall not discuss the validity of these assumptions. Specifically, the assumption of ideality of the mixture is a serious one and is discussed in Sec. 2.3.4. Here, we shall describe the model and how it can lead to the prediction of the existence of temperature of maximum density.

Let i and p stand for the icy and the packed components, at equilibrium:



The condition for chemical equilibrium is:

$$\mu_i = \mu_p \quad (2.3.2)$$

⁸A partial list of references is: Davis and Bradley (1966), Arakawa *et al.* (1969), Arakawa and Sasaki (1969), Davis and Jarzynski (1972), Grunwald (1986), Cho *et al.* (1997), Vedamuthu *et al.* (1994), Eyring and co-workers (1964, 1966), Arakawa and co-workers (1969a,b, 1970, 1977), Weres and Rice (1972), Marchi and Eyring (1964), Jhon and Eyring (1976), Sanchez *et al.* (1987), and Braibanti and co-workers (1996).

⁹Ben-Naim (1972b, 1973, 1974).

Assuming that the two components form a symmetrical ideal solution, we can write¹⁰

$$\mu_i = \mu_i^p + k_B T \ln x_i \quad (2.3.3)$$

$$\mu_p = \mu_p^p + k_B T \ln x_p \quad (2.3.4)$$

where x_i and x_p are the mole fractions of the two forms i and p , respectively, and μ_i^p and μ_p^p are the chemical potentials of the two components in their pure states at the same temperature and pressure.

From (2.3.3) and (2.3.4), one can get the equilibrium constant for the “reaction” (2.3.1):

$$K = \frac{x_p}{x_i} = \exp[-\beta(\mu_p^p - \mu_i^p)] \quad (2.3.5)$$

Assuming some numerical values for the chemical potentials of pure i and p , one can get the dependence of the mole fraction x_i on the temperature. The temperature dependence of the volume is obtained as follows. We write the molar volume of water as

$$V_w = x_i V_i^p + x_p V_p^p \quad (2.3.6)$$

where V_i^p and V_p^p are the molar volumes of the “pure” forms of i and p . The temperature dependence of the volume is

$$\left(\frac{\partial V_w}{\partial T} \right)_P = \left[x_i \frac{\partial V_i^p}{\partial T} + x_p \frac{\partial V_p^p}{\partial T} \right] + (V_i^p - V_p^p) \left(\frac{\partial x_i}{\partial T} \right)_P \quad (2.3.7)$$

Furthermore, the derivative $(\partial x_i / \partial T)_P$ can be obtained from (2.3.5):

$$\left(\frac{\partial x_i}{\partial T} \right)_P = \frac{x_i x_p (H_i^p - H_p^p)}{k_B T^2} \quad (2.3.8)$$

¹⁰Note that the letter “ p ” in (2.3.3) and (2.3.4) is used both for “packed” as a subscript and for “pure” as a superscript.

Pause to consider the meaning of this relationship. The concentration of component i will *increase* or *decrease* with increasing temperature according to whether $H_i^p - H_p^p$ is *positive* or *negative*.¹¹

Hence, from (2.3.7) and (2.3.8) we get:

$$\left(\frac{\partial V_w}{\partial T}\right)_P = \left[x_i \frac{\partial V_i^p}{\partial T} + x_p \frac{\partial V_p^p}{\partial T} \right] + \frac{x_i x_p}{k_B T^2} \Delta H \Delta V \quad (2.3.9)$$

where $\Delta H = H_i^p - H_p^p$ and $\Delta V = V_i^p - V_p^p$.

The interpretation of the negative temperature dependence of the volume of water, based on this TSM is as follows. One assumes that the pure components i and p behave normally, i.e. that they both expand upon increasing the temperature. Therefore, the first term in the square brackets in (2.3.9) is expected to be positive. The second term depends on the product of the mole fractions $x_i x_p$. This specific form results from assuming an ideal solution. However, the qualitative argument below is independent of this assumption. See also Sec. 2.3.4.

For normal liquids, the second term on the right-hand side of (2.3.9) is expected to be positive. $V_i^p - V_p^p$ is, by definition of the two components, positive. We have defined the i component as the more “open” component. In normal liquids, “more open” means larger intermolecular separation, and larger separation means weaker interactions. Hence, we expect $H_i^p - H_p^p$ to be positive too (note that in this case the enthalpy change is nearly equal to the energy change¹²). Therefore, the term on the right-hand side of (2.3.9) will be positive for normal liquids at room temperature and atmospheric pressure. In water, the situation

¹¹This is an example of Le Chatelier’s principle.

¹²At atmospheric pressure, $P = 1$ atm, ΔV is at most $18 \text{ cm}^3 \text{ mol}^{-1}$. Hence, at $P = 1$ atm, we have: $P\Delta V \approx 0.44 \text{ cal mol}^{-1}$ ($1 \text{ cal} = 41.3 \text{ cm}^3 \text{ atm}$). On the other hand, ΔE is of the order of 6 kcal mol^{-1} . Therefore, $\Delta H = \Delta E + P\Delta V \approx \Delta E$.

is quite different. Again, $V_i^p - V_p^p$ is positive, by definition (or by choice of the two components). However, $H_i^p - H_p^p$ would be negative, i.e. the interaction energy among the molecules in the “open” structure is *larger* (more negative) than the interactions in the close-packed structure. This is an essential difference between liquid water and other “normal” liquids, one manifestation of the “principle” discussed in Sec. 2.1. As we shall show in Chapter 3, this principle is also involved in the interpretation of the outstanding properties of aqueous solutions of inert molecules.

The qualitative interpretation of the negative temperature dependence of the volume is very simple. As we increase the temperature, both of the components i and p expand. In addition, one component — that which has lower energy or enthalpy — melts upon heating. Since the component of lower energy is also the component with larger molar volume, the second term in (2.3.9) will be negative. In liquid water at very low temperatures the second term on the right-hand side of (2.3.9) is the dominant one, probably because of the large values of ΔH and ΔV and because $x_i x_p$ is not negligible. As we continue to increase the temperature beyond 4°C, there are two effects that cause a decrease of the second term on the right-hand side of (2.3.9). First, this term depends on T^{-2} , and will therefore rapidly decrease with increasing temperature. Second, as the temperature increases, the component i “melts” according to (2.3.8), and hence the concentration of x_i decreases, and at some point x_i becomes so small that $x_i x_p$ becomes small too.

The second quantity that we shall discuss within this simple TSM is the heat capacity of water. Again, we view the system as composed of two components and write the molar enthalpy of the water as [see (2.3.6)]:

$$H_w = x_i H_i^p + x_p H_p^p \quad (2.3.10)$$

The molar heat capacity at constant pressure is¹³

$$C_{P,w} = \left(\frac{\partial H_w}{\partial T} \right)_P = \left[x_i \frac{\partial H_i^p}{\partial T} + x_p \frac{\partial H_p^p}{\partial T} \right] + (H_i^P - H_p^P) \left(\frac{\partial x_i}{\partial T} \right)_P \quad (2.3.11)$$

Compare this with (2.3.7). Here, H_i^p and H_p^p are the molar enthalpies of the pure i and p forms.

Using again the derivative in (2.3.8), we rewrite (2.3.11) as

$$C_{P,w} = \left[x_i \frac{\partial H_i^p}{\partial T} + x_p \frac{\partial H_p^p}{\partial T} \right] + \frac{(H_i^P - H_p^P)^2 x_i x_p}{k_B T^2} \quad (2.3.12)$$

Again, we assume that the term in the square brackets on the right-hand side of (2.3.12) is “normal” in the sense that it is an average of the heat capacities of the two components i and p each having a value of the order of pure ice or pure simple non-hydrogen bonding liquid. The second term on the right-hand side of (2.3.12) is always positive. It is this term that is responsible for the outstandingly large value of the heat capacity of water.

Note that in contrast to the temperature derivative of the volume, here the second term on the right-hand side of (2.3.12) is independent of the sign of $H_i^P - H_p^P$. It does not matter in which direction the relative concentrations of the two components change; all that matters is the size of the difference $|H_i^P - H_p^P|$. Another important factor that appears both in (2.3.9) and (2.3.12) is the product $x_i x_p$. This particular product is a result of the assumption of symmetrical ideal solutions. Clearly, the same product would appear had we assumed that the system were dilute ideal, i.e. if either $x_i \ll 1$ or $x_p \ll 1$. In any case, it is clear that if either component is chosen in such a way that

¹³Note that in (2.3.11), capital P is for “pressure,” subscript p is for “close packed,” and superscript p is for “pure.”

its mole fraction is very small, the product $x_i x_p$ will be small. As we shall see in the next section, the explanation provided by this model for both $\partial V/\partial T$ and $C_{P,w}$ is independent of the assumption of ideality of the solution.

Because the interpretation of the high value of the heat capacity of water does not depend on the correlation between local energy and local density, we can expect that other liquids with strong interactions, such as ammonia, will also have high heat capacity.¹⁴

A slightly different way of interpreting the high heat capacity is the following. Let us write

$$C_P = \frac{\Delta Q}{\Delta T} \quad (2.3.13)$$

where ΔQ and ΔT are small increments in the heat transferred to the system and the change in the temperature, respectively.

Suppose heat flows into the system by the amount ΔQ . Some of this energy will cause an increase in the kinetic energy of the particles, let us say, ΔQ_K , and another part ΔQ_M will be absorbed by the system in “melting” one component into another. Hence, we have

$$\Delta Q = \Delta Q_K + \Delta Q_M \quad (2.3.14)$$

We know that ΔT will be proportional to ΔQ_K , and hence we can write $\Delta T = \alpha \Delta Q_K$ ($\alpha > 0$) and

$$C_P = \frac{\Delta Q_K + \Delta Q_M}{\Delta T} = \frac{\Delta Q_K + \Delta Q_M}{\alpha \Delta Q_K} = \frac{1}{\alpha} + \frac{\Delta Q_M}{\Delta Q_K} \quad (2.3.15)$$

¹⁴Note that by high heat capacity we mean high with respect to what we expect from the heat capacity of a molecule with three translational degrees of freedom ($3k_B T/2$), and three rotational degrees of freedom ($3k_B T/2$), assuming that vibrational and electronic states are not excited at these temperatures. Thus, the expected value of C_P is about $6 \text{ cal mol}^{-1} \text{ K}^{-1}$.

Clearly, the larger the ratio $\Delta Q_M/\Delta Q_K$, the larger the heat capacity of the system will be.

If there are no chemical processes that absorb heat, then all the heat transfer ΔQ will go into the kinetic energy of the particles, and the heat capacity will be α^{-1} . (This will be the case, for example, for a monoatomic ideal gas.) If there exists a mechanism that can absorb a large amount of heat (e.g. melting the ice-like form), then $\Delta Q_M/\Delta Q_K$ will be very large; hence, the rise in temperature will be small and the heat capacity large.

An extreme case is when we have two phases at equilibrium, say, solid and liquid. In this case, if we add ΔQ to the system, as long as there are two phases at equilibrium, all the added energy will go to melt the solid into the liquid, the temperature of the system will not change, and the heat capacity will be infinity.

Exercise E.2.1: Write the expression for the pressure dependence of the volume within this TSM. Explain the analog of Eq. (2.3.9) for this case.

Exercise E.2.2: Look at Wada's paper (1961). Use the parameter he uses or choose your own parameters for the model. Examine the conditions under which the volume has a minimum as a function of temperature. Examine numerically the competition between the two terms on the right-hand side of Eq. (2.3.9).

Exercise E.2.3: Examine the conditions for a high value of heat capacity and a minimum in the heat capacity as a function of temperature.

Exercise E.2.4: Do the same as in E.2.3 for the isothermal compressibility in this model.

We have discussed the specific model worked out by Wada, but the interpretation of the temperature dependence of the volume is the same for any other *MM* of water. Also, one should note that the assumption of symmetrical ideal solutions was explicitly introduced in this model. We shall further discuss the inappropriateness of this assumption in Sec. 2.3.4.

2.3.3. *An exact MM approach to the theory of liquids*

In this section, I shall describe the theoretical foundation of the mixture-model (*MM*) approach to any liquid. In contrast to what was originally believed, the *MM* approach does not need, and is not based on, experimental evidence. There is a valid question regarding the usefulness of this approach. We shall discuss this aspect in the following section. However, the general *MM* approach is firmly established in statistical mechanical terms. In fact, the *MM* approach is part of a more general formalism that was originally referred to as the generalized molecular distribution function.¹⁵ Here, we shall be concerned with the *singlet* generalized molecular distribution function only.

A comment on terminology is in order. We use the term *mixture model* though no *model* is involved. The reason is that originally the *MM* approach was based on various choices of *models* for each of the components comprising the mixture. We shall use the term *MM*, though a more appropriate term would be the mixture view or the mixture approach to a one-component system. As we shall see below one can use a discrete *MM* or a continuous *MM*. This is quite different from the characterization of models as being an *MM* or a continuous model.¹⁶

¹⁵See Ben-Naim (1973, 1974).

¹⁶It is not uncommon yet somewhat puzzling to see that some authors categorize their theory as “belonging” to an *MM* or a continuous model. I believe this distinction is now obsolete.

2.3.3.1. *The singlet generalized molecular distribution function*

Consider the ordinary singlet molecular distribution function (MDF) in a one-component liquid¹⁷:

$$\begin{aligned} N_L^{(1)}(\mathbf{S}_1)d\mathbf{S}_1 &= d\mathbf{S}_1 \int \cdots \int d\mathbf{R}^N P(\mathbf{R}^N) \sum_{i=1}^N \delta(\mathbf{R}_i - \mathbf{S}_1) \\ &= Nd\mathbf{S}_1 \int \cdots \int d\mathbf{R}^N P(\mathbf{R}^N) \delta(\mathbf{R}_1 - \mathbf{S}_1) \end{aligned} \quad (2.3.16)$$

Here, $N_L^{(1)}(\mathbf{S}_1)d\mathbf{S}_1$ is the average number¹⁸ of particles occupying the element of volume $d\mathbf{S}_1$. For the present treatment, we limit our discussion to spherical molecules only. The quantity defined in (2.3.16) can be assigned two different meanings. The first follows from the first form on the right-hand side of (2.3.16), which is identified as an average quantity in the T, V, N ensemble. The second form on the right-hand side of (2.3.16) is N times the probability of finding particle 1 in the element of volume $d\mathbf{S}_1$. Clearly, this probability is given by $N_L^{(1)}(\mathbf{S}_1)d\mathbf{S}_1/N$. The function $\delta(\mathbf{R}_i - \mathbf{S}_1)$ in (2.3.16) is the Dirac delta function. We shall also use the same notation for the Kronecker delta function below.

We now systematize the generalization procedure of (2.3.16) as follows. Let us rewrite (2.3.16) in a somewhat different way. For each configuration $\mathbf{R}^N$ of the entire system, we define the property of the particle i as

$$L_i(\mathbf{R}^N) = \mathbf{R}_i \quad (2.3.17)$$

The property of particle i defined in (2.3.17) is simply its *location* $\mathbf{R}_i$. This is the reason for using the letter L in the definition of the function $L_i(\mathbf{R}^N)$.

¹⁷We assume for simplicity that the particles are spherical. All the results of this section are valid for non-spherical particles.

¹⁸Note that $N_L^{(1)}(\mathbf{S}_1)$ is the density of the particles at point $\mathbf{S}_1$.

Next, we define the *counting function* of the property L by

$$N_L^{(1)}(\mathbf{R}^N, \mathbf{S}_1) d\mathbf{S}_1 = \sum_{i=1}^N \delta[L_i(\mathbf{R}^N) - \mathbf{S}_1] d\mathbf{S}_1 \quad (2.3.18)$$

which is the number of particles whose property L attains a value within $d\mathbf{S}_1$ at $\mathbf{S}_1$ given the specific configuration $\mathbf{R}^N$. The average number (here in the T, V, N ensemble) of such particles is

$$\begin{aligned} N_L^{(1)}(\mathbf{S}_1) d\mathbf{S}_1 &= \langle N_L^{(1)}(\mathbf{R}^N, \mathbf{S}_1) \rangle d\mathbf{S}_1 \\ &= d\mathbf{S}_1 \int \cdots \int d\mathbf{R}^N P(\mathbf{R}^N) \sum_{i=1}^N [L_i(\mathbf{R}^N) - \mathbf{S}_1] \end{aligned} \quad (2.3.19)$$

which is the same as (2.3.16).

We now illustrate a few examples of properties that may replace L in (2.3.18) and which are useful in the study of water.

2.3.3.2. Coordination number

A simple property which has been the subject of many investigations is the coordination number (CN). We recall that the average coordination number can be obtained from the pair distribution function (Sec. 1.4). Here, we are interested in the more detailed information on the *distribution* of CNs.

Let R_C be a fixed number, serving as the radius of the first coordination shell. If σ is the effective diameter of the particles of the system, a reasonable choice of R_C for our purposes is $\sigma \leq R_C \leq 1.5\sigma$. The range given above seems to be in conformity with the commonly accepted concept of the radius of the first coordination sphere around a given particle. In what follows, we assume that R_C has been fixed.

The property to be considered here is the CN of the specific particle i given a configuration $\mathbf{R}^N$ of the system. This is

defined by

$$CN_i(\mathbf{R}^N) = \sum_{j=1, j \neq i}^N H(|\mathbf{R}_j - \mathbf{R}_i| - R_C) \quad (2.3.20)$$

where $H(x)$ is a unit step function, defined by

$$H(x) = \begin{cases} 0 & \text{if } x > 0 \\ 1 & \text{if } x \leq 0 \end{cases} \quad (2.3.21)$$

Each term in (2.3.20) contributes unity whenever $|\mathbf{R}_j - \mathbf{R}_i| < R_C$, i.e. whenever the center of particle j falls within the coordination sphere of particle i . Hence, $CN_i(\mathbf{R}^N)$ is the number of particles ($j \neq i$) that falls in the coordination sphere of particle i for a given configuration $\mathbf{R}^N$. Next, we define the counting function for this property by

$$N_{CN}^{(1)}(\mathbf{R}^N, K) = \sum_{i=1}^N \delta[CN_i(\mathbf{R}^N) - K] \quad (2.3.22)$$

Here, $\delta(x - K)$ is the Kronecker delta function. (The more common notation is $\delta_{x,K}$.) The meaning of δ as a Dirac or Kronecker delta should be clear from the context. In the sum (2.3.22) we scan all the particles ($i = 1, 2, \dots, N$) of the system in a given configuration $\mathbf{R}^N$. Each particle whose CN is exactly K contributes unity to the sum (2.3.22), and zero otherwise. Hence, the sum in (2.3.22) *counts* all particles whose CN is K for the particular configuration $\mathbf{R}^N$. The average number of such particles is

$$\begin{aligned} N_{CN}^{(1)}(K) &= \langle N_{CN}^{(1)}(\mathbf{R}^N, K) \rangle \\ &= N \int \cdots \int d\mathbf{R}^N P(\mathbf{R}^N) \delta[CN_1(\mathbf{R}^N) - K] \end{aligned} \quad (2.3.23)$$

We define the following quantity:

$$\begin{aligned} x_{CN}(K) &= \frac{N_{CN}^{(1)}(K)}{N} \\ &= \int \cdots \int d\mathbf{R}^N P(\mathbf{R}^N) \delta[CN_1(R^N) - K] \end{aligned} \quad (2.3.24)$$

From the definition of $N_{CN}^{(1)}(K)$ in (2.3.23), it follows that $x_{CN}(K)$ is the mole fraction of particles whose coordination number is equal to K . On the other hand, the second form on the right-hand side of (2.3.24) provides the probabilistic meaning of $x_{CN}(K)$, i.e. this is the probability that a *specific* particle, say 1, will be found with CN equal to K .

The quantity $x_{CN}(K)$ can be viewed as a component of a vector

$$\mathbf{x}_{CN} = (x_{CN}(0), x_{CN}(1), \dots) \quad (2.3.25)$$

which gives the “composition” of the system with respect to the classification according to the CN s, i.e. each component of this vector gives the mole fraction of particles with a given CN . The average CN of particles in the system is given by¹⁹

$$\langle K \rangle = \sum_{K=0}^{\infty} K x_{CN}(K) \quad (2.3.26)$$

The CN as defined above may be viewed as a property conveying the local density around the particles. The larger the CN of a specific particle, the larger its local density. By a simple transformation, we can make this statement more precise. The local density around the particle i for a given configuration $\mathbf{R}^N$

¹⁹Note that $\langle K \rangle$, as defined in (2.3.26), coincides with the definition of the average CN given in Sec. 1.4 provided that we choose R_C of the present section to coincide with R_M in Sec. 1.4.

and for a given R_C is defined by

$$D_i(\mathbf{R}^N) = CN_i(\mathbf{R}^N) \left(\frac{4}{3}\pi R_C^3 \right)^{-1} \quad (2.3.27)$$

Hence, the average number of particles having local density equal to η is

$$N_D^{(1)}(\eta) = \left\langle \sum_{i=1}^N \delta[D_i(\mathbf{R}^N) - \eta] \right\rangle \quad (2.3.28)$$

Another quantity conveying a similar meaning is the volume of the Voronoi polyhedron, which is essentially the inverse of the local density.

2.3.3.3. Volume of the Voronoi polyhedron

A local property of interest in the study of liquids is the Voronoi polyhedron (VP), or the Dirichlet region, defined as follows. Consider a specific configuration $\mathbf{R}^N$ and a particular particle i . Draw all the segments $l_{ij}(j = 1, \dots, N, j \neq i)$ connecting the centers of particles i and j . Let P_{ij} be the plane perpendicular to and bisecting the line l_{ij} . Each plane P_{ij} divides the entire space into two parts. Denote by V_{ij} the part of space that includes the point $\mathbf{R}_i$. The VP of particle i for the configuration $\mathbf{R}^N$ is defined as the intersection of all the regions $V_{ij}(j = 1, \dots, N, j \neq i)$:

$$(VP)_i = \bigcap_{j=1, j \neq i}^N V_{ij}(\mathbf{R}_i, \mathbf{R}_j) \quad (2.3.29)$$

A two-dimensional illustration of a construction of a VP is shown in Fig. 2.2. It is clear from the definition that the region $(VP)_i$ includes all the points in space that are *nearer* to $\mathbf{R}_i$ than to any $\mathbf{R}_j(j \neq i)$. Furthermore, each VP contains the center of one and only one particle.²⁰

²⁰Rogers (1964) and Salsburg (1966).

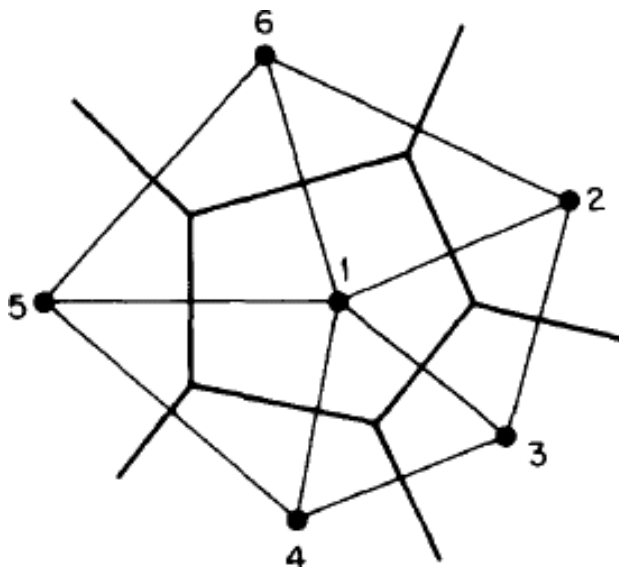


Fig. 2.2 The Voronoi polygon of particle 1 in a two-dimensional system of spherical particles.

The concept of *VP* can be used to generate a few local properties.²¹ The one of interest here is the *volume* of the *VP*, which we denote by

$$\psi_i(\mathbf{R}^N) = \text{volume of } (VP)_i \quad (2.3.30)$$

The counting function for this property is

$$N_{\psi}^{(1)}(\mathbf{R}^N, \phi) d\phi = d\phi \sum_{i=1}^N \delta[\psi_i(\mathbf{R}^N) - \phi] \quad (2.3.31)$$

and its average is

$$N_{\psi}^{(1)}(\phi) d\phi = d\phi \left\langle \sum_{i=1}^N \delta[\psi_i(\mathbf{R}^N) - \phi] \right\rangle \quad (2.3.32)$$

²¹Note that the *form* of the *VP* is also a property which can be considered in the context of this section. Other properties of interest are the number of faces of the *VP*, the surface area of the *VP*, etc.

Clearly, $N_{\psi}^{(1)}(\phi)d\phi$ is the average number of particles whose VP has a volume between ϕ and $\phi + d\phi$.

We note here that the volume of a system in the (T, P, N) ensemble can be written as

$$V(T, P, N) = \int_0^{\infty} \phi N_{\psi}^{(1)}(\phi) d\phi$$

where

$$N = \int_0^{\infty} N_{\psi}^{(1)}(\phi) d\phi$$

In this representation of the volume, ϕ may be viewed as the “partial molar volume” of the species, the VP of which is equal to ϕ (for details, see Appendix E).

2.3.3.4. *Binding energy*

The next property is referred to as binding energy (BE) and is defined for particle i and a fixed configuration $\mathbf{R}^N$ as follows:

$$BE_i(\mathbf{R}^N) = U_N(\mathbf{R}_1, \dots, \mathbf{R}_{i-1}, \mathbf{R}_i, \mathbf{R}_{i+1}, \dots, \mathbf{R}_N) - U_{N-1}(\mathbf{R}_1, \dots, \mathbf{R}_{i-1}, \mathbf{R}_{i+1}, \dots, \mathbf{R}_N) \quad (2.3.33)$$

This is the change of energy in bringing a particle from an infinite distance, with respect to all other particles, to the position $\mathbf{R}_i$. For a system of pairwise additive potentials, (2.3.33) reduces to

$$BE_i(\mathbf{R}^N) = \sum_{j=1, j \neq i}^N U(\mathbf{R}_i, \mathbf{R}_j) \quad (2.3.34)$$

which is the total interaction energy of particle i with all other particles being at a fixed configuration.

The counting function for this property is

$$N_{BE}^{(1)}(\mathbf{R}^N, \nu) d\nu = d\nu \sum_{i=1}^N \delta[BE_i(\mathbf{R}^N) - \nu] \quad (2.3.35)$$

which is the number of particles having BE between ν and $\nu + d\nu$ for the specified configuration $\mathbf{R}^N$. Note that since ν is a continuous variable, the δ -function in (2.3.35) is the Dirac delta function. The average number of particles having BE between ν and $\nu + d\nu$ is

$$N_{BE}^{(1)}(\nu) d\nu = d\nu \left\langle \sum_{i=1}^N \delta[BE_i(\mathbf{R}^N) - \nu] \right\rangle \quad (2.3.36)$$

The corresponding mole fraction is

$$x_{BE}(\nu) d\nu = \frac{N_{BE}^{(1)}(\nu) d\nu}{N} \quad (2.3.37)$$

The function $x_{BE}(\nu)$ is referred to as the *distribution of BE*. By analogy with the vector (2.3.25), which has discrete components, we often write $\mathbf{x}_{BE}$ for the whole distribution function, the components of which are $x_{BE}(\nu)$.

Note also that the total energy of a system in the T, P, N ensemble may be written as

$$\begin{aligned} E(T, P, N) &= E^K + \langle U_N \rangle \\ &= E^K + \frac{1}{2} \int_{-\infty}^{\infty} \nu N_{BE}^{(1)}(\nu) d\nu \\ &= \int_{-\infty}^{\infty} \left(\varepsilon^K + \frac{\nu}{2} \right) N_{BE}^{(1)}(\nu) d\nu \end{aligned}$$

where ε^K is the average kinetic energy of a particle in the system.

In this representation the quantity $(\varepsilon^K + \nu/2)$ may be interpreted as the “partial molar energy” of the species, the BE of which is ν (see also Appendix E).

2.3.3.5. *Combination of properties*

One way of generating new distribution functions from previous ones is by combining properties. For instance, the counting function for *BE* and the volume of the *VP* is

$$N_{B,\psi}^{(1)}(\mathbf{R}^N, \nu, \phi) d\nu d\phi = d\nu d\phi \sum_{i=1}^N \delta[BE_i(\mathbf{R}^N) - \nu] \delta[\psi_i(\mathbf{R}^N) - \phi] \quad (2.3.38)$$

which counts the number of particles having *BE* between ν and $\nu + d\nu$ and the volume of the *VP* between ϕ and $\phi + d\phi$. The average number of such particles is

$$N_{B,\psi}^{(1)}(\nu, \phi) d\nu d\phi = d\nu d\phi \left\langle \sum_{i=1}^N \delta[BE_i(\mathbf{R}^N) - \nu] \delta[\psi_i(\mathbf{R}^N) - \phi] \right\rangle \quad (2.3.39)$$

Note that although we have combined *two* properties, we still have a *singlet* generalized *MDF*. A related singlet generalized *MDF* which conveys similar information to the one in (2.3.39) but is simpler for computational purposes is constructed by the combination of *BE* and *CN*, i.e.

$$N_{B,C}^{(1)}(\nu, K) d\nu = d\nu \left\langle \sum_{i=1}^N \delta[BE_i(\mathbf{R}^N) - \nu] \delta[CN_i(\mathbf{R}^N) - K] \right\rangle \quad (2.3.40)$$

Note that the first δ on the right-hand side of (2.3.40) is a Dirac delta function, whereas the second is a Kronecker delta function.

2.3.3.6. *Some numerical examples*

Here, we present some examples of singlet generalized *MDFs*. All illustrations provided in this section were obtained by a Monte Carlo computation on a two-dimensional system

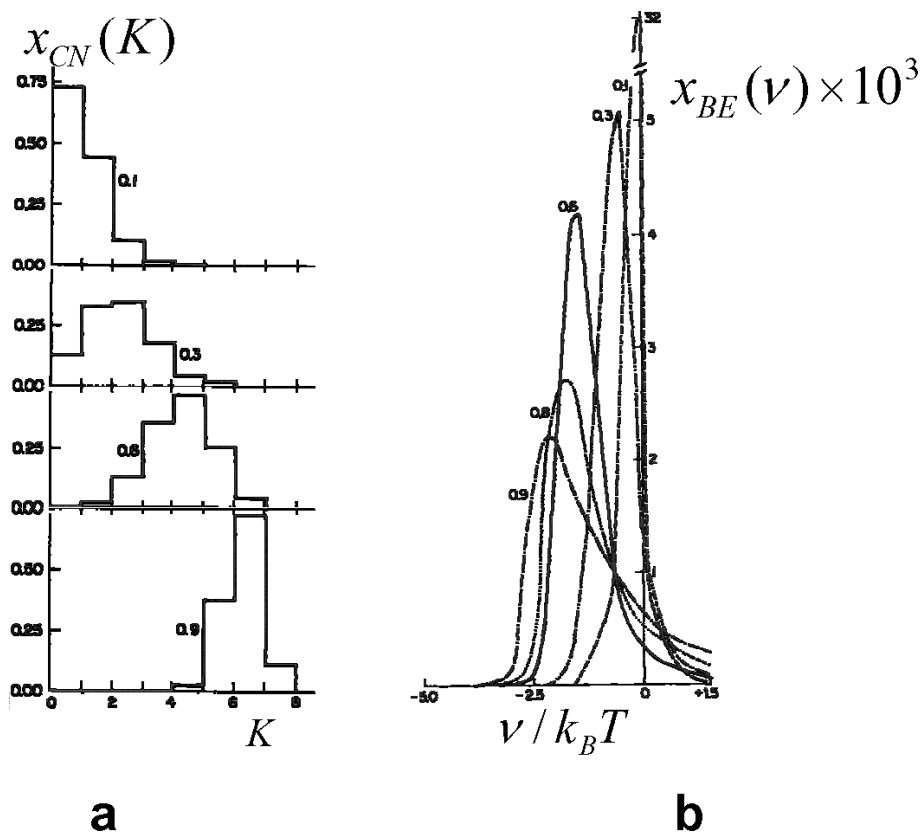


Fig. 2.3 The distribution function (a) of coordination number $x_{CN}(K)$ and (b) of the binding energy $x_{BE}(v)$ in a two-dimensional system of spherical particles. The number densities are shown next to each curve.

consisting of 36 Lennard-Jones particles for which the pair potential is of the form

$$U(R) = 4\varepsilon[(\sigma/R)^{12} - (\sigma/R)^6] \quad (2.3.41)$$

Figure 2.3a shows the distribution of CN, $x_{CN}(K)$, and its density dependence. The Lennard-Jones parameters for these computations are

$$\sigma = 1.0, \quad \varepsilon/k_B T = 0.5 \quad (2.3.42)$$

We use σ as the unit of length, and hence the densities refer to particles per unit area σ^2 . The radius of the first coordination sphere is chosen as $R_C = 1.5\sigma$. The distributions of CN as shown in Fig. 2.3a are according to our intuitive expectations. As the density increases, the mole fraction of particles with relatively higher CN increases. Figure 2.3b shows the distribution of BE and its dependence on the density. The most pronounced feature of all these curves is the essentially single peak — and that the location of the peak shifts to the left as the density increases.

Note that the average value of the BE of a particle $\langle v \rangle$ is related to the total average interaction energy in the system by

$$\langle U \rangle = \frac{N}{2} \langle v \rangle \quad (2.3.43)$$

$\langle v \rangle$ is the average binding energy of a single particle. Multiplying by N gives the BE of all the particles. In this counting, the interaction energy between each pair of particles is counted twice: from i to j and from j to i . Hence, we must divide by two to obtain the total average interaction energy of the system.

In Fig. 2.4a, we show the distribution function $x_{BE,CN}(v, K)$ for the combined properties of BE and CN for the same system described in (2.3.41) and (2.3.42). As can be seen from this figure, when the coordination number K increases, the distribution shifts to the right, i.e. to stronger BE. This is what we expect from simple liquids, i.e. higher CN is correlated with stronger BE. Figure 2.5a shows the conditional average of BE as a function of the coordination number. We see again that the larger the CN, the stronger the average BE. We shall return to discussing this property in Sec. 2.6 in connection with water-like particles. Figures 2.4b and 2.5b show the same quantities calculated for “water-like” particles discussed in Sec. 2.6.

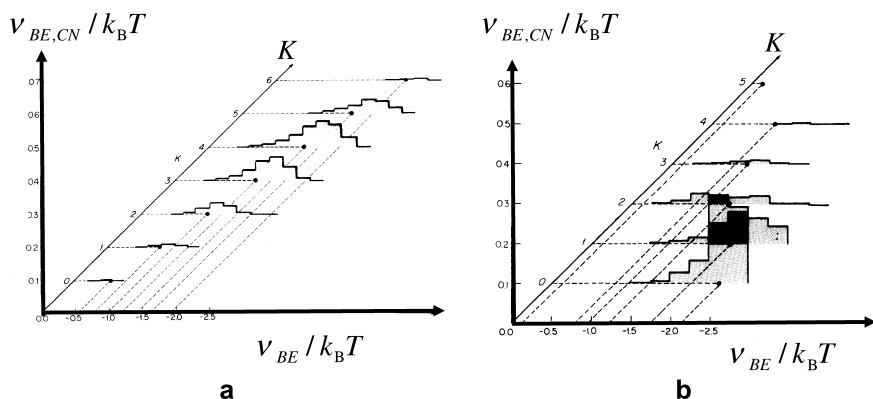


Fig. 2.4 The distribution of the combined properties of coordination number (CN) and binding energy (BE) (a) for spherical particles and (b) for water-like particles in two dimensions (Sec. 2.6). The number densities are shown next to each curve.

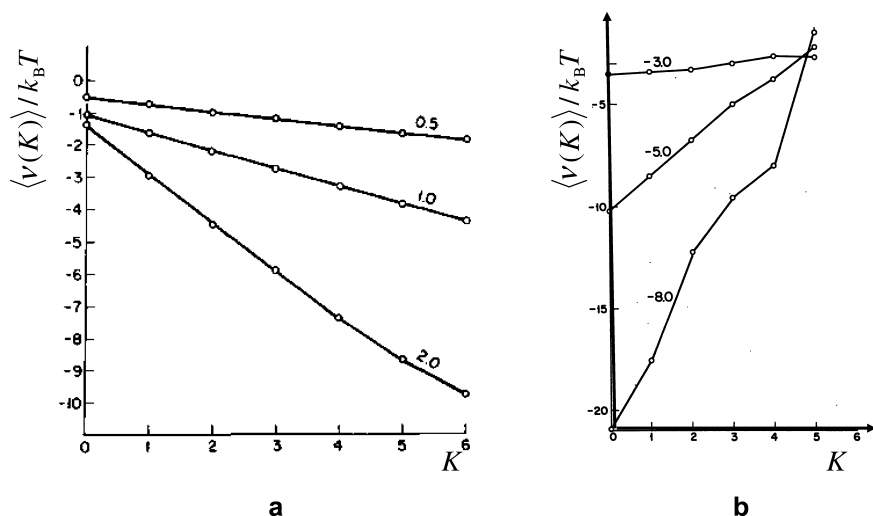


Fig. 2.5 The conditional average binding energy of particles having a fixed coordination number K in a two-dimensional system of (a) spherical particles for different LJ parameter ε (as indicated next to each curve) and (b) of water-like particles for different hydrogen bond energies ε_{HB} (Sec. 2.6).

2.3.3.7. *The mixture-model approach to liquids*

The idea of an *MM* approach is very simple and quite old. Here, we present the general idea of the *MM* approach based on the singlet generalized *MDF*.

Consider, for instance, the singlet generalized *MDF* based on the coordination number:

$$x_{CN}(K) = \frac{N_{CN}^{(1)}(K)}{N} = \int \cdots \int d\mathbf{R}^N P(\mathbf{R}^N) \delta[CN_1(\mathbf{R}^N) - K] \quad (2.3.44)$$

This quantity may be interpreted in two ways. First, this is the mole fraction of particles having *CN* equal to *K*. Second, $x_{CN}(K)$ is the probability that a specific particle, say 1, will be found with a *CN* equal to *K*.

Because of the first interpretation, we may refer to the vector

$$\mathbf{x}_{CN} = (x_{CN}(0), x_{CN}(1), \dots) \quad (2.3.45)$$

as a quasi-component distribution function (*QCDF*). This provides the “composition” of the system when viewed as a mixture of quasi-components. The normalization condition for $\mathbf{x}_{CN}$ is

$$\sum_{K=0}^{\infty} x_{CN}(K) = 1 \quad (2.3.46)$$

Note, however, that since the particles exert strong repulsive forces when brought very close to each other, the occurrence of a large *CN* for a given particle must be a very improbable event. Therefore, the sum over *K* in (2.3.46) effectively extends from *K* = 0 to, say, *K* ≈ 12 (depending of course, on the choice of *R_C*), i.e. the mole fractions $x_C(K)$, with *K* > 12, will in general be negligible.

A mixture of quasi-components must be distinguished from a mixture of real components in essentially two respects. First, the quasi-components do not differ in their *chemical* composition;

they are characterized by their local environment, which in the above example is the CN . A more important difference is that a system of quasi-components cannot be “prepared” in any desired composition, i.e. the components of a vector $\mathbf{x}_{CN}$ cannot be chosen at will. One consequence of this restriction is that quasi-components do not exist in the pure state.

Note also that the same molecule can “belong” to different species at different times. This is quite different from a regular mixture having a fixed composition but similar to a mixture of inter-converting molecules at equilibrium.

In the above example, we elaborated on a classification procedure based on a discrete parameter, the value of the CN . It can easily be generalized to any other *property* used for constructing the various singlet generalized $MDFs$. For instance, the quantity $x_{BE}(\nu)d\nu$ defined in (2.3.37) is the mole fraction of molecules having BE between ν and $\nu+d\nu$. This is an example of a $QCDF$ function based on a continuous parameter, ν . Another example is the function $x_{\psi}(\phi)d\phi = N_{\psi}^{(1)}(\phi)d\phi/N$ based on the volume of the VP of the particles.

It should be noted that in all of the above-mentioned examples the adoption of the MM approach depends solely on the rule of classification of molecules into various groups. In each case, the rule must be unique and exhaustive, i.e. for each configuration $\mathbf{R}^N$ of the system, each particle belongs to one and only one group.

In the next section, we shall discuss the application of an exact two-structure model based on the MM approach.

2.3.4. *Application of an exact two-structure model*

The simplest version of the MM approach and the one that has most often been applied is the two-structure model (TSM). Again, we stress that the exact TSM does not involve any *model*

of the liquid. The models that have been used in the study of water may be derived from the exact *MM* by defining the components that comprise the system. Examples of such models are the Wada model discussed in Sec. 2.3.2 or the Pauling model discussed in Sec. 2.4.2. Here, we discuss some examples of exact *TSMs* that are derivable from any one of the quasi-component distributions discussed in Sec. 2.3.3. Consider, for instance, the distribution based on the concept of coordination number (*CN*). We have denoted by $x_{CN}(K)$ the mole fraction of molecules having a *CN* equal to K . The vector $\mathbf{x}_{CN} = (x_{CN}(0), x_{CN}(1), \dots)$ describes the *composition* of the system when viewed as a mixture of quasi-components, distinguishable according to their *CN*. From this distribution we can construct a *TSM*; those whose *CN* is smaller than or equal to some number, say K^* , and those whose *CN* is larger than K^* . The two corresponding mole fractions are

$$x_L = \sum_{K=0}^{K^*} x_{CN}(K), \quad x_H = \sum_{K=K^*+1}^{\infty} x_{CN}(K) \quad (2.3.47)$$

where x_L may be referred to as the mole fraction of the species with low (L) local density and x_H as that of the species with relatively high (H) local density. The new vector composed of two components (x_L, x_H) is also a quasi-component distribution function and gives the composition of the system when viewed as a mixture of two components, which we may designate as L and H molecules. Starting with the same vector $\mathbf{x}_{CN} = (x_{CN}(0), x_{CN}(1), \dots)$, we may derive many other *TSMs* differing from the one in (2.3.47). A possibility which may be useful for liquid water is

$$x_A = x_{CN}(4), \quad x_B = 1 - x_A \quad (2.3.48)$$

where we distinguish between molecules with *CN* equal to four in one group (A), and all other molecules in the second group (B).

Instead of the CN , we can use the number of HB s for our classification into species. For instance, we can consider the four HB ed species as one species of the TSM and refer to the other species (with $n = 0, 1, 2, 3$) collectively as a second species.

As a second example, consider the quasi-component distribution function based on the concept of binding energy (BE). We recall that the vector (or the function) $\mathbf{x}_{BE}$ gives the composition of the system when viewed as a mixture of molecules differing in their BE . Thus, $x_{BE}(\nu)d\nu$ is the mole fraction of molecules with BE between ν and $\nu + d\nu$. A possible TSM constructed from this function is

$$x_A = \int_{-\infty}^{\nu^*} x_{BE}(\nu)d\nu \quad x_B = 1 - x_A \quad (2.3.49)$$

where x_A is the mole fraction of molecules whose BE is below a certain value ν^* , and x_B is the mole fraction whose BE is larger than ν^* . Again, we have a new quasi-component distribution function composed of two components (x_A, x_B).

The above examples illustrate the general procedure by which we construct a TSM from any quasi-component distribution function. From now on, we assume that we have made a classification into two components, L and H , without referring to a specific example. The arguments we use will be independent of any specific classification procedure. We will see that in order for such a TSM to be useful in interpreting the properties of water, we must assume that each component in itself behaves “normally” (in the sense discussed below). The outstanding properties of water are then interpreted in terms of “structural changes,” i.e. redistribution of the molecules into various species that take place in the liquid.

Let N_L and N_H be the equilibrium numbers of L and H molecules, respectively, and N_w be the total number of water molecules in the system, $N_w = N_L + N_H$. Viewing the system as a mixture of two components, we write the total volume of

the system using the Euler theorem as²²

$$V = N_L \bar{V}_L + N_H \bar{V}_H \quad (2.3.50)$$

where $\bar{V}_L$ and $\bar{V}_H$ are the partial molar (or molecular) volumes of L and H , respectively.²³

The total differential of $V(T, P, N_L, N_H)$ is

$$\begin{aligned} dV = & \left(\frac{\partial V}{\partial T} \right)_{P, N_L, N_H} dT + \left(\frac{\partial V}{\partial P} \right)_{T, N_L, N_H} dP + \left(\frac{\partial V}{\partial N_L} \right)_{T, P, N_H} \\ & \times dN_L + \left(\frac{\partial V}{\partial N_H} \right)_{T, P, N_L} dN_H \end{aligned} \quad (2.3.51)$$

The temperature dependence of the volume, along the equilibrium line with respect to the reaction $L \rightleftharpoons H$ (keeping P and N_w constant; hence, $dN_L + dN_H = 0$), is

$$\left(\frac{\partial V}{\partial T} \right)_{P, N_w, eq} = \left(\frac{\partial V}{\partial T} \right)_{P, N_L, N_H} + (\bar{V}_L - \bar{V}_H) \left(\frac{\partial N_L}{\partial T} \right)_{P, N_w, eq} \quad (2.3.52)$$

The first term on the right-hand side of (2.3.52) gives the temperature dependence of the volume of the “frozen-in” system, and can be written as

$$\left(\frac{\partial V}{\partial T} \right)_{P, N_L, N_H} = N_L \left(\frac{\partial \bar{V}_L}{\partial T} \right)_{P, N_L, N_H} + N_H \left(\frac{\partial \bar{V}_H}{\partial T} \right)_{P, N_L, N_H} \quad (2.3.53)$$

This quantity may be referred to as the “frozen-in” part of the total temperature dependence of the volume.

²²See Appendix E. Note here that we must use the *partial* molar volumes of L and H . In Sec. 2.3.2, we used the *molar* volumes of the *pure* components; see, for example, Eq. (2.3.6).

²³Note again that the *partial* molecular volume is different from the actual molecular volume of the particle.

The second term on the right-hand side of (2.3.52) may be referred to as the *relaxation* part of the total temperature dependence of the volume. It is quite clear that this term contains the contribution to the temperature dependence of the volume that is associated with the “structural changes” in the system. In the context of this section, the term “structural changes” refers only to the inter-conversion between the two species L and H arising from the change in temperature, or equivalently the redistribution of molecules between the two species.

We now use the following identity from Appendix F:

$$\left(\frac{\partial N_L}{\partial T}\right)_{P, N_w, eq} = (\mu_u - 2\mu_{LH} + \mu_{HH})^{-1} \left(\frac{(\bar{H}_L - \bar{H}_H)}{T}\right) \quad (2.3.54)$$

where $\mu_{ij} = \partial^2 G / \partial N_i \partial N_j$.

With (2.3.54) we can write the temperature dependence of the molar volume within the exact MM approach as

$$\left(\frac{\partial V}{\partial T}\right)_{P, N_w, eq} = \left(\frac{\partial V}{\partial T}\right)_{P, N_L, N_H} + \frac{(\bar{H}_L - \bar{H}_H)(\bar{V}_L - \bar{V}_H)}{T(\mu_{LL} - 2\mu_{LH} + \mu_{HH})} \quad (2.3.55)$$

where $\mu_{LL} - 2\mu_{LH} + \mu_{HH} > 0$ (see Appendix F). Equation (2.3.55) should be compared with Eq. (2.3.9) obtained for a symmetrical ideal solution. Note that for ideal solutions we have

$$\mu_{LL} - 2\mu_{LH} + \mu_{HH} = \frac{k_B T}{N_w x_L x_H} \quad (2.3.56)$$

In general, this quantity can be written as

$$\begin{aligned} & \mu_{LL} - 2\mu_{LH} + \mu_{HH} \\ &= \frac{k_B T}{x_L x_H V [\rho_L + \rho_H + \rho_L \rho_H (G_{LL} + G_{HH} - 2G_{HL})]} \end{aligned} \quad (2.3.57)$$

This equality follows from the Kirkwood–Buff theory of solutions, where G_{ij} are the *KB* integrals,²⁴ defined in Sec. 1.5.

Note that if the system is a symmetric ideal solution, then $G_{LL} - 2G_{LH} + G_{HH} = 0$, and (2.3.57) reduces to (2.3.56), with $(\rho_L + \rho_H)V = N_w$.

In order to use (2.3.55) for interpreting the anomalous negative temperature dependence of the volume of water between 0 and 4°C, we must choose a classification procedure so that: (i) the “frozen-in” term in (2.3.55) behaves normally, i.e. each of the derivatives in (2.3.53) is positive; such an assumption is invoked either explicitly or implicitly in the various *ad hoc* TSMs for water, and (ii) the relaxation term in (2.3.52) must be negative and large enough (in absolute magnitude) to overcompensate for the positive value of the “frozen-in” part.

Regarding the first condition, there is no general rule that guarantees that the “frozen-in” term is “normal.” In the simplified *ad hoc* TSMs, this assumption is quite natural. For instance, if one species is ice-like and the second one is, say, monomeric water molecules, then it is natural to assume that each of the partial molar volumes has a normal temperature dependence.

The analysis of the second condition leads to somewhat more interesting insights as to the origin of negative temperature dependence of the volume. Consider first the sign of the relaxation term in (2.3.55). Clearly, in order that this term be negative, we must have (note that $\mu_{LL} - 2\mu_{LH} + \mu_{HH} > 0$; see Appendix F):

$$(\bar{V}_L - \bar{V}_H)(\bar{H}_L - \bar{H}_H) < 0 \quad (2.3.58)$$

This means that $\bar{V}_L - \bar{V}_H$ and $\bar{H}_L - \bar{H}_H$ must have opposite signs. Next, in order to get a large negative value for the relaxation term in (2.3.55), two conditions must be fulfilled: (i) The

²⁴See Ben-Naim (2006) and Sec. 1.5.

two components L and H must be very different since otherwise the differences $\bar{V}_L - \bar{V}_H$ and $\bar{H}_L - \bar{H}_H$ will be very small, and (ii) neither of the mole fractions x_L or x_H may be too small since otherwise the product $x_L x_H$ will be small, and we will get a small relaxation term in (2.3.55).

Let us further examine the above two conditions. Suppose we define L and H in such a way that L has a low local density and H has a relatively high local density; we can express the difference in the partial molar volumes in terms of molecular distribution functions using the Kirkwood–Buff theory²⁵:

$$\begin{aligned}\bar{V}_L - \bar{V}_H &= \frac{\rho_H(G_{HH} - G_{LH}) - \rho_L(G_{LL} - G_{HL})}{\eta} \\ &= \frac{\rho_w}{\eta}(G_{wH} - G_{wL})\end{aligned}\quad (2.3.59)$$

Thus, the requirement that $\bar{V}_L - \bar{V}_H$ be positive is equivalent to the statement that the overall excess of water molecules around H is larger than the overall excess of water molecules around L . This is precisely the meaning of the requirement that H is a molecule with a relatively higher local density than L .

It is clear that the fulfillment of one condition, $\bar{V}_L - \bar{V}_H > 0$, can be achieved by proper definition of the two components. The question that arises is: Under what circumstances is the second condition, $\bar{H}_L - \bar{H}_H < 0$, also fulfilled?

In order to understand the characteristic nature of the packing of water molecules in the liquid state, consider first a simple fluid such as argon. Suppose that we define two components L and H having a low and high local density, respectively. For instance, we use the mole fraction in (2.3.47) with $K^* = 6$. In this case, we have $\bar{V}_L - \bar{V}_H > 0$ by virtue of the definition of

²⁵See Appendix F for the meaning of G_{wH} and G_{wL} .

the two components. However, since an argon molecule having more than six neighbors will have more neighbors to interact with, it is likely to have a lower partial molar energy or enthalpy. Hence, we expect that $\bar{H}_L - \bar{H}_H > 0$ (i.e. the conversion of a molecule from H to L is accompanied by an increase in enthalpy). Such a TSM would not work for our purposes: the condition (2.3.58) is not fulfilled. A different case is obtained with the choice of $x_H = x_{CN}$ ($K \geq 13$). Clearly, in this case, we also have $\bar{V}_L - \bar{V}_H > 0$. (The H component has a very high local density.) In addition, because of this particular choice of H , it is clear that the transformation $H \rightarrow L$ is likely to involve a decrease in enthalpy (since most of the neighbors must exert strong repulsive forces on the H -molecule, so that its conversion to an L releases energy). Hence, $\bar{H}_L - \bar{H}_H$ is expected to be negative. This choice will satisfy the condition (2.3.58) for a negative relaxation term. However, with the particular choice of the component H , it is very likely that $x_H \approx 0$ (a CN higher than 13 must be a very rare event). Hence, the product $x_L x_H$ is very small and the whole relaxation term in (2.3.55) will be negligibly small, though having a negative sign.²⁶

The situation in water is different since we know that the strong directional forces (hydrogen bonds) are responsible for maintaining low local density. Hence, it is possible to define two components L and H in such a way that

$$\bar{V}_L - \bar{V}_H > 0, \quad \bar{H}_L - \bar{H}_H < 0 \quad (2.3.60)$$

and, at the same time, none of the mole fractions x_L and x_H is too small. If this is indeed the case, then we will have a large, negative relaxation term in (2.3.55), which will dominate the temperature dependence of the volume. Of course, in order to make a

²⁶Note that when x_H is very small, the mixture becomes a dilute ideal solution and one can use Eq. (2.3.56) in Eq. (2.3.55).

more quantitative statement about the magnitudes of $\bar{V}_L - \bar{V}_H$, $\bar{H}_L - \bar{H}_H$ and x_L , we must choose a particular model and a specific set of parameters. That is exactly what has been done in Wada's model (Sec. 2.2), and we shall do that again in Sec. 2.4.

Two pieces of experimental evidence are in conformity with the requirements in (2.3.60). One is the relation between the molar volume and energy of the high pressure polymorphs of ice pointed out in Sec. 1.3. There, we noted that structures having a relatively large coordination number have also internal energies less negative than the corresponding internal energy of ordinary hexagonal ice. Second, in Chapter 1 we pointed out the slight increase in the average coordination number of water as we increase the temperature (see Sec. 1.4.5), i.e.

$$\frac{d}{dT} \left[\sum K x_{CN}(K) \right] > 0 \quad (2.3.61)$$

which means that the average of the distribution $x_{CN}(K)$ shifts towards higher values of K as the temperature increases. On the other hand, since the heat capacity is always positive, addition of heat to any system at equilibrium will shift the distribution of species towards those that have higher energy. In other words, the "structural changes" in the system will always be in that direction so that part of the heat is absorbed by the system. Therefore, using the distribution $x_{CN}(K)$ as in (2.3.47) with $K^* = 4$, we can conclude that the shift towards higher coordination number is correlated with the shift towards less negative binding energy.

At the molecular level, the condition (2.3.58) can be formulated in terms of the quasi-component distribution function $x_{BE,CN}(\nu, K)$. For a normal liquid, we expect that the average binding energy of species having a fixed coordination number will be a decreasing function of K (see Fig. 2.5a). On the other hand, in water we expect that this function will increase

with K , at least for some range of P and T . This has indeed been demonstrated for two-dimensional water-like particles (see Fig. 2.5b) and also by Monte Carlo simulation on 3-D water²⁷ (see Sec. 2.7).

Thus, the unique temperature dependence of the volume of water is due to the unique packing of water molecules in such a way that an open local structure is correlated with large (negative) binding energy. This unique feature of the interaction has been built in the model of Sec. 2.5 to show a negative thermal expansion coefficient in a one-dimensional system. We shall also see in Chapter 3 that this unique property is also responsible for some outstanding properties of aqueous solutions of non-polar solutes.

Consider next the heat capacity (at constant pressure) which, in the *TSM* formalism, can be obtained as follows. The total enthalpy of the system is written as

$$H = N_L \bar{H}_L + N_H \bar{H}_H \quad (2.3.62)$$

and the heat capacity is given by

$$C_P = \left(\frac{\partial H}{\partial T} \right)_{P, N_w, eq} = \left(N_L \frac{\partial \bar{H}_L}{\partial T} + N_H \frac{\partial \bar{H}_H}{\partial T} \right) + (\bar{H}_L - \bar{H}_H) \left(\frac{\partial N_L}{\partial T} \right)_{P, N_w, eq} \quad (2.3.63)$$

where again we have split the heat capacity into two terms. The first is the heat capacity of the “frozen-in” system and the second is the corresponding relaxation term. We stress again that the split into these two terms depends on the choice of the particular classification procedure used to define L and H .

²⁷Swaminathan and Beveridge (1977) and Mezei and Beveridge (1982).

Using the identity (F.6) from Appendix F, we can rewrite the relaxation term in (2.3.63) as

$$\begin{aligned} (\bar{H}_L - \bar{H}_H) \left(\frac{\partial N_L}{\partial T} \right)_{P, N_w, eq} &= \frac{(\bar{H}_L - \bar{H}_H)^2}{T(\mu_{LL} - 2\mu_{LH} + \mu_{HH})} \\ &= \frac{(\bar{H}_L - \bar{H}_H)^2 x_L x_H \eta V}{k_B T^2} \end{aligned} \quad (2.3.64)$$

where η is given by

$$\eta = \rho_L + \rho_H + \rho_L \rho_H (G_{LL} - G_{HH} - 2G_{LH}) \quad (2.3.65)$$

and G_{ij} are the KB integrals (Sec. 1.5).

Clearly, the relaxation term in (2.3.64) is always positive, independent of the definition of L and H . Of course, the magnitude of the relaxation term depends on the particular choice of the classification procedure. In order to explain the high value of the heat capacity of liquid water, one assumes that the “frozen-in” term, i.e. the first term on the right-hand side of (2.3.63), has a “normal” value. The excess heat capacity is then attributed to the relaxation term. In order for the latter to be large, we must have two components which differ appreciably in their partial molar enthalpy [otherwise $(\bar{H}_L - \bar{H}_H)^2$ cannot be large], and none of the mole fractions x_L and x_H can be too small.

We note again that the requirements for a large value of the relaxation term of the heat capacity are weaker than those needed for a large relaxation term of the thermal expansion coefficient. As we have seen, the peculiar relation between $\bar{V}_L - \bar{V}_H$ and $\bar{H}_L - \bar{H}_H$ supplemented by the requirement that x_L and x_H not be too small is probably a unique feature of liquid water. On the other hand, the requirement that $(\bar{H}_L - \bar{H}_H)^2$ be large is certainly a result of the existence of strong interaction energy between water molecules. This is of course a result of the hydrogen bonds. However, as we shall see in Sec. 2.5, the HB s are not essential for the large heat capacity.

As a final example, we discuss the expression for the isothermal compressibility in the *TSM*:

$$\begin{aligned} \kappa_T = \frac{-1}{\bar{V}} \left(\frac{\partial V}{\partial P} \right)_{T, N_w, eq} &= \frac{-1}{\bar{V}} \left[N_L \frac{\partial \bar{V}_L}{\partial P} + N_H \frac{\partial \bar{V}_H}{\partial P} \right] \\ &\quad - \frac{1}{\bar{V}} (\bar{V}_L - \bar{V}_H) \left(\frac{\partial N_L}{\partial P} \right)_{T, N_w, eq} \end{aligned} \quad (2.3.66)$$

The relaxation term can be rewritten using identity (F.8) from Appendix F.

$$\begin{aligned} -\frac{1}{\bar{V}} (\bar{V}_L - \bar{V}_H) \left(\frac{\partial N_L}{\partial P} \right)_{T, N_w, eq} &= -\frac{(\bar{V}_L - \bar{V}_H)^2}{V(\mu_{LL} - 2\mu_{LH} + \mu_{HH})} \\ &= -\frac{(\bar{V}_L - \bar{V}_H)^2 x_L x_H \eta}{k_B T} \end{aligned} \quad (2.3.67)$$

We note that this term is always negative, independent of the particular definitions of *L* and *H*. The relaxation term depends only on $\Delta V = \bar{V}_L - \bar{V}_H$, not on the particular correlation between ΔH and ΔV .

We conclude this long section with a consideration of the nature of the mixture of *L* and *H*. The question is whether the mixture may be assumed to be ideal and, if so, in what sense. First, suppose that we have defined *L* and *H* in such a way that one component is very dilute in the other, which can easily be achieved. For instance, if we take $K^* = 12$ in (2.3.47), then it is likely that $x_H \approx 0$. Hence, such a solution will be dilute ideal and we have

$$\mu_{LL} - 2\mu_{LH} + \mu_{HH} = \frac{k_B T}{N_w x_L x_H} \quad (2.3.68)$$

However, the fact that one component is very dilute in the other implies that the product $x_L x_H$ is very small. Hence, all the relaxation terms in (2.3.55), (2.3.63), and (2.3.67) are very small, and the whole treatment is rendered useless.

A second possibility is to define L and H in such a way that the two components are “similar,” so that the solution is symmetrically ideal,²⁸ i.e.

$$G_{LL} + G_{HH} - 2G_{LH} = 0 \quad (2.3.69)$$

In this case, $\eta = \rho_L + \rho_H = \rho_w$, or equivalently (2.3.56). However, care must be exercised in applying the symmetric ideal assumption to the TSM of water. We saw that in order to get large relaxation terms in (2.3.55), (2.3.63), and (2.3.67) we must assume that the two components L and H are very *different*, i.e. ΔH and ΔV are large. This, in general, will contradict the assumption of similarity in the sense of (2.3.69).

We recall that condition (2.3.69) is essentially a condition on the *similarity* between the two species, in the sense that the local environments of L and H are similar. In a real mixture of two components A and B , similarity of the molecules (chemical composition structure, etc.) A and B implies similarity in their local environments as well. In the MM approach for water, we start with two components which are *identical* in their chemical composition. (Both L and H are water molecules!) Therefore, it is very tempting to assume that these two components are also similar in the sense of (2.3.69); hence, they form a symmetric ideal solution. However, since we require the two components to be very *different* in their local environments, they must be very dissimilar, thereby, invalidating the assumption of ideality.

²⁸For details, see Ben-Naim (2006).

2.4. Lattice Models for Water

2.4.1. *Introduction*

Lattice models for liquids were very common between the 1930s and 1950s but are rarely used nowadays. The main reason for their falling out-of-fashion was the recognition that solids are fundamentally different from liquids. Therefore, lattice models for liquids were largely discarded. One would have expected that this were true for liquid water as well. Yet quite surprisingly lattice models for water were used, and still are used, in the study of water.²⁹

The main reason they endure is that water, although a liquid, does contain a high concentration of ice-like molecules. As we have seen in Chapter 1, Sec. 1.4, this is true only locally. Some of the two-structure models for water assumed explicitly that water contains patches of ice-like regions. This assumption has been criticized³⁰ on the grounds that if liquid water contained some “seeds” of ice, then it would be unlikely that supercooled water could exist at such lower temperature below the melting point of ice. Perhaps the Pauling model was designed to answer that criticism. Instead of ice-like structure, Pauling assumed that liquid water contains clathrate-like structures. These structures still resemble ice in terms of energy and local density but do not have the hexagonal structure of ice.

The model presented in this section is of interest for three reasons. First, it is the simplest interstitial model having features in common with many models proposed for water and used successfully to explain some of the outstanding properties of water and aqueous solutions. Second, this model may be viewed either

²⁹A partial list is: Lavis and Southern (1984), Weres and Rice (1972), Pretti and Buzano (2004), and Girardi and Figueiredo (2004).

³⁰Koefoed (1957).

as one component or as a mixture of two components. Therefore, one can switch between the language of a one-component liquid and the language of the MM. The two points of view are completely equivalent. The MM view has some advantages since in this view one can study “what goes on” at a molecular level when we change the temperature or the pressure. Finally, this is a simple solvable example of a system at constant T, P, N and as such it also has pedagogical value.

The interstitial model has a serious drawback, however, which is similar to the shortcomings of applying a lattice model to a fluid in general. It is therefore important to make a clear-cut distinction between results that pertain strictly to the model and results that have more general validity. In this section, we shall describe a simplified version of Pauling’s model and briefly outline some of the results. The details are left as an exercise for the reader. A partial theoretical treatment of Pauling’s model was carried out by Frank and Quist (1961).

2.4.2. The Pauling model and its solution

The system consists of N_w water molecules at a some temperature T and pressure P . A total of N_L molecules participate in the formation of a regular lattice with a well-defined structure, which for our purposes need not be specified. [It may be an ice I_h structure as in the Samoilov (1957) model, or a clathrate type of structure as in the Pauling (1960) model.] The lattice is presumed to contain empty spaces, or holes. We let N_0 be the number of holes per lattice molecule, i.e. $N_0 N_L$ is the total number of holes formed by N_L lattice molecules. We assume that the system is macroscopically large, so that surface effects are negligible; hence, N_0 is considered to be independent of N_L . In the case of ice I_h , we have $N_0 = \frac{1}{2}$. Each hole is surrounded by

12 molecules, but each molecule participates in six holes; hence, the number of holes per lattice molecule is $\frac{1}{2}$.

The remaining $N_H = N_w - N_L$ molecules are assumed to occupy the holes and may be referred to as interstitial molecules.³¹ A schematic illustration of such a model in two dimensions is shown in Fig. 2.6.

To keep the complexity of the model at a minimum, we require the following simplifying assumptions: (i) All the holes have the same structure. (ii) A hole can accommodate at most

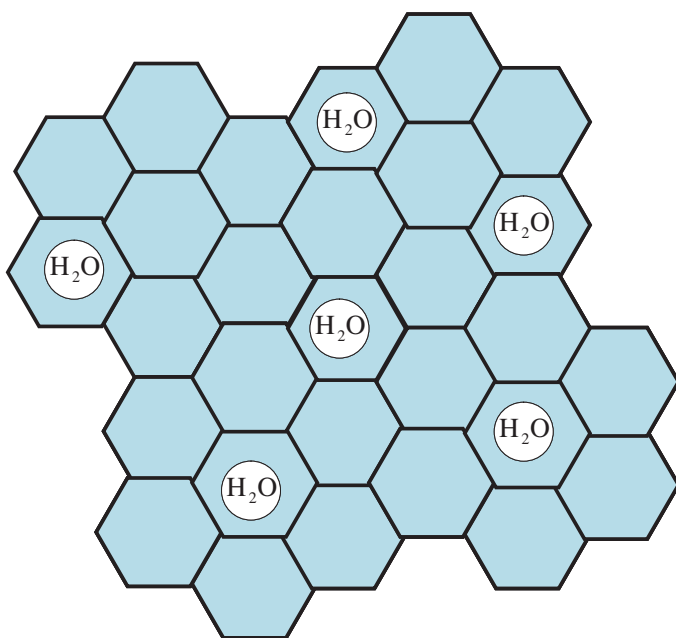


Fig. 2.6 A schematic description of a two-dimensional interstitial model for water. The lattice molecule occupies the vertices of the hexagons. The interstitial water molecules occupy the holes in the lattice.

³¹In the clathrate model, the holes are occupied by a solute. In this case the lattice serves as a host for the solute molecule. In the lattice model for water the host and the guest molecules are water molecules.

one water molecule in such a way that it does not distort the lattice structure to a significant extent. (iii) The interstitial molecules do not “see” each other, i.e. there is no direct interaction between interstitial molecules in adjacent holes. Hence, occupancy of a certain hole does not affect the probability of an adjacent hole being occupied or unoccupied. (iv) The lattice molecules are assumed to hold the equilibrium lattice points, and each is characterized by an energy E_L . An interstitial molecule interacts with its surrounding molecules by a constant energy parameter E_H . No other degrees of freedom are ascribed to the interstitial molecules.

Clearly, the condition $N_H < N_0 N_L$ must be satisfied. Alternatively, the mole fraction of interstitial molecules is restricted to vary between the limiting values:

$$0 \leq x_H = \frac{N_H}{N_w} \leq \frac{N_0}{(1 + N_0)} \quad (2.4.1)$$

For instance, in the model depicted in Fig. 2.6, $N_0 = \frac{1}{2}$, i.e. each lattice particle “belongs” to three holes, but each hole is built up by six particles, so that each particle contributes half a hole. Thus, the mole fraction of interstitial molecules cannot exceed $\frac{1}{3}$.

The total energy of the system E_T is composed only of the interaction energies among the molecules:

$$E_T = N_L E_L + N_H E_H \quad (2.4.2)$$

where E_L is the lattice energy per lattice molecule and E_H is the interaction energy of an interstitial molecule with its surroundings. E_L is of the order of the HB energy. We also assume that $E_L < E_H$.

The canonical partition function for this model is

$$\begin{aligned}
 Q(T, V, N_w) &= \sum_{\text{all states}} \exp[-\beta E_T] \\
 &= \sum_{\text{configurations}} \exp[-\beta(N_L E_L + N_H E_H)] \\
 &= \sum_{E_T} \Omega(E_T, V, N_w) \exp[-\beta(N_L E_L + N_H E_H)]
 \end{aligned} \tag{2.4.3}$$

In Eq. (2.4.3) we started from the definition of the *PF* as the sum over all states or all configurations of the system. In the last form on the right-hand side of (2.4.3), we have collected all the terms in the partition function corresponding to the same value of the total energy E_T , which is Ω -fold degenerate. Clearly, the total energy depends only on the number N_L (E_L and E_H are assumed to be fixed, and $N_H = N_w - N_L$). Hence, to compute the degeneracy of a given energy E_T , it is sufficient to compute the number of ways we can arrange N_H interstitial molecules in $N_0 N_L$ holes. This number is³²

$$\Omega(E_T, V, N_w) = \frac{(N_0 N_L)!}{N_H! (N_0 N_L - N_H)!} \tag{2.4.4}$$

Furthermore, in this particular model, the total volume V can be written as

$$V = N_L V_L \tag{2.4.5}$$

where V_L is the volume of the system per lattice molecule. (Interstitial molecules do not contribute to the volume.) The condition (2.4.5) considerably simplifies the evaluation of the

³²Frank and Quist (1961) referred to the entropy associated with Ω as the mixing entropy. Clearly, this quantity has nothing to do with mixing. See also Ben-Naim (2008).

partition function in (2.4.3). In the canonical ensemble, the volume V is fixed, and hence, from (2.4.5), the number N_L is fixed too. This, in turn, determines the total energy through (2.4.2). Therefore, the canonical PF (2.4.3) reduces to a single term, namely

$$Q(T, V, N_w) = \frac{(N_0 N_L)!}{N_H! (N_0 N_L - N_H)!} \exp[-\beta(N_L E_L + N_H E_H)] \quad (2.4.6)$$

This is sufficient to calculate all the thermodynamic quantities of the system. However, it is instructive to transform the PF Q into the T, P, N_w partition function. This is more convenient for later applications in which various thermodynamic quantities are evaluated. The T, P, N_w partition function is

$$\begin{aligned} \Delta(T, P, N_w) &= \sum_{V=V_{\min}}^{V_{\max}} Q(T, V, N_w) \exp(-\beta P V) \\ &= \sum_{N_L=N_{L,\min}}^{N_w} \frac{(N_0 N_L)!}{N_H! (N_0 N_L - N_H)!} \\ &\quad \times \exp[-\beta(N_L E_L + N_H E_H + P N_L V_L)] \end{aligned} \quad (2.4.7)$$

In the second term form on the right-hand side, we have transformed the summation over all possible volumes of the system to a sum over N_L , which determines the volume through (2.4.5). The summation is carried out from the minimum value of N_L to the maximum value of N_L , which is N_w . This completes our description of the model.

From (2.4.7), we can derive all the required thermodynamic quantities by standard relations. Before discussing applications of (2.4.7) it is worthwhile pausing to consider the equivalence of viewing the system as either a single component or as a mixture of two components. As in any mixture-model approach, we

start with a one-component system described by the variables T, P, N_w . If we prefer, we can switch to the language of the *MM* approach. Once we have defined the species L and H , then we can view the system as a mixture of two components.

To see the relation between the two views, let us rewrite (2.4.7) as

$$\Delta(T, P, N_w) = \sum_{N_L} \Delta(T, P, N_w; N_L) \quad (2.4.8)$$

Each term $\Delta(T, P, N_w; N_L)$ in the sum on the right-hand side of (2.4.8) is the partition function of a system in which the conversion reaction $L \rightleftharpoons H$ has been “frozen in.” In other words, the system is viewed as a mixture of two components L and H .³³

Using a connection between this partition function and the Gibbs energy, we can rewrite (2.4.8) as

$$\exp[-\beta G(T, P, N_w)] = \sum_{N_L} \exp[-\beta G(T, P, N_w; N_L)] \quad (2.4.9)$$

We next show that the two approaches, the one component view and the *MM* view, are equivalent. We denote by N_L^* (and $N_H^* = N_w - N_L^*$) the value of N_L for which $G(T, P, N_w; N_L)$ is minimum. The condition for this minimum is

$$\begin{aligned} \frac{(N_0 N_L^*)^{N_0} N_H^*}{(N_0 N_L^* - N_H^*)^{N_0+1}} &= \exp[\beta(E_L - E_H + PV_L)] \\ &\equiv K(T, P) \end{aligned} \quad (2.4.10)$$

The conventional mole fractions of the L and H species are: $x_L = N_L/N_w$, $x_H = 1 - x_L$.

The equilibrium condition (2.4.10) can be written more conveniently in terms of the “mole fractions” of empty and occupied

³³Since $N_w = N_L + N_H$, the partition function of the mixture is actually a function of one variable N_L .

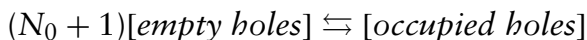
holes, which are defined, respectively, as

$$y_0 = \frac{(N_0 N_L - N_H)}{N_0 N_L}, \quad y_1 = \frac{N_H}{N_0 N_L} \quad (2.4.11)$$

With these variables, the equilibrium condition (2.4.10) is rewritten as

$$\frac{y_1^*}{(y_0^*)^{N_0+1}} = K(T, P) = \exp[\beta(E_L - E_H + PV_L)] \quad (2.4.12)$$

which has a simple interpretation as an equilibrium constant for the reaction



The stoichiometry of this reaction is as follows. In order to create one mole of occupied holes, we must cancel one mole of empty holes. In addition, in order to fill these holes, we need one mole of water molecules, which must come from the lattice. Hence, N_0 empty holes must also be eliminated. Altogether, we need $N_0 + 1$ moles of empty holes to be converted to one mole of occupied holes.

Recall that N_L^* is the value of N_L that minimizes $G(T, P, N_w, N_L)$. Hence, N_L^* is also the value of N_L that maximizes the term $\exp[-\beta G(T, P, N_w, N_L)]$. We now replace the sum on the right-hand side of (2.4.9) by the maximal term to obtain³⁴

$$\begin{aligned} \exp[-\beta G(T, P, N_w)] &= \sum_{N_L} \exp[-\beta G(T, P, N_w; N_L)] \\ &\cong \exp[-\beta G(T, P, N_w; N_L^*)]. \end{aligned} \quad (2.4.13)$$

Note that $G(T, P, N_w)$ is the Gibbs energy of the system with N_w molecules. On the other hand, $G(T, P, N_w; N_L^*)$ is the Gibbs

³⁴This procedure of replacing a sum by a maximal term is very common in statistical thermodynamics. For more details, see Ben-Naim (2008a).

energy of the system viewed as a mixture of *two components*. However, the two views of the system are equivalent when N_L^* is determined from the equilibrium condition (2.3.10). See also Appendix D.

The Gibbs energy of the system with any arbitrary composition N_L, N_H is

$$G(T, P, N_w; N_L) = (N_L E_L + N_H E_H + P N_L V_L) - k_B T \ln \left[\frac{(N_0 N_L)!}{N_H! (N_0 N_L - N_H)!} \right] \quad (2.4.14)$$

For the specific value of $N_H = N_H^*$ which minimizes $G(T, P, N_w; N_L)$, we get the near equality

$$G(T, P, N_w) \cong G(T, P, N_w; N_L^*) \quad (2.4.15)$$

Note that on the left-hand side of (2.3.15), we have the Gibbs energy of the one-component system characterized by T, P, N_w . On the right-hand side of (2.3.15), we have a *different* system. This is a system where the conversion between the two species L and H is “frozen-in” at the specific value of N_L^* (and $N_H^* = N_w - N_L^*$). This is a different system since we do not allow the conversion between the two species. Nevertheless, the Gibbs energies of the two systems are equal (in the thermodynamic limit). We shall soon see that this kind of equality is not shared by all thermodynamic quantities of the system.

In the general case, it is difficult to solve (2.4.10) for x_L^* explicitly. As a simple case, we take $N_0 = 1$ and rewrite (2.4.10) in terms of the mole fraction $x_L = N_L/N_w$:

$$\frac{x_L^*(1 - x_L^*)}{(2x_L^* - 1)^2} = K \quad (2.4.16)$$

There are two solutions to this equation, namely

$$x_L^* = \frac{1}{2} \pm \frac{1}{2} \left(\frac{1}{4K + 1} \right)^{1/2} \quad (2.4.17)$$

From these two possible solutions, only one is physically acceptable. In order to determine the correct solutions for the physical model, we can check one limiting case. For instance, for given T and P , and the choice of $E_L \ll E_H$, x_L^* must tend to unity as $K \rightarrow 0$. From (2.4.17), we have in this limit

$$x_L^* \xrightarrow{K \rightarrow 0} \frac{(1 \pm 1)}{2} \quad (2.4.18)$$

Hence, the *plus* sign is the acceptable one in (2.4.17).

The chemical potential of water, viewed as a single component, is defined by $\mu_w = (\partial G / \partial N_w)_{T,P}$. In the MM view, one can define two chemical potentials:

$$\begin{aligned} \mu_L &= \left(\frac{\partial G}{\partial N_L} \right)_{T,P,N_H} \\ &= E_L + PV_L - k_B T N_0 \ln \frac{N_0 N_L}{N_0 N_L - N_H} \\ &= E_L + PV_L - k_B T N_0 \ln \frac{N_0 x_L}{N_0 x_L - x_H} \end{aligned} \quad (2.4.19)$$

$$\begin{aligned} \mu_H &= \left(\frac{\partial G}{\partial N_H} \right)_{T,P,N_L} \\ &= E_H + k_B T \ln \frac{N_H}{N_0 N_L - N_H} \\ &= E_H + k_B T \ln \frac{x_H}{N_0 x_L - x_H} \end{aligned} \quad (2.4.20)$$

Note that the chemical potentials μ_L and μ_H are *definable* only in the frozen-in system, since we require N_H and N_L to be kept constant in (2.4.19) and (2.4.20), respectively. In the special case where $N_L = N_L^*$ and $N_H = N_H^*$, we get the equality

$$\mu_L = \mu_H \quad (2.4.21)$$

Clearly, the mixture of L and H is not ideal, neither in the dilute nor in the symmetrical sense. Note that L and H are both

water molecules. They are *identical* molecules, yet they are not similar in the sense of (2.3.69). By their very definition, the two components L and H differ markedly in their local environment; hence, it is unlikely that they obey the condition for symmetric ideal solutions.

The entropy of the system is

$$\begin{aligned}
 -S &= \left(\frac{\partial G}{\partial T} \right)_{P, N_w} \\
 &= \left(\frac{\partial G}{\partial T} \right)_{P, N_L, N_H} + \left[\left(\frac{\partial G}{\partial N_L} \right)_{T, P, N_H} - \left(\frac{\partial G}{\partial N_H} \right)_{T, P, N_L} \right] \left(\frac{\partial N_L}{\partial T} \right)_{P, N_w} \\
 &= \left(\frac{\partial G}{\partial T} \right)_{P, N_L, N_H} \quad (2.4.22)
 \end{aligned}$$

Note carefully that the entropy of the system is in general different for different values of N_L . However, for $N_L = N_L^*$, the condition of equilibrium (2.4.21) leads to the last equality on the right-hand side of (2.4.22).

Exercise E.2.6: Write the analog of (2.4.22) for the enthalpy of the system. What can be said about the enthalpy of the system described by T, P, N_w and by T, P, N_L, N_H when $N_L = N_L^*$?

The volume of the system is

$$V = \left(\frac{\partial G}{\partial P} \right)_{T, N_w} = \left(\frac{\partial G}{\partial P} \right)_{T, N_L, N_H} = N_L V_L \quad (2.4.23)$$

which is the expected result for this model.

The enthalpy and the internal energy are similarly obtained from

$$H = G + TS = N_L E_L + N_H E_H + P N_L V_L \quad (2.4.24)$$

$$E = H - PV = N_L E_L + N_H E_H \quad (2.4.25)$$

All the quantities calculated above are indifferent to the freezing in of the conversion between L and H , provided we did the freezing at the equilibrium point, $N_L = N_L^*$.

The temperature dependence of the volume is

$$\begin{aligned} \left(\frac{\partial V}{\partial T}\right)_{P, N_w, eq} &= \left(\frac{\partial V}{\partial T}\right)_{P, N_L, N_H} \\ &+ \left[\left(\frac{\partial V}{\partial N_L}\right)_{T, P, N_H} - \left(\frac{\partial V}{\partial N_H}\right)_{T, P, N_L} \right] \left(\frac{\partial N_L}{\partial T}\right)_{P, N_w, eq}; \end{aligned} \quad (2.4.26)$$

In this particular model we have the result

$$\left(\frac{\partial V}{\partial T}\right)_{P, N_w, eq} = \frac{V_L(E_L - E_H + PV_L)(N_0 N_L^* - N_H^*)x_L^* x_H^*}{k_B T^2 N_0} \quad (2.4.27)$$

Since $V_L > 0$, $N_0 N_L \geq N_H$, and $x_L x_H \geq 0$, the sign of (2.4.27) is determined by the quantity $E_L - E_H + PV_L$. In most interstitial models, $E_L - E_H$ is of the order of about $-10^3 \text{ cal mol}^{-1}$. At 1 atm and with V_L of the order of $18 \text{ cm}^3 \text{ mol}^{-1}$, we have $PV_L \approx 18/41 = 0.44 \text{ cal mol}^{-1}$. Thus, the PV_L term is negligible compared to $E_L - E_H$, and therefore, the sign of (2.4.27) is negative. This is the essence of the "explanation" of the temperature dependence of the volume of water. If we assume that V_L is temperature dependent, then

instead of (2.4.27), we have

$$\left(\frac{\partial V}{\partial T}\right)_{P,N_w,eq} = N_L \left(\frac{\partial V_L}{\partial T}\right)_{P,N_L,N_H} + (\bar{V}_L - \bar{V}_H) \left(\frac{\partial N_L}{\partial T}\right)_{P,N_w,eq} \quad (2.4.28)$$

Exercise E.2.7: Explore numerically the temperature and the pressure dependence of the molar volume and the heat capacity in this model. Choose values of $E_L < 0$ and $E_H < 0$ and $V_L > 0$ as the molecular parameters. Follow the mole fractions x_L , x_H as a function of T and P . Suppose that $E_L - E_H < 0$, i.e. the energy per lattice molecule is lower than the interstitial molecule. In this case, we always find that x_L decreases with increase in temperature. Explain why.

Qualitatively, we can associate the lattice component with the more *structured* component or the more *ordered* form. Therefore, the decrease in x_L upon increasing the temperature can be interpreted as *melting* of the ice-like form, or equivalently as an increase in the extent of disorder in the system.

What happens when we choose E_L and E_H such that $E_L - E_H > 0$? Can one still say that the ice-like form *melts*, or the *order* in the system decreases upon raising the temperature?

Finally, it should be noted that the molecular reason underlying the negative temperature dependence of the volume is the same as in real liquid water, namely the unique correlation between binding energy and local density. The principle for this particular model is depicted in Fig. 2.7.

If we assume that the first term on the right-hand side of (2.4.28) is positive (i.e. the lattice expands with increasing temperature), then we have competition between two terms of opposite signs, which happen to cancel out at about 4°C.

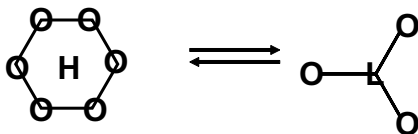


Fig. 2.7 The implementation of the *principle* in the lattice model described in Sec. 2.4.1. A lattice (L) molecule is at equilibrium with an interstitial molecule (H).

2.4.3. The heat capacity and the isothermal compressibility

The heat capacity at constant pressure is given by

$$\begin{aligned}
 C_P &= \left(\frac{\partial H}{\partial T} \right)_{P, N_w, eq} \\
 &= \left(\frac{\partial H}{\partial T} \right)_{P, N_L, N_H} + (\bar{H}_L - \bar{H}_H) \left(\frac{\partial N_L}{\partial T} \right)_{P, N_w, eq} \quad (2.4.29)
 \end{aligned}$$

This is the general expression for the heat capacity in the mixture-model approach. In our model, the first term on the right-hand side of (2.4.29) is zero and for the second term we have

$$\begin{aligned}
 C_P &= (E_L - E_H + PV_L) \left(\frac{\partial N_L}{\partial T} \right)_{P, N_w, eq} \\
 &= \frac{(E_L - E_H + PV_L)^2 (N_0 N_L^* - N_H^*) x_L^* x_H^*}{k_B T^2 N_0} \quad (2.4.30)
 \end{aligned}$$

In this particular model, all the heat capacity is due to the conversion between H and the L species. Note again that the heat capacity is zero in the frozen-in system.

As a final example of quantities in this group, we compute the pressure dependence of the volume (related to the isothermal

compressibility) for this model:

$$\begin{aligned}
 V\kappa_T &= - \left(\frac{\partial V}{\partial P} \right)_{T, N_w, eq} \\
 &= - \left[\left(\frac{\partial V}{\partial P} \right)_{T, N_L, N_H} + (\bar{V}_L - \bar{V}_H) \left(\frac{\partial N_L}{\partial P} \right)_{T, N_w, eq} \right] \\
 &= \frac{V_L^2 (N_0 N_L^* - N_H^*) x_L^* x_H^*}{k_B T N_0}
 \end{aligned} \tag{2.4.31}$$

which is always positive.

We conclude this section with a general comment on interstitial models. The study of such models is useful and quite rewarding in providing us insight into the possible mechanism by which water exhibits its anomalous behavior. One should be careful not to conclude that the numerical results obtained from the model are an indication of the extent of the reality of the model. It is possible, by a judicious choice of the molecular parameters, to obtain thermodynamic results which are in agreement with experimental values measured for real water. Such agreement can be achieved by quite different models. The important point is not the quantitative results of the model but the qualitative explanation that the model offers for the various properties of water. We shall use the same model in Sec. 3.6 to explain some aspects of aqueous solutions of simple solutes.

2.5. A One-Dimensional Model for Water

2.5.1. Introduction

A one-dimensional (1-D) model for water may sound like an extremely unrealistic model for such a complex liquid. Indeed, it is! If the aim is to calculate thermodynamic quantities and to compare them to the corresponding experimental quantities of

real water, then clearly a 1-D model is useless. However, if the aim is to *understand* the outstanding properties of water at a molecular level, then any model in any dimension could be very useful. The motivation for the construction and the study of the 1-D model for water is the following:

It has long been recognized that the unique properties of water are related to the *open structure* or the *ice-like* character of liquid water. The idea that water contains some kind of *structure* related to the structure of ice is very old (see Sec. 2.1). This idea was the underlying motivation for constructing various mixture models for water.

In all of these models, the *hydrogen bonds*, or the *structure* of liquid water, were traditionally emphasized as the main molecular reasons for the anomalous behavior exhibited by liquid water.³⁵ However, underlying this relatively ill-defined concept of structure (which was much later defined in statistical mechanical terms; see Sec. 2.7) lies a more fundamental principle which can be defined in molecular terms, and which does not explicitly mention the concept of structure yet is responsible for the unusual properties of liquid water. This principle was first formulated in terms of generalized molecular distribution functions in 1973.³⁶ It states that there exists a range of temperatures and pressures at which the water-water interactions produce a unique correlation between high local density and a weak binding energy. Clearly, this principle does not mention *structure*. As will be demonstrated in this section, it is this principle, not the *structure per se*, which is responsible for the unique properties of water as well as of aqueous solutions.³⁷

³⁵See, for example, Stillinger (1980).

³⁶Ben-Naim (1973, 1974).

³⁷A similar view was expressed by Jirsak and Nezbeda (2007) and Oliveira *et al.* (2006).

A simpler version of the same principle uses the language of the mixture-model approach to liquid water. Within this approach, the principle states that there exists a range of temperatures and pressures at which there are non-negligible concentrations of two species: one characterized by large partial molar volume and large absolute value of the partial molar enthalpy, and a second characterized by a smaller partial molar volume and smaller absolute value of the partial molar enthalpy. In order to obtain the outstanding properties of water, one also needs to assume that the concentrations of these two species are of comparable magnitude (see Sec. 2.3 for details).³⁸

Figure 2.8b is a schematic illustration of this principle when applied to a 1-D model. On the left-hand side, we have close-packed and weakly bound molecules; on the right-hand side, we have an open structure with strong “hydrogen bonds.”

This principle was first used implicitly in the construction of the first successful pair potential for water molecules.³⁹ Later, it was used explicitly in constructing pair potentials that exhibit

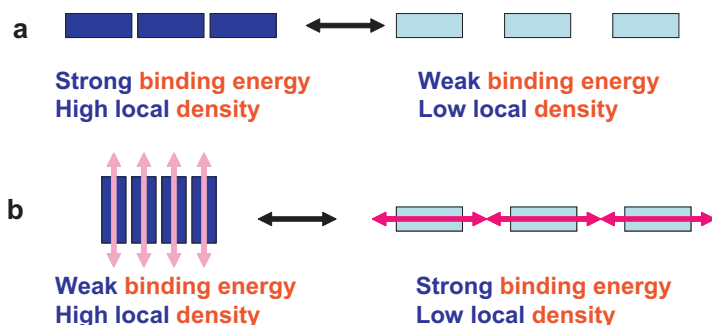


Fig. 2.8 The correlation between local density and binding energy in a one-dimensional model for (a) normal fluid and (b) water-like particles.

³⁸As was pointed out in Sec. 2.3, the peculiar type of correlation between local density and local binding energy can also be obtained at high pressure. However, in this case one of the components would have negligible concentration.

³⁹Ben-Naim and Stillinger (1972).

water-like behavior in 3-D, 2-D, and 1-D models. The most amazing finding was that even in a 1-D world, which is very far from real liquid water, the implementation of this principle was sufficient to produce most of the characteristic behavior of liquid water. The success of this principle in explaining the properties of both water and aqueous solutions was so compelling that I have quite often said that this principle is *necessary* and *sufficient* for any successful model for water, as discussed in the preface.

It should be said that even the most seemingly “realistic” 3-D models for water are in fact very far from being realistic. An effective pair potential for water, even when it can lead to a perfect agreement between computed and experimental results, is far from being close to the *real* pair potential function between two water molecules. Conversely, even if we had a perfect pair potential between *two* water molecules, it is doubtful that its employment in a theory of water would reproduce the properties of water. We shall further discuss this aspect of the pair potential in Sec. 2.7.

In applying a model for water, the most we can say — and this is true for any model — is that *certain features of the pair potential lead to certain macroscopic properties of water*. In this respect, the 1-D model has the advantage of providing the same connection between molecular and bulk properties, but in this case the connection can be written exactly.

The 1-D model for water described in this section is referred to as the *primitive model*. It has almost no other features but the principle of correlation between low local density and strong binding energy. This feature is built-in in the pair potential described in Sec. 2.5.2. A more “complicated” potential was published earlier⁴⁰ as a textbook example and was shown to

⁴⁰Ben-Naim (1992). In the original model, a double-well potential was constructed. The primitive model used in this section is a simplification of the double-well potential. I was quite surprised to see that Bell used a similar model in 1969.

reproduce the anomalous temperature dependence of the volume. I shall refer to this version of the pair potential as the BN1D potential.

Essentially, the same model and the same results were published four years later by Cho *et al.* (1996). A more extensive study of this model was carried out by Sadr-Lahijany *et al.* (1999). Both of these authors used the older version of the 1-D model but perhaps did not realize that the double-well character of the older version is not essential for the reproduction of the properties of water.

One-dimensional models for water had been discussed earlier. Perhaps, the first one was considered by Bell (1969), who devised a lattice type of 1-D model. This model was extended by Elkoshi and Ben-Naim (1979) to study hydrophobic interactions (see Chapter 4). A more detailed model of water was discussed by Ben-Naim and Lovett (1969). We shall discuss this model in Sec. 2.5.4 and in Chapter 3.

In this section, we present two simplified models that manifest many of the outstanding properties of water and aqueous solutions. The first is referred to as the primitive 1-D model, a simplified version of the earlier 1-D model published in 1992. It has the advantage of taking into account nothing but the “principle” mentioned above. It is shown that a double well is not really necessary. The implementation of the principle is achieved by defining only two distances: the hard core “diameter” σ_1 and the “hydrogen-bonding” (*HB*) distance σ_2 with the requirement that $\sigma_2 > \sigma_1$.

The second model is a simplified version of a model by Lovett and Ben-Naim published in 1969. It is referred to as the primitive cluster model for water. This model produces the same results for water as the primitive model. However, it has two advantages. First, one can follow the “molecular mechanism” underlying the characteristic behavior of liquid water. Second, it

is easier to apply in the study of aqueous solutions of simple solutes. This will be discussed in Sec. 3.9.

2.5.2. The primitive model and the corresponding partition function

Consider a system consisting of N water-like particles denoted w , in one dimension (Fig. 2.9a). We take only nearest-neighbor interactions between pairs of consecutive particles into account. The potential function is described in Fig. 2.10d and is defined as

$$U_{ww}(R) = \begin{cases} \infty & 0 \leq R < \sigma_1 \\ 0 & \sigma_1 \leq R < \sigma_2 \\ \varepsilon_{HB} & \sigma_2 \leq R < \sigma_2 + \delta_2 \\ 0 & R \geq \sigma_2 + \delta_2 \end{cases} \quad (2.5.1)$$

Here, σ_1 is the hard-rod “diameter” of the particles. Between σ_1 and $\sigma_2 > \sigma_1$, there exists a flat region [in the previous model this region contained an additional square well potential; see Ben-Naim (1992)]. ε_{HB} is referred to as the hydrogen bond (HB) energy and its range is between σ_2 and $\sigma_2 + \delta_2$. In this

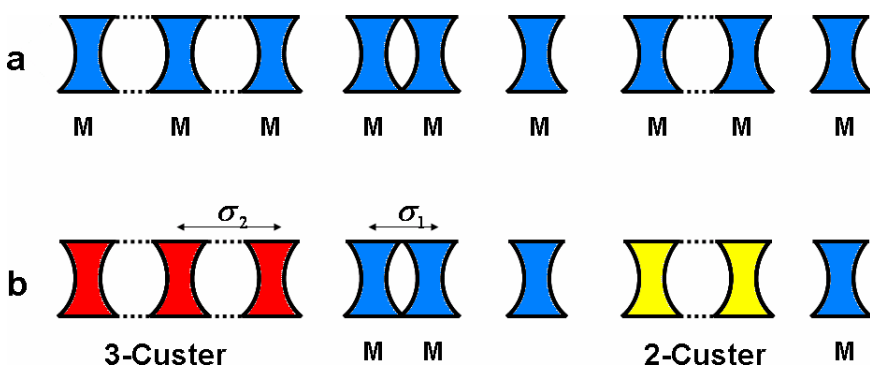


Fig. 2.9 (a) The primitive model and (b) the primitive cluster model for water-like particles in one dimension. In the latter, each sequence of bonded molecules is viewed as a different “component.”

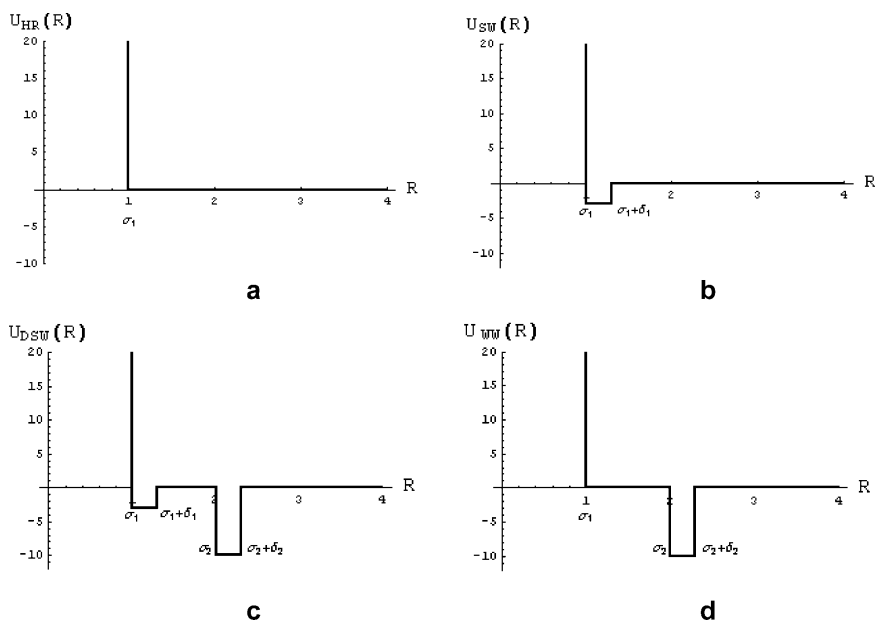


Fig. 2.10 The various pair potentials used in the study of water in 1-D: (a) the hard rod (HR), (b) the square well (SW), (c) the double square well (referred to as the BN1D potential), and (d) the pair potential for the primitive model referred to as the hydrogen bonded, or the water-water (WW), potential.

section, we use dimensionless parameters. The Planck constant and the Boltzmann constant are chosen as unity; hence, ε_{HB} has the same units as the temperature T . The unit of length is chosen as $\sigma_1 = 1$.

It is already clear from the definition (2.5.1) and from Fig. 2.10d that this potential fulfills the requirement of the “principle” mentioned in Sec. 2.5.1. Particles that are closer to each other (in the range from σ_1 to σ_2) experience “weaker” binding energy, while at larger distances (in the range from σ_2 to $\sigma_2 + \delta_2$) they experience a stronger binding energy. This feature of the pair potential is enough to produce the required correlation between low local density and strong binding energy. In this model, one can refer to the *HBed* particles as the

more “structured” component, but this view is not essential for understanding the behavior of the system (as well as the behavior of real liquid water).

We describe here only briefly the construction of the partition function (*PF*) of this system. More details are given in Ben-Naim (1992, 2008c).

The total interaction energy is written as

$$U_N(R_1, R_2, \dots, R_N) = \sum_{i=1}^{N-1} U_{ww}(R_{i,i+1}) \quad (2.5.2)$$

where R_i is the location of the i th particle, and $R_{i,i+1}$ is the distance between two consecutive particles i and $i + 1$. Thus, the total interaction energy is assumed to be the sum of the interactions between consecutive pairs of particles.

The classical canonical *PF* is

$$\mathcal{Q}(T, L, N) = \frac{1}{\Lambda^N N!} \int_0^L \cdots \int_0^L d\mathbf{R}^N \exp[-\beta U_N(\mathbf{R}^N)] \quad (2.5.3)$$

where $\beta = T^{-1}$, and Λ is the momentum *PF* in one dimension, which in our case is

$$\Lambda = \frac{h}{\sqrt{2\pi m k_B T}} \quad (2.5.4)$$

$\mathbf{R}^N = R_1, \dots, R_N$ and $d\mathbf{R}^N = dR_1 \cdots dR_N$. We do not ascribe any internal *PF* to the particles. (In the primitive model, we choose $h = 1$, $k_B = 1$, and $m = 1$.) The integration for each particle ranges from 0 to L . In a 1-D system, we can *order* the particles and rewrite the configurational *PF* as

$$\begin{aligned} & \frac{1}{N!} \int_0^L \cdots \int_0^L d\mathbf{R}^N \exp[-\beta U_N(\mathbf{R}^N)] \\ &= \int_0^L dR_N \int_0^{R_N} dR_{N-1} \cdots \int_0^{R_2} dR_1 \exp[-\beta U_N(\mathbf{R}^N)] \end{aligned} \quad (2.5.5)$$

Note that once the particles are ordered, they can be labeled as first, second, etc., and we can delete the factor $N!$.

One can take the Laplace transform of the right-hand side of (2.5.5), which transforms from the variables T, L, N into the variables T, P, N , where P is the one-dimensional pressure.

Denoting by

$$\psi_{ww}(P, T) = \int_0^\infty dR \exp[-\beta PR - \beta U_{ww}(R)] \quad (2.5.6)$$

we can apply the convolution theorem to obtain the isothermal-isobaric PF ,⁴¹ namely

$$\Delta(T, P, N) = \frac{\psi_{ww}^N(P, T)}{\Lambda^N} \quad (2.5.7)$$

Thus, for any given pair potential $U(R)$, we can calculate the PF (2.5.7), and from there all the thermodynamic quantities. The fundamental relation between $\Delta(T, P, N)$ and the Gibbs energy of the system is

$$G(T, P, N) = -T \ln \Delta(T, P, N) \quad (2.5.8)$$

2.5.3. *Selected illustrative results for the primitive model*

In this section, we present some results for the thermodynamic quantities for the 1-D model of particles interacting through the potential function (2.5.1) (Fig. 2.10d). We shall compare these results with results for a reference liquid which consists of hard rods (HR). The interaction between the particles in the “normal” reference system is (Fig. 2.10a)

$$U_{HR}(R) = \begin{cases} \infty & 0 \leq R < \sigma_1 \\ 0 & R \geq \sigma_1 \end{cases} \quad (2.5.9)$$

⁴¹For details, see Ben-Naim (1992).

Hence

$$\begin{aligned}\psi_{HR} &= \int_0^\infty dR \exp[-\beta PR - \beta U_{HR}(R)] \\ &= \frac{\exp[-\beta P\sigma_1]}{\beta P}\end{aligned}\quad (2.5.10)$$

We shall refer to the reference system of the *HR* system and the water-like system as the *HB* system.

(i) Temperature dependence of the average volume

We start with the most unusual and well-known property of liquid water: the temperature dependence of the molar volume.

The molar “volume” is the average length per particle and is given by

$$\langle l \rangle = \frac{\langle L \rangle}{N} = \frac{1}{N} \frac{\partial G}{\partial P} = \frac{\partial \mu}{\partial P} \quad (2.5.11)$$

In Fig. 2.11, we show the temperature dependence of the average length per particle $\langle L \rangle/N$ as a function of temperature for the following parameters:

$$\sigma_1 = 1, \quad \sigma_2 = 2, \quad \delta_2 = 0.3, \quad \varepsilon_{HB} = -10 \quad (2.5.12)$$

As expected, for the *HR* system, the average volume always increases with temperature both at low and at high pressures. Note also that in the limit of $T \rightarrow 0$, the molar volume of the *HR* system tends to $\sigma_1 = 1$, as expected. On the other hand, for the water-like molecules, interacting through the pair potential $U_{ww}(R)$, Eq. (2.5.1), we find a quite different behavior.

First, note that at low pressure and high temperature, the system behaves “normally,” i.e. the molar volume increases monotonically with increasing temperature or decreasing pressure. On the other hand, in the limit of very low temperatures $T \rightarrow 0$, we have two distinctly different limiting volumes. At low pressures, the limit of the molar volume tends to σ_2 (here $\sigma_2 = 2$).

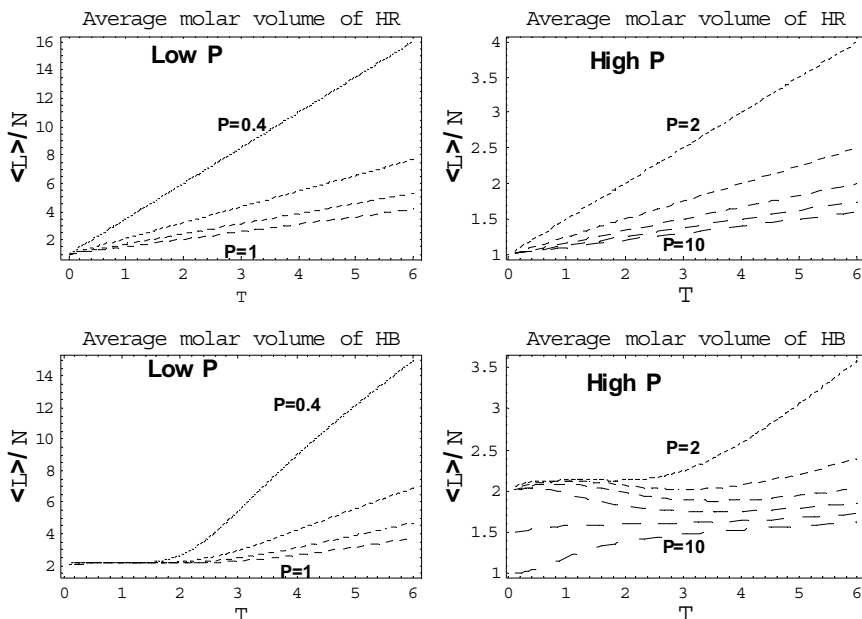


Fig. 2.11 The temperature dependence of the average length per particle (the molar “volume”) as a function of the temperature for a few values of the pressure. The upper panel corresponds to the reference hard particles or hard rods (*HR*), and the lower panel to the hydrogen bonded (*HB*) water-like system. In this figure, as well as in the following figures, we indicate only a few values of the pressure (or temperatures) next to the corresponding curves. The in-between curves have in-between pressures.

This corresponds to the “ice-like” open structure where all pairs attain the distance between σ_2 and $\sigma_2 + \delta_2$. On the other hand, at higher pressure (here $P \approx 9$), the limiting value of the molar volume is that of the close-packed system as in the case of the *HR* system.

The most interesting behavior, which is a direct result of the particular pair potential (2.5.1), is for pressures in the range $4 \leq P \leq 9$ and temperatures in the range $2 \leq T \leq 5$. In this range we observe a negative temperature dependence of the volume. This behavior is unique to liquid water and it is quite surprising

that such a “primitive” model exhibits the same behavior. On the other hand, it is not surprising to see such a behavior since the *principle* has been built into the model.

In the next section, we shall follow the molecular *reason* for this behavior. As we have learned in Sec. 2.4, by studying simple mixture models, the outstanding behavior of liquid water is due to *structural changes* (in the sense discussed in Sec. 2.4) that are induced by changing either the temperature or the pressure (or the added solute in Chapter 3).

Note that as the pressure increases, the location of the minimum of the volume initially shifts to the right (i.e. to higher temperature), then to the left, but becomes more and more shallow. At high pressures ($P \geq 9$), the minimum disappears, and the system's volume behaves “normally” (as is the case for real liquid water at high pressures). This is very similar to the experimental data on the temperature dependence of the volume shown in Fig. 1.22. More details on the molar volume as a function of pressure near the minimum is shown in Fig. 2.12.

The pressure dependence of the molar volume of the *HR* system and the water-like system is shown in Fig. 2.13. Note that for the *HR* system the molar volume is always a monotonically decreasing function of the pressure. On the other hand, for the water-like system, as we decrease the temperature, the molar volume shows an almost phase transition from the open structure (of molar volume $\sigma_2 = 2$) to the close-packed structure (of molar volume $\sigma_1 = 1$). As the temperature is lowered, the transition becomes sharper and sharper.

Figure 2.14 shows the “isotope” effect on the temperature of a minimum volume of the system for three different values of the *HB* energy, $\varepsilon_{HB} = -8, -9, -10$. The results shown in Fig. 2.14 are qualitatively similar to the corresponding experimental data on H_2O , D_2O , and T_2O (shown in Fig. 1.21). Two important aspects of the volume minimum in Fig. 2.14 should be noted.

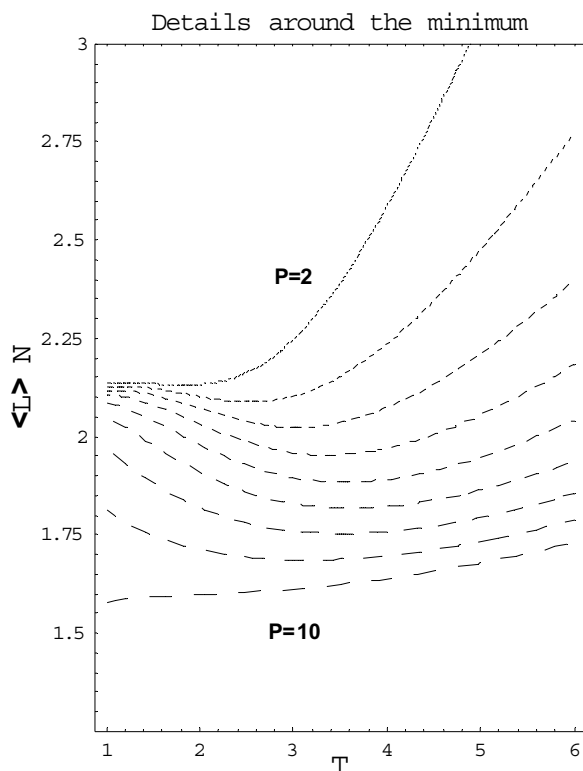


Fig. 2.12 Details of the temperature dependence of the molar volume near the minimum of the volume at various pressures.

First, upon increasing the *HB* energy (keeping all other parameters constant), the location of the minimum is shifted to the right. (It is well-known that H_2O and D_2O have almost exactly the same geometries, i.e. the OH distance and the HOH angles are the same. The only significant difference is the strength of the *HB* energy, which in the 1-D model is represented by the parameter ε_{HB} .) Second, the molar volume of the “isotopes” in the neighborhood of the minimum increases with the strength of the *HB* energy. This reflects the higher degree of the “structure” of the system having the stronger *HB*s (though the geometry of

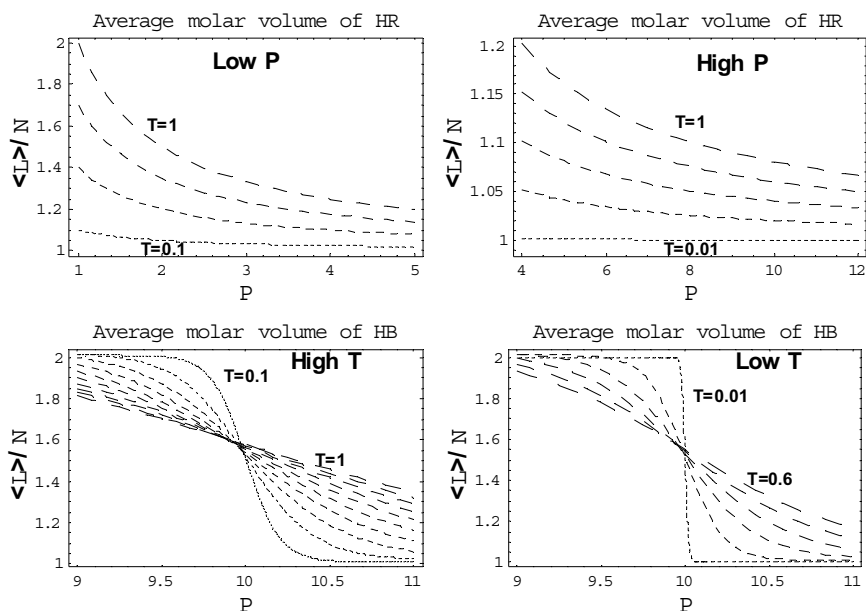


Fig. 2.13 The pressure dependence of the molar volume for different values of the temperature.

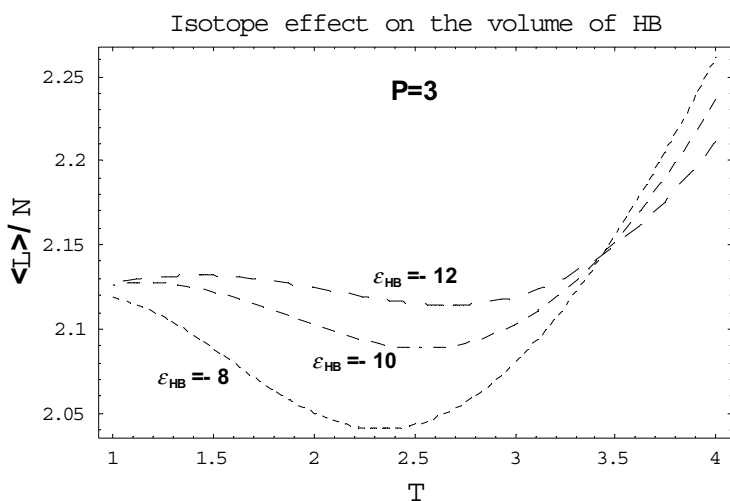


Fig. 2.14 The “isotope” effect on the molar “volume” near the minimum for three values of the HB energy parameter ϵ_{HB} .

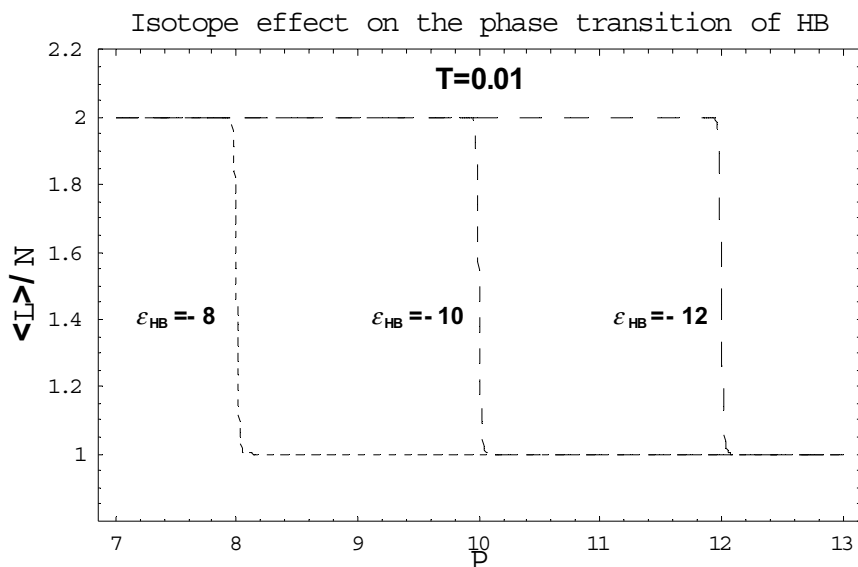


Fig. 2.15 The “isotope” effect on the pressure dependence of the “volume” of the water-like particles near the “phase transition.”

the HB is the same). These two features are similar to the isotope effect in real water. We shall further discuss the relation between the strength of the hydrogen bond and the degree of structure of the system in Sec. 2.7.

Finally, we show in Fig. 2.15 the “isotope” effect on the pressure dependence of the volume near the phase transition. We chose one low temperature $T = 0.01$ and plotted the volume as a function of pressure for the three values of $\epsilon_{HB} = -8, -10, -12$. In the three cases, there is a sharp transition from the open structure to the close-packed structure as we increase the pressure. The location of the transition-pressure is different for the different cases. As $|\epsilon_{HB}|$ increases, i.e. the HB s are stronger, the open-structure becomes more stable, and a higher pressure is required to produce the transition.

(ii) The isothermal compressibility

The isothermal compressibility in the 1-D system is defined by

$$\kappa_T = -\frac{1}{\langle L \rangle} \left(\frac{\partial \langle L \rangle}{\partial P} \right)_T \quad (2.5.13)$$

where $\langle L \rangle$ is the average volume of the system in the T, P, N ensemble. Figure 2.16 shows some results for the dependence of the compressibility as a function of temperature for the systems of HRs and water-like particles. For the HRs, the isothermal compressibility is a monotonically increasing function of temperature. It tends to zero at very low temperature (solid phase). At high temperatures, we obtain the expected “ideal gas”

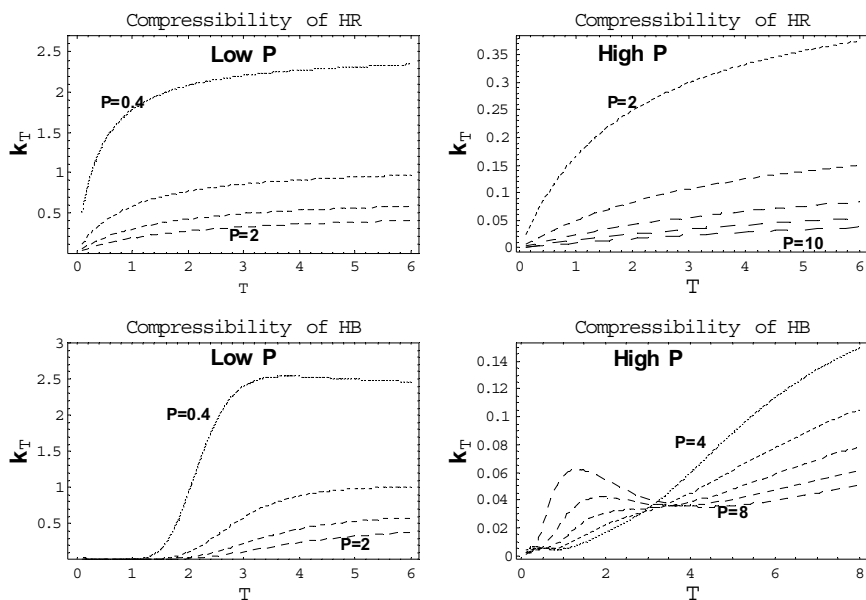


Fig. 2.16 The temperature dependence of the isothermal compressibility of the HR and the HB models.

behavior, i.e.

$$\kappa_T \rightarrow \frac{1}{P} \quad \text{at } T \rightarrow \infty \quad (2.5.14)$$

Normally, the compressibility decreases with increase in the pressure. However, for the *HB* system, at some range of temperatures ($2 \leq T \leq 3$) and pressures ($4 \leq P \leq 8$) we observe a different behavior. The compressibility shows a maximum followed by a minimum as a function of temperature. A more detailed examination of this behavior of the compressibility around the minimum shows that the minimum becomes shallower as we increase the pressure, and at about $P \approx 16$ it disappears. This is also the behavior of real liquid water. It was pointed out long ago by Bridgman⁴² that at high pressures water behaves “normally.”

The pressure dependence of the compressibility is shown in Fig. 2.17. The *HR* system exhibits “normal” behavior, i.e. κ_T decreases monotonically with increasing pressure. However, for the water-like system the behavior is quite different. The compressibility increases with pressure, reaches a maximum value, and then decreases. The high value of the compressibility at low temperatures and the intermediate pressure of $P \approx 10$ is a result of large fluctuations in the volume near the phase-transition-like pressure we saw in Fig. 2.15. This typical behavior is completely absent in the *HR* system. Note also that liquid water has a relatively small value of compressibility compared to other “normal” liquids. In the two-structure model, a negative contribution to the compressibility is obtained from structural rearrangement in the system induced by changes in the pressure (see Sec. 2.4). In the next section, we shall study the possible molecular “mechanism” that determines the value of the compressibility.

⁴²Bridgman (1912).

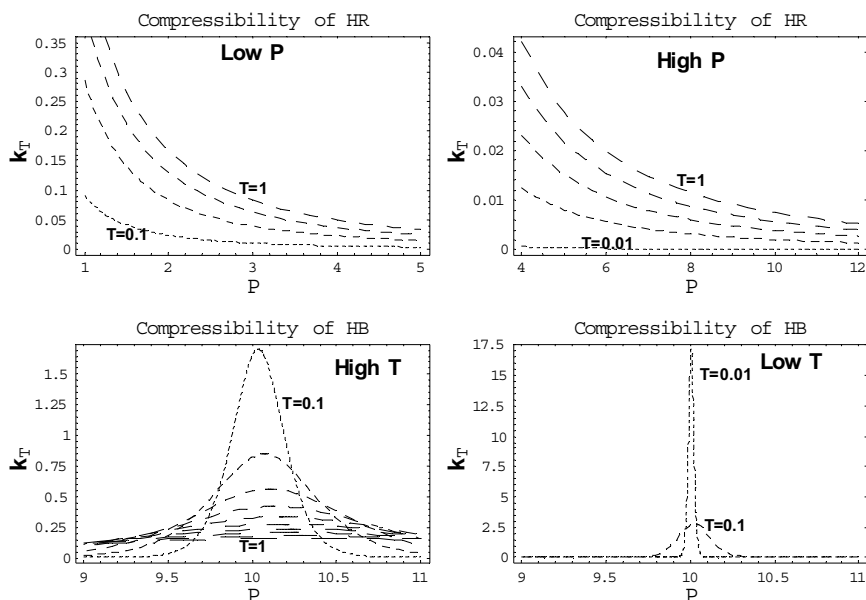


Fig. 2.17 The pressure dependence of the isothermal compressibility for the HR and the HB models.

In Fig. 2.18, we show the isotope effect on the compressibility near the minimum for three different values of the *HB* energy, $\varepsilon_{HB} = -8, -10, -12$. The location of the minimum first shifts to the right (towards higher T), then to the left. In all cases, the minimum is deeper for larger values of the *HB* energy. This is in contrast with the experimental data on real light and heavy water⁴³ (see also Fig. 1.26).

Finally, in Fig. 2.19, we show the “isotope” effect on the compressibility at and around the maximum for two temperatures. The three curves correspond to the same model with the same parameters but varying the strength of the hydrogen bond energy, $\varepsilon_{HB} = -8, -10, -12$. It is interesting to note that the *value* of the maximum compressibility is almost unchanged,

⁴³Millero and Lepple (1970, 1971).

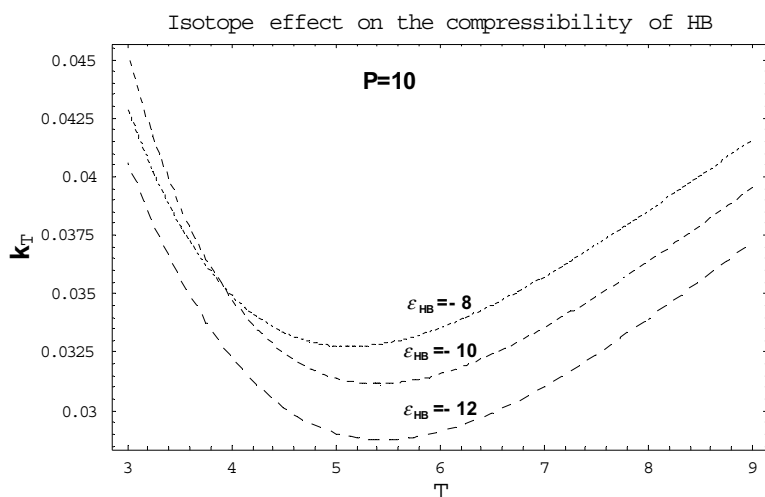


Fig. 2.18 The “isotope” effect on the isothermal compressibility near the minimum.

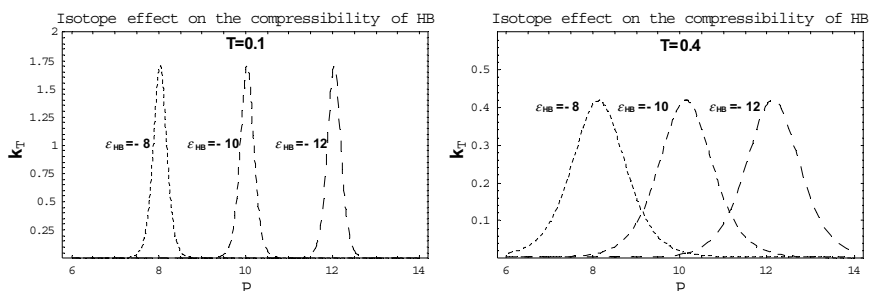


Fig. 2.19 The “isotope” effect on the isothermal compressibility of the *HB* model as a function of pressure at two temperatures.

but the location of the maximum is shifted to high pressures as we increase the hydrogen bond energy. Similar curves for $T = 0.4$ are shown in the same figure. The trend is the same, however. The value of the maximum compressibility is smaller and the width of each curve is much larger than at the lower temperature. Again, an understanding of these phenomena at a

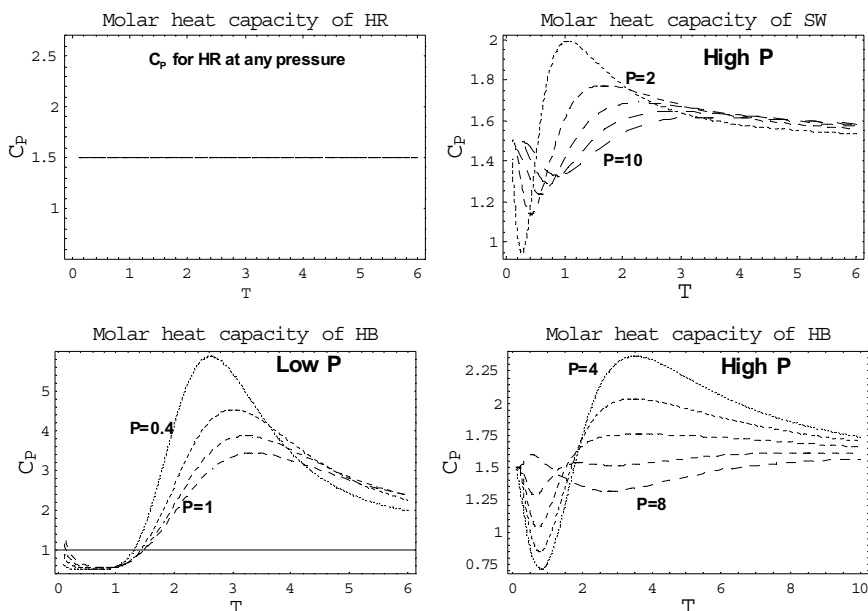


Fig. 2.20 The molar heat capacity of the *HR*, *SW*, and *HB* models as a function of the temperature for different pressures.

molecular level is rendered possible through the mixture-model approach to liquid water.

(iii) The heat capacity at constant pressure

Figure 2.20 shows the molar heat capacity computed from the second derivative of the chemical potential

$$C_p = \frac{\partial(H/N)}{\partial T} = T \frac{\partial(S/N)}{\partial T} = -T \frac{\partial^2 \mu}{\partial T^2} \quad (2.5.15)$$

Note that for the *HR* system, the chemical potential is

$$\mu = k_B T \ln \Lambda / \psi_{HR} \quad (2.5.16)$$

with

$$\psi_{HR} = \frac{\exp[-\beta P \sigma_1]}{\beta P} \quad (2.5.17)$$

Therefore, the molar heat capacity is constant (note $k_B = 1$):

$$C_P = \frac{3}{2} \quad (2.5.18)$$

In Fig. 2.20, we also show the molar heat capacity for a square-well (SW) potential with $\sigma_1 = 1$ and $\varepsilon = -1$. Here also, we have a maximum of molar heat capacity of about two. The “additional” heat capacity in this case is due to the “structural changes” induced by the change in temperature. These structural changes occur in any liquid, as was discussed in Sec. 2.4.

For the *HB* system, we observe a much larger heat capacity at low pressures, but not at high pressures. As we have seen in Sec. 2.4, the large values of the heat capacity of real water is due to the large difference in the enthalpy of the two components, or equivalently the large fluctuations in the enthalpy of the system. In Fig. 2.21, the molar heat capacity for the two models — the *SW* and the *HB* models with $\varepsilon = -1, \dots, -10$ — are shown as a function of temperature at $P = 2$. Note that the curves in this case are almost the same for the *SW* and the *HB* systems. The larger ε (or ε_{HB}) is, the larger the heat capacity is. This is an important observation and is in accordance with the conclusion reached in Sec. 2.4, namely that the large heat capacity depends

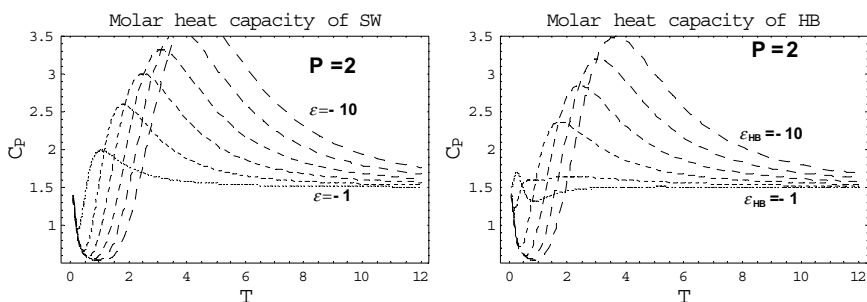


Fig. 2.21 The molar heat capacity of the *SW* and the *HB* models.

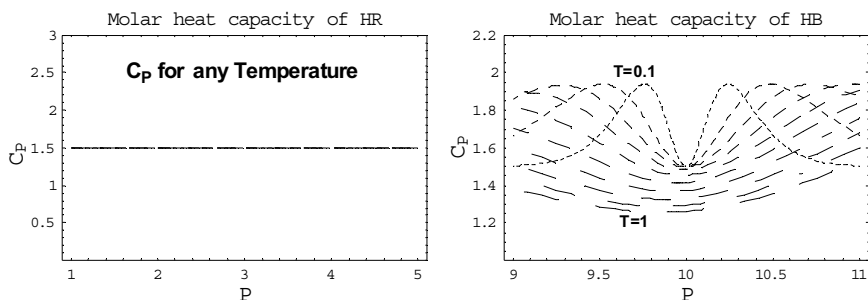


Fig. 2.22 The pressure dependence of the molar heat capacity of the *HR* and *HB* models at different temperatures.

only on the strength and the spread of the values of the binding energies of the species in the system, and not on the particular correlation between local density and local binding energy.

The pressure dependence of the heat capacity for the *HR* and the *HB* models is shown in Fig. 2.22. As expected for the *HR* model, $C_p = 1.5$ and is independent of the pressure and the temperature. For the *HB* system, the behavior is much more complex but it is not similar to the dependence of the heat capacity for real water in the range of T and P for which water is liquid.

(iv) The average number of hydrogen bonds in the primitive model

As we have discussed in Sec. 2.4 the best way of understanding the behavior of liquid water, as well as its solutions, is to follow the “structural changes” in the system — as we change the temperature or the pressure (and the solute concentration in the case of solutions; see Chapter 3). In this primitive model, the simplest way to follow the “structural changes” is through the average number of *HBs* in the system. This is simply defined as the average number of pairs of nearest-neighbor particles which are at a distance between σ_2 and $\sigma_2 + \delta_2$. The probability distribution for the nearest-neighbor distances can be obtained directly from

the partition function (2.5.7) by taking the functional derivative of the PF with respect to the pair potential.⁴⁴ In the 1-D model, the result is

$$\text{Pr}(R) = \frac{\exp[-\beta PR - \beta U_{ww}(R)]}{\int_0^\infty \exp[-\beta PR - \beta U_{ww}(R)] dR} \quad (2.5.19)$$

The average number of $H\text{Bed}$ pairs per particle is obtained from (2.5.19) by simply integrating over the range of distances between σ_2 and $\sigma_2 + \delta_2$ ⁴⁵:

$$\langle X_{HB} \rangle = \frac{\int_{\sigma_2}^{\sigma_2 + \delta_2} \exp[-\beta PR - \beta U_{ww}(R)] dR}{\int_0^\infty \exp[-\beta PR - \beta U_{ww}(R)] dR} \quad (2.5.20)$$

Figure 2.23 shows the average number of HB s per water molecule as a function of temperature. At low pressures and low temperatures, the system is initially fully $H\text{Bed}$, and the average number of HB s decreases with increasing temperature. At higher pressures, the behavior is quite different. At pressures

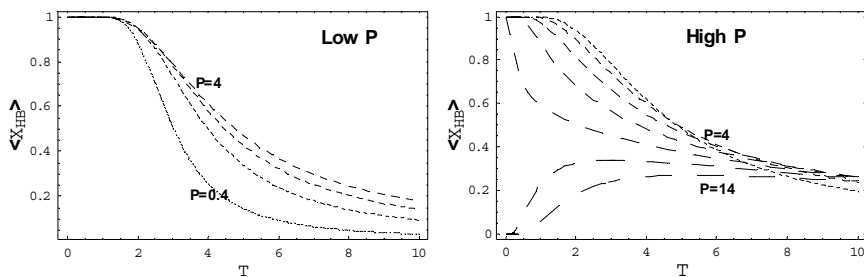


Fig. 2.23 The average number of HB s per particle as a function of temperature for the primitive model at different pressures.

⁴⁴For details, see Ben-Naim (2006).

⁴⁵This is the probability of finding two *consecutive* particles within a range of distances between σ_2 and $\sigma_2 + \delta_2$. Therefore, this is also the mole fraction of nearest neighbors that are hydrogen bonded. Since the number of nearest-neighbor bonds is equal to the number of particles in the system, the quantity $\langle X_{HB} \rangle$ is also the average number of HB s per particle in the system.

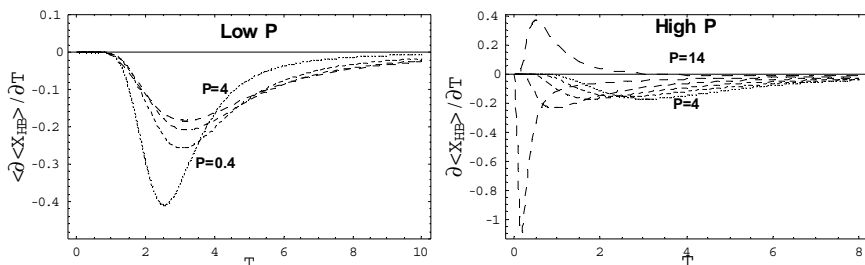


Fig. 2.24 The slope of $\langle X_{HB} \rangle$ with respect to temperature at low and high pressures.

above $P = 10$, the system starts with zero HB s, and the average number of HB s increases with increasing temperature. For the purposes of understanding the anomalous behavior of water, we need to follow the slope of the quantity $\langle X_{HB} \rangle$ with respect to temperature. This is shown in Fig. 2.24. Note that in the range of interest, i.e. for $2 < T < 3$ and $0.4 < P < 4$, we find a negative slope, corresponding to the breaking of the HB s upon the raising of the temperature. A different behavior is observed at higher pressures.

The pressure dependence of the average number of HB s is shown in Fig. 2.25a. Again, we see a sharp transition from the fully HB ed system to the fully non- HB ed system, similar to the transition we observed in Fig. 2.15. The derivative of the quantity $\langle X_{HB} \rangle$ with respect to temperature, as recorded in Fig. 2.24a, is shown in Fig. 2.25b, but now as a function of pressure.

Note that at high temperature the slope is almost zero and pressure independent. On the other hand, at low temperature ($T = 0.01$) there is a sharp transition from negative to positive slope as we cross a pressure of about $P \approx 12.5$.

In the next section, we shall examine in more detail the “structural changes” that occur in the system using the primitive cluster model. The information relevant to understanding the behavior of water is the same in the two models. The only

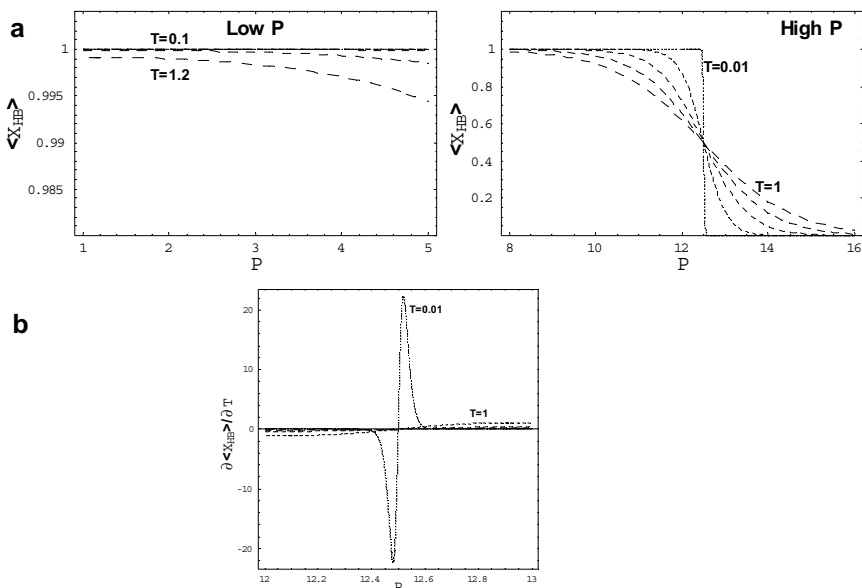


Fig. 2.25 The pressure dependence of $\langle X_{HB} \rangle$.

difference is that with the cluster model it is easier to calculate not only the average number of HBs but also the concentration of each type of cluster.

(v) Pair correlation function

In Fig. 2.26 we show the pair correlation function $g(R)$ for the square-well potential (Fig. 2.10b) and for the primitive model (Fig. 2.10d).⁴⁶ These two should represent the “normal” liquid and the “water-like” liquid. Note that in the case of the “normal” liquid (Fig. 2.26a) the height of the first peak of $g(R)$ *increases* as we increase the density of the liquid. We have seen this behavior in Sec. 1.4, Fig. 1.28.

As can be seen in Fig. 2.26a at very low density ($\rho = 0.001$), $g(R) = \exp[-\beta U(R)]$. As the density increases, the height of the

⁴⁶The calculations of $g(R)$ were made with a computer program prepared by Andres Santos, for which I am very grateful.

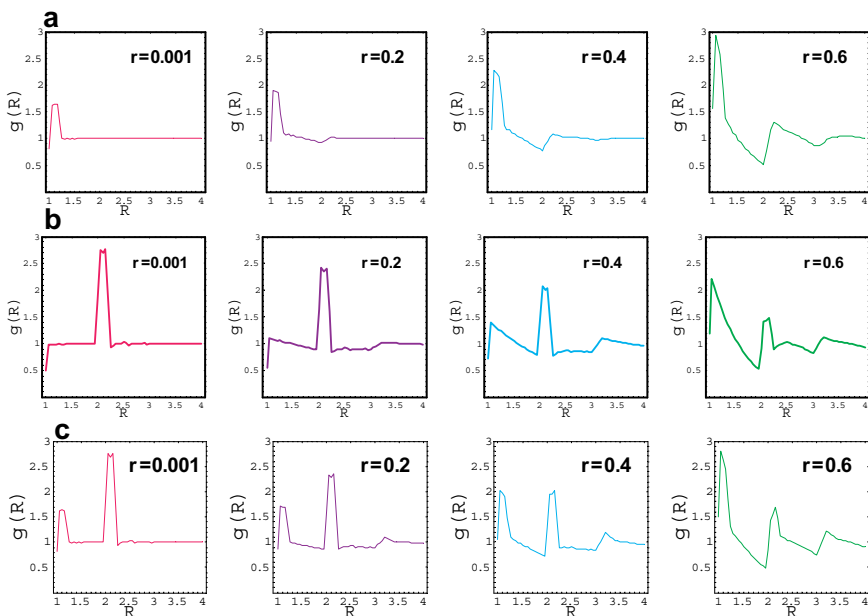


Fig. 2.26 The pair correlation function for 1-D models: (a) square-well potential with $\sigma = 1$ and $\varepsilon/k_B T = 0.5$, (b) primitive model with $\sigma_2 = 2\varepsilon_{HB}/k_B T = -1$ and (c) double-well potential with $\varepsilon_{HB}/k_B T = -0.5$ and $\varepsilon_{HB}/k_B T = -1$.

first peak *increases*. At the same time, a second and a third peak at 2σ and 3σ , etc. develop. This is the behavior of a normal liquid of simple spherical particles.

In Fig. 2.26b we show the pair correlation function for the primitive model for water (see Fig. 2.10d). Here, we see a strong peak at $R = 2$ corresponding to the *HB*ing distance. The height of this peak *diminishes* as we increase the density while a new peak at $R = 1$ develops. At $\rho = 0.6$, the peak at $R = 1$ is even higher than the one at $R = 2$. Clearly, at this density the average intermolecular distance is smaller than $R = 2$, and hence the particles are more closely packed.

In real water we observe only one peak at about $R = 2.8 \text{ \AA}$. The reason is that the “hard-core” diameter and the distance of

*H*Bing are very close to each other, and therefore the $g(R)$ does not resolve into two peaks. We shall see similar phenomena for water-like particles in Sec. 2.6.

In Fig. 2.26c we also show the pair correlation function for the double-well potential (Fig. 2.10c). Again, we see that initially the peak at $R = 2$ is higher but as the density increases a new peak develops at $R \approx 1$ and becomes dominant at $\rho = 0.6$.

2.5.4. *The primitive cluster model for water and its partition function*

In this section, we introduce what is essentially an equivalent model to the one described in Sec. 2.5.2. This model, referred to as the primitive cluster model, has several features that make it more useful in the study of the molecular “mechanism” underlying the anomalous behavior of liquid water and aqueous solutions. For water, as we shall see below, the two models provide essentially the same results. However, with the cluster model, we can get a deeper insight into the “mechanism” underlying the anomalies of water, namely the structural changes (here, essentially the change in the cluster-size distribution) in the liquid that lead to the anomalous behavior. As we shall see in Sec. 3.9, the cluster model is also more convenient for the study of some of the most outstanding properties of aqueous solutions of simple solutes.

The model is a simplified version of a model first developed by Lovett and Ben-Naim (1969). The idea is to define a sequence of n *H*Bed particles as an n -cluster (mimicking the ice-like clusters of *H*Bed molecules in liquid water). In doing so, we include all the *H*Bing in the cluster as part of the “internal” partition function of the n -cluster. The interaction potential between any pair of clusters (including the 1-cluster, i.e. the monomers, or non-*H*Bed particle), is now the hard-rod (*HR*) potential. (In the original model, this part was chosen to be a square-well potential. As with the primitive model discussed in Sec. 2.5.2, the

primitive version of the model discussed in this section removes the square-well potential and leaves only the *HR* repulsive part.)

The primitive cluster model is essentially the same as the primitive model as depicted in Fig. 2.9a. We could have left all the interactions between the particles exactly the same as in the primitive models, in which case the models would be identical except for the two different views of the system, the one-component and the *MM* views. As we have seen in Sec. 2.3, these two views are completely equivalent. In Fig. 2.9b the primitive cluster model is depicted. Clearly, the only difference is in renaming a sequence of *HBed* molecules as a cluster. For computational simplicity, we also assume that the interactions between all non-*HBed* particles are simply the *HR* types of potential.

We present a brief derivation of the partition function for the cluster model. It is basically the same as the one derived by Lovett and Ben-Naim (1969), except for the simplification of the pair interactions. In the following, we treat the case of pure water. We shall revert to this model for the study of aqueous solutions in Sec. 3.9.

The system consists of monomers, the interaction potential between which is the *HR* potential as described in Sec. 2.5.2. In addition, we have clusters of different sizes. An *n*-cluster consists of *n* monomers connected by “hydrogen bonds.” Once we have defined a cluster as a sequence of *HBed* monomers, the system may be viewed as a mixture of different species: monomers, 2-clusters, 3-clusters, etc. The grand partition function for such a fluid mixture is

$$\begin{aligned} & \Xi(T, L, \lambda_1, \dots, \lambda_N) \\ &= \sum_{N_1, N_2, \dots, N_n=0}^{\infty} \prod_{i=1}^n \frac{\lambda_i^{N_i}}{N_i! \Lambda_i^{N_i}} \\ & \quad \times \int_0^L \dots \int_0^L d\mathbf{R}^{N_1} \dots d\mathbf{R}^{N_n} \exp[-\beta U_N] \end{aligned} \quad (2.5.21)$$

where U_N is the total potential energy of interaction in the system. We assume that the maximal size of the cluster is n . In principle, one can take $n = \infty$, but for very large n the probability of such a cluster becomes negligibly small.

For the HB potential within the cluster, we simply take a harmonic potential of the form $U_{HB}(R) = \frac{1}{2}k(R - a)^2$, and an energy parameter ε_{HB} (Fig. 2.27). We also denote

$$\eta(T, P) = \exp[-\beta\varepsilon_{HB}]\psi_{HB}$$

$$\psi_{HB} = \int_0^\infty dR \exp[-\beta PR - \beta \frac{k}{2}(R - a)^2] \quad (2.5.22)$$

There is a standard procedure to proceed from (2.5.21) to obtain the Laplace transform of the grand partition function with respect to the length variable L ,⁴⁷ i.e.

$$\psi[\Xi(T, L, \lambda)] = \int_0^\infty \exp[-\beta PL] \Xi(T, L, \lambda) \quad (2.5.23)$$

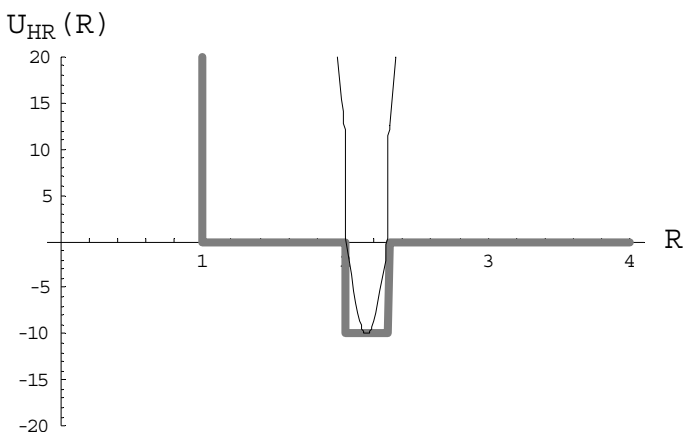


Fig. 2.27 The potential of the HB in the primitive model (thick line) and the harmonic potential between monomers forming a cluster of HB ed molecules (thin line).

⁴⁷For details, see Ben-Naim (1992).

By choosing a specific ordering of the species then applying the convolution theorem, the Laplace transform of the grand partition function can be rewritten as

$$\psi[\Xi(T, L, \lambda)] = \sum_{N=0}^{\infty} \text{Tr}[\mathbf{M}^N] \quad (2.5.24)$$

where $\text{Tr}[\mathbf{M}^N]$ is the trace of the matrix $\mathbf{M}^N$. The elements of the symmetric matrix $\mathbf{M}$ are

$$\begin{aligned} M_{1,1} &= \frac{\lambda_1}{\Lambda_1} \psi_{HR} \\ M_{1,n} &= M_{n,1} = \left[\frac{\lambda_1 \lambda_n}{\Lambda_1^{n+1}} \psi_{HB}^{n-1} \exp[-\beta(n-1)\varepsilon_{HB}] \right]^{1/2} \psi_{HR} \\ M_{n,m} &= M_{m,n} = \left[\frac{\lambda_n \lambda_m}{\Lambda_1^{n+m}} \psi_{HB}^{n+m-1} \exp[-\beta(n+m-1)\varepsilon_{HB}] \right]^{1/2} \psi_{HR} \end{aligned} \quad (2.5.25)$$

where ψ_{HB} is defined in (2.5.22). Note that a factor ψ_{HR} is assigned to each interaction between adjacent clusters, and a factor ψ_{HB} is assigned for an HB within the cluster.

If γ_i is the i th eigenvalue of the matrix $\mathbf{M}$, then we can rewrite (2.5.24) as

$$\psi[\Xi(T, L, \lambda)] = \sum_i \sum_{N=0}^{\infty} \gamma_i^N = \sum_i (1 - \gamma_i)^{-1} \quad (2.5.26)$$

Normally, to recover the grand partition function, one needs to take the inverse Laplace transform of (2.5.26). However, in our case, we can view the Laplace transform of $\Xi(T, L, \lambda)$ as the “generalized” partition function, and we can obtain all the thermodynamic quantities of the system from the eigenvalues of the matrix $\mathbf{M}$.⁴⁸

⁴⁸See, for example, Fisher (1961) and Ben-Naim (2008c).

Define the auxiliary quantities

$$t_1^2 = \frac{\lambda_1}{\Lambda_1} \quad \text{and} \quad t_n^2 = \frac{\lambda_n}{\Lambda_n} \psi_{HB}^{n-1} \exp[-\beta(n-1)\varepsilon_{HB}]. \quad (2.5.27)$$

The matrix $\mathbf{M}$ can be transformed into

$$\mathbf{M} = \psi_{HR} \begin{pmatrix} t_1^2 & t_1 t_2 & t_1 t_3 \\ t_1 t_2 & t_2^2 & t_2 t_3 \\ \vdots & \vdots & \vdots \end{pmatrix} \quad (2.5.28)$$

Fortunately, this matrix can be transformed by an orthogonal transformation into a matrix of the form⁴⁹

$$\mathbf{M}' = \psi_{HR} \begin{pmatrix} \sum t_i^2 & 0 & 0 & 0 & \cdots \\ 0 & 0 & 0 & 0 & \\ 0 & 0 & 0 & 0 & \end{pmatrix} \quad (2.5.29)$$

Clearly, this matrix has only one eigenvalue, γ , which is obtained from

$$\psi_{HR} t^2 - \gamma = 0 \quad (2.5.30)$$

where $t^2 = \sum_{i=1}^{\infty} t_i^2$.

In order to use the Laplace transform of the grand partition function in (2.5.26), γ must be equal to 1; hence, the sum on the right-hand side of (2.5.26) diverges.⁵⁰ This leads to the implicit equation of state of the form

$$\psi_{HR}(T, P) t^2(T, P, \lambda) = 1 \quad (2.5.31)$$

Note that in this equation of state t^2 is a sum over all the clusters in the system viewed as different components. Because of the chemical equilibrium among all the species, we must have $\mu_i = i\mu_1$, or equivalently $\lambda_i = \lambda_1^i$, where λ_1 is the absolute activity of the monomers, which is also the absolute activity of

⁴⁹Note that the trace of the matrix $\mathbf{M}$ is the same as that of $\mathbf{M}'$.

⁵⁰For details, see Ben-Naim (1992).

water (when all the clusters are at equilibrium). After inserting the condition of chemical equilibrium into t^2 , we can now carry out the summation over all species i :

$$t^2 = \sum_{i=1}^{\infty} t_i^2 = \frac{\lambda_1}{\Lambda_1} + \sum_{i=2}^{\infty} \frac{\lambda_1^i}{\Lambda_1^i} \eta^i = \frac{\lambda_1/\Lambda_1}{1 - \eta\lambda_1/\Lambda_1} \quad (2.5.32)$$

At this stage, we have only one absolute activity, i.e. the system is viewed as one component. We write $\lambda = \lambda_1$ and rewrite the equation of state (2.4.31) as

$$\psi_{HR}(T, P) \frac{\lambda/\Lambda_1(T)}{1 - \eta(T, P)\lambda/\Lambda_1(T)} = 1 \quad (2.5.33)$$

This is an implicit equation from which we can eliminate the chemical potential μ in the form

$$\mu(T, P) = T \ln \lambda = T \ln \left[\frac{\Lambda_1}{\psi_{HR} + \eta} \right] \quad (2.5.34)$$

where

$$\psi_{HR} = \int_0^{\infty} \exp[-\beta PR] \exp[-\beta U_{HR}(R)] dR = \frac{\exp[-\beta P\sigma_1]}{\beta P} \quad (2.5.35)$$

From the chemical potential, we can get all the required thermodynamics of the system. As we have pointed out earlier, by choosing σ_1 and ε_{HB} as in the primitive model and choosing a to be equal to $\sigma_2 + \delta_2/2$, in the primitive model there remains only one parameter, the force constant k , to be chosen in such a way that the results of this model will be almost identical to the results obtained in Sec. 2.5.3.

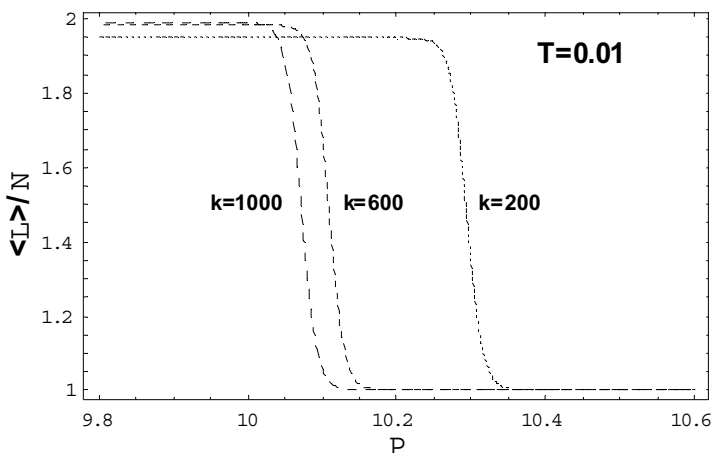


Fig. 2.28 The pressure dependence of the volume for the primitive cluster model as in Fig. 2.13 but for different choices of the force constant k in Eq. (2.5.22).

Formally, the identity of the two models, for a fixed T and P , can be obtained by requiring that ψ_{ww} of Sec. 2.5.6 be equal to

$$\psi_{ww} = \psi_{HR} + \eta \quad (2.5.36)$$

Once we have chosen the parameters $\sigma_1, \sigma_2 = a, \delta_2$ and ϵ_{HB} , with some experimentation, one finds that with $k = 1000$ one gets almost identical results to those obtained in Sec. 2.5.2. We show in Fig. 2.28 one example of the dependence of the volume as a function of pressure for different values of k . It is clear that the qualitative form of the curves is similar to that in Fig. 2.13. Note, however, that the larger the k value, the closer the limit of the volume to two. This is so because the HB in this case is more sharply defined (see Fig. 2.27).

2.5.5. Cluster's size distribution

We now turn to examining the cluster's size distribution and its dependence on T and P . To do this, we need to go back

to the equation of state in (2.5.31) *before* the insertion of the equilibrium condition. We write the equation of state as

$$F(T, P, \lambda) = \psi_{HR}(T, P) \sum_{i=1}^{\infty} t_i^2(T, P, \lambda_i) = 1 \quad (2.5.37)$$

where all the λ_i here are considered as independent variables (this is equivalent to a system where the equilibrium among all the species is frozen in). The Gibbs–Duhem relation is

$$SdT - LdP + \sum N_i d\mu_i = 0 \quad (2.5.38)$$

from which we can obtain all the densities of all the species:

$$\rho_i = \frac{N_i}{\langle L \rangle} = - \frac{\partial F / \partial \mu_i}{\partial F / \partial P} = \frac{- \frac{\partial F}{\partial \lambda_i} \frac{\partial \lambda_i}{\partial \mu_i}}{\partial F / \partial P} \quad (2.5.39)$$

After the differentiation of F with respect to λ_i , we can insert the condition of equilibrium $\lambda_i = \lambda^i$ to obtain the densities at *equilibrium*. This leads to

$$\rho_j = \frac{-\beta \lambda^j \eta(T, P)^{j-1}}{\Lambda^j \partial F / \partial P} \quad (2.5.40)$$

The total number of water molecules is

$$\rho_w = \sum_{i=1}^{\infty} i \rho_i \quad (2.5.41)$$

We now define the mole fraction of the j -clusters as

$$X(j) = \frac{\rho_j}{\sum_{i=1}^{\infty} i \rho_i} \quad (2.5.42)$$

Note that the normalization of $X(j)$ is

$$\sum_{j=1}^{\infty} j X(j) = 1 \quad (2.5.43)$$

Since an n -cluster contains $(n - 1)$ hydrogen bonds, the average number of HBs per particle is

$$\langle X_{HB} \rangle = \frac{\sum (j - 1)\rho_j}{\sum i\rho_i} = \sum_j (j - 1)X(j) \quad (2.5.44)$$

It is easily shown that $X(j)$ is related to $\langle X_{HB} \rangle$ by the relation⁵¹

$$X(j) = \frac{(1 - \langle X_{HB} \rangle)^2}{\langle X_{HB} \rangle^{j-1}} \quad (2.5.45)$$

2.5.6. Selected results for the primitive cluster model

In this section, we present some results on the cluster-size distribution and related quantities. The calculations are performed for the following set of parameters:

$$\sigma_1 = 1, \quad \sigma_2 = a = 2, \quad k = 1000, \quad \varepsilon_{HB} = -10 \quad (2.5.46)$$

Figure 2.29 shows the mole fraction of monomers that are engaged in the j -cluster, $jX(j)$, as a function of j . As expected, at low temperatures the distribution is very broad, but as the temperature increases the larger clusters “melt down” and the distribution becomes sharper, and eventually all the molecules become monomeric, i.e. $j = 1$.

More detailed temperature dependence for each type of cluster is shown in Fig. 2.30. As expected, the mole fraction of the monomers increases monotonically as a function of T , eventually reaching $X(1) = 1$ at high temperatures.

For $j \neq 1$, there is initially an increase in the mole fraction $X(j)$, but it eventually decreases at very high temperature. As expected, the larger the cluster size, the lower the maximum of $X(j)$. Figure 2.30 shows the temperature dependence of $X(j)$ for three sets of j : small, intermediate, and large.

⁵¹Lovett and Ben-Naim (1969).

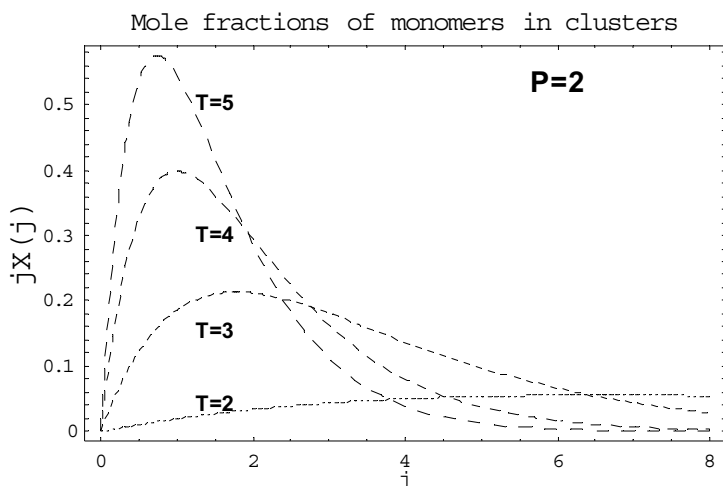


Fig. 2.29 The mole fraction of monomers $jX(j)$ participating in various j -clusters.

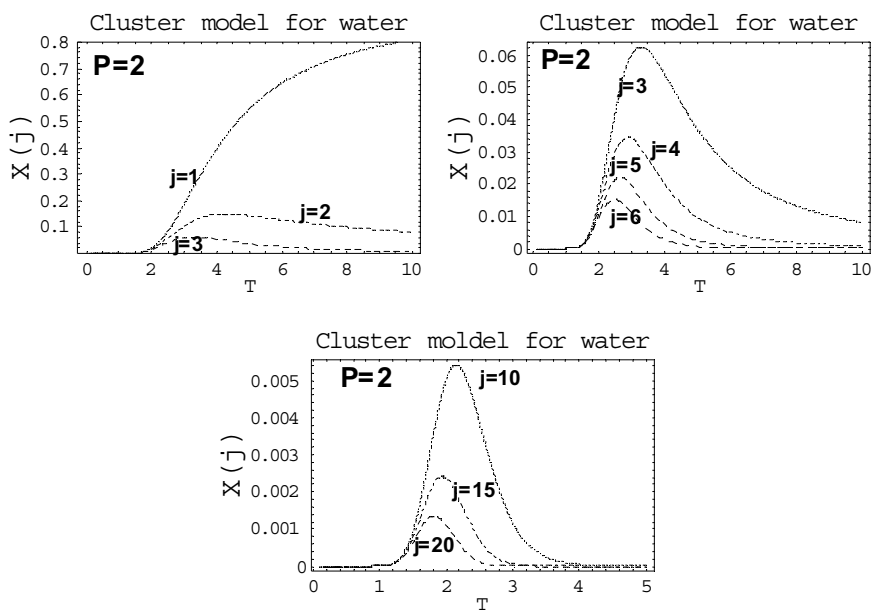


Fig. 2.30 The dependence of the mole fractions of the clusters $X(j)$ on the temperature for different cluster sizes j .

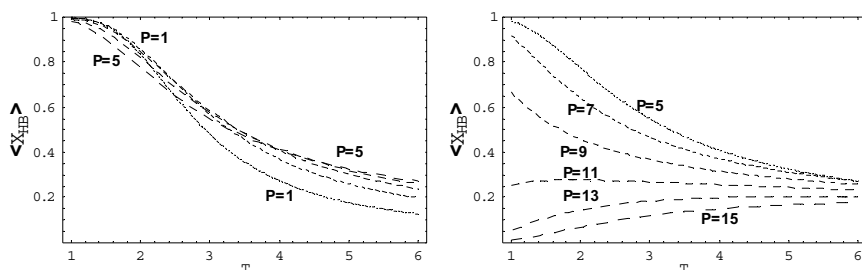


Fig. 2.31 The temperature dependence of the average number of *HBs* per molecule at different pressures.

The overall “structural changes” in this system are captured by the quantity $\langle X_{HB} \rangle$. This is the analog of the average number of *HBs* per particle, as discussed in Sec. 2.5.3, which in real liquid water is also a measure of the overall *structure* of the system.

Figure 2.31 shows the temperature dependence of $\langle X_{HB} \rangle$ for several values of the pressure. Note that at lower temperatures ($T \leq 2$), we find $\langle X_{HB} \rangle \approx 1$, i.e. almost all the particles in the system are *HBed*. Increasing the pressure causes a breakdown of *HBs*; hence, $\langle X_{HB} \rangle$ decreases. At higher temperature ($T \geq 4$), this trend is reversed, i.e. increasing the pressure causes the formation of more *HBs*. This behavior is typical for low pressures, $P \leq 10$. At higher pressures ($P \geq 11$) and low temperature, all the particles are close-packed with no *HBs*. Hence, as expected, increasing the temperature causes an increase in $\langle X_{HB} \rangle$.

In order to gain insight into the molecular mechanism underlying the anomalous behavior of liquid water (as well as of aqueous solutions, discussed in Chapter 3), we need to examine the temperature and the pressure derivatives of the quantity $\langle X_{HB} \rangle$. To see this, it is sufficient to consider a simple two-structure model for water. Let x_{HB} be the *HBed* component (or the ice-like species in the traditional mixture-model theories of water).

Then we can write the molar volume of water as (see Sec. 2.3):

$$V = x_{HB} \bar{V}_{HB} + (1 - x_{HB}) \bar{V}_{NHB} \quad (2.5.47)$$

where $\bar{V}_{HB}$ and $\bar{V}_{NHB}$ are the partial molar volumes of the *H*B₂O and non-*H*B₂O species, respectively. The temperature dependence of the volume is

$$\begin{aligned} \left(\frac{\partial V}{\partial T} \right)_P &= x_{HB} \frac{\partial \bar{V}_{HB}}{\partial T} + (1 - x_{HB}) \frac{\partial \bar{V}_{NHB}}{\partial T} \\ &\quad + (\bar{V}_{HB} - \bar{V}_{NHB}) \left(\frac{\partial x_{HB}}{\partial T} \right)_P \end{aligned} \quad (2.5.48)$$

The first two terms on the right-hand side of the equation are presumed to be positive (i.e. the two-component mixture would behave “normally” if the concentrations of the two species were constants). Since $(\bar{V}_{HB} - \bar{V}_{NHB})$ is presumed to be positive (due to the relatively more open structure of the *H*B₂O species), we can expect a large negative contribution from the third term on the right-hand side of Eq. (2.5.48). As we have seen in Sec. 2.3, in order to get a net negative temperature dependence of the molar volume, we need to get a large negative contribution from the third term on the right-hand side of Eq. (2.5.48). (Similar arguments apply to the compressibility, heat capacity, etc.) Therefore, in the next two figures we examine the quantities

$$\frac{\partial \langle X_{HB} \rangle}{\partial T} \quad \text{and} \quad \frac{\partial \langle X_{HB} \rangle}{\partial P} \quad (2.5.49)$$

in the range of temperatures and pressures where the system shows the characteristic anomalous behavior.

Figure 2.32 shows $\partial \langle X_{HB} \rangle / \partial T$ as a function of T for several pressures. This quantity measures the overall “structure changes” in the system caused by the increase of temperature. First, note that as expected, at low pressures this quantity is always negative (the “ice-like” component melts as the temperature increases). For each pressure, the quantity $\partial \langle X_{HB} \rangle / \partial T$ goes through a minimum. These minima correspond to the maximal

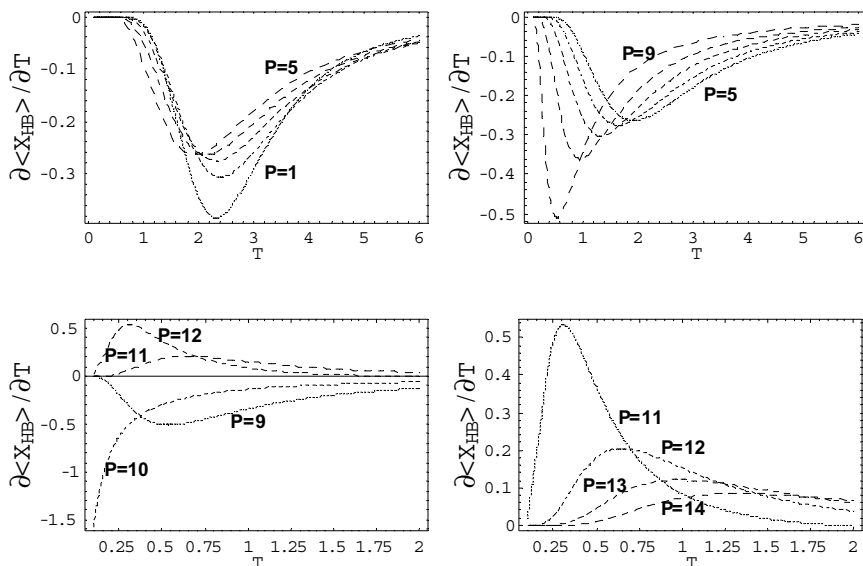


Fig. 2.32 The temperature dependence of the slope $\partial\langle X_{HB}\rangle/\partial T$ for several pressures.

structural changes induced by the change in the temperature. It is clear that these minima also occur in the ranges of T and P at which we have observed the anomalous temperature dependence of the volume, namely $2 \leq T \leq 3$ and $4 \leq P \leq 9$. (See Sec. 2.5.3. Note, however, that in Sec. 2.5.3 we studied the primitive model, but as we have pointed out the cluster model exhibits the same behavior as the primitive model). Once we increase the pressure beyond $P \approx 10$, the system is highly compressed and the quantity $\partial\langle X_{HB}\rangle/\partial T$ becomes positive, i.e. increasing the temperature causes an expansion from the close-packed structure into the open, *HB*ed structure.

Figure 2.33 shows the quantity $\partial\langle X_{HB}\rangle/\partial P$ as a function of T for various pressures. This quantity is relevant to the compressibility of water. At low pressures, $\partial\langle X_{HB}\rangle/\partial P$ is positive, i.e. *HB*s are formed by increasing the pressure. At higher pressures, the quantity $\partial\langle X_{HB}\rangle/\partial P$ becomes negative. It should be noted that $\partial\langle X_{HB}\rangle/\partial P$ plays the same role for the pressure dependence

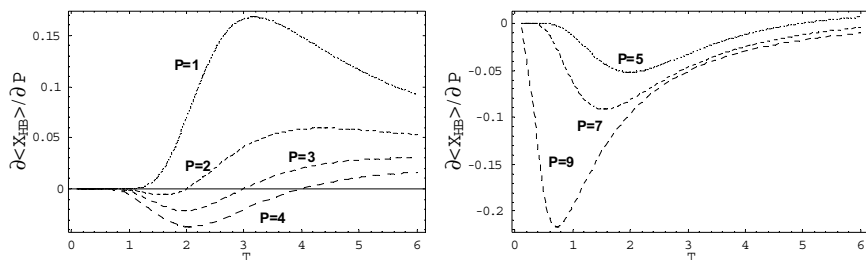


Fig. 2.33 The temperature dependence of the slope $\partial\langle X_{HB}\rangle/\partial P$ for several pressures.

of the volume as $\partial\langle X_{HB}\rangle/\partial T$ plays for the temperature dependence of the molar volume. For a simple two-structure model, the analog of Eq. (2.5.48) is

$$\left(\frac{\partial V}{\partial P}\right)_T = x_{HB} \frac{\partial \bar{V}_{HB}}{\partial P} + (1 - x_{HB}) \frac{\partial \bar{V}_{NHB}}{\partial P} + (\bar{V}_{HB} - \bar{V}_{NHB}) \left(\frac{\partial x_{HB}}{\partial P}\right)_T \quad (2.5.50)$$

Here, $(\bar{V}_{HB} - \bar{V}_{NHB}) > 0$, and in order to produce a large contribution to the compressibility, due to structural changes in the system, we need a large value of $\partial x_{HB}/\partial P$. In the cluster model, the relevant quantity is $\partial\langle X_{HB}\rangle/\partial P$. Note also that the above argument can be used to explain the value of the compressibility. In order to explain the minimum of the isothermal compressibility of water, we need to examine the second derivative of $\langle X_{HB}\rangle$ with respect to both T and P .

2.5.7. *Some concluding remarks regarding the 1-D model for water*

In spite of the admittedly “unrealistic” nature of the 1-D system, I believe that a great deal of understanding about water can be achieved at a molecular level by studying these simple models. In particular, the fact that such primitive models succeed

in reproducing the most unusual properties of water corroborates the conjecture that the peculiar correlation between local density and local binding energy is both *sufficient* and *necessary* for understanding the behavior of liquid water. We shall see in Sec. 3.9 that this principle is also essential for the understanding of some of the most outstanding properties of aqueous solutions of inert solutes. Nevertheless, it seems to me that the significance of this principle was not appreciated even by authors who used this model to explain the properties of water. I shall present here two such examples that might indicate, at least in my view, that authors who used the primitive 1-D model have missed the *main point* of the merits of the specific potential function constructed for the study of liquid water.

The first comment refers to the work of Cho *et al.* (1996), who used an earlier version of the primitive model for water⁵² (the one referred to as the BN1D potential in Fig. 2.10c). In their conclusion, the authors wrote: “It might be necessary, in order to reproduce the known temperature and pressure effects, to *insert* empirically the appropriate *double-well* feature into the water potential.” (italics added)

In my view, this conclusion demonstrates that the authors did not appreciate the significance of the principle. First, as we have seen in the previous sections, the *double-well* potential as constructed earlier is not essential for the study of the outstanding properties of water. Second, and more importantly, in designing the original 3-D pair potential for water the main goal was to find a model potential for water that would lead to typical water behavior. Although it was not stated explicitly, *the principle* — low local density correlated with strong binding energy — was a *built-in* feature of the potential function. It was only later recognized as a “necessary” and “sufficient” feature. That was also the motivation for constructing the 1-D as well as

⁵²The double-well potential was published earlier in Ben-Naim (1992). See Fig. 2.10c.

the 2-D potentials for water-like particles. Therefore, the suggestion made by Cho *et al.* that the *double-well* feature of the potential should be implemented in the 3-D models is the same as suggesting to implement an irrelevant feature of the potential function. As we have seen, the double-well potential used earlier (Ben-Naim, 1992) is not essential, and the essential part of the potential is already contained in the potential functions designed for water in the 3-D as well as in the 2-D models (see Sec. 2.6). The essential feature of the potential is already there and need not be further implemented!⁵³

The work of Cho *et al.* (1996) was criticized by Velasco *et al.* (1997) stating that “to our knowledge, there has not been a report of any anomalous behavior in $\rho()$ for multiple well interaction potential in 3-D,” and concluded that “therefore the anomaly is a genuine feature of the 1-D case.” It seems to me that this criticism is leveled at the conclusions of the Cho *et al.* paper and not at the merits of the potential itself. Clearly, Velasco *et al.* missed the main point of this 1-D potential. This is not a model for *water* but a model of a *phenomenon*. It is certainly not a realistic model for water, yet it is a very useful model for understanding the outstanding behavior of water. Although I agree that the double-well feature should not be implemented in a 3-D model, I do not agree that “the anomaly is a genuine feature of the 1-D case.”

The second comment is in the same vein as the first. It might sound like a matter of semantics, but in my view it is more

⁵³It is clear to me that had these authors *designed* the double-well potential, they would not have arrived at this conclusion. It is more likely that they used the BN1D potential published by Ben-Naim (1992) but overlooked the main motivation for designing this specific form of the potential function. The emphasis on the “double-well” feature of the pair potential can also be misleading. In fact, it did mislead a few authors who published works where the “double-well” feature was implemented in a 3-D model. This is a futile effort. The implementation of the *principle*, in a 3-D model does not add anything new to what we already know in the 1-D model. See Lyubartsev and Ben-Naim (to be published 2009–2010).

than that. The title of the Sadr-Lahijany *et al.* (1999) article is: “Water-like anomalies for *core-softened* model of fluids: one dimension.” In their conclusion (as well as in the abstract and the introduction) the authors state: “We used a 1-D core-softened potential which mimics the effect of hydrogen-bonding....” I believe that this statement indicates that the authors have missed the main point of the potential function they used. It is *not* the softening of the hard-core potential that mimics the effect of hydrogen bonding. The softening of the hard-core part of the potential does not lead to any anomalies of water! As was demonstrated in this section, the primitive model consists of an un-softened hard core (at σ_1). The important feature of the potential has nothing to do with the softening of the hard core. It was only accidental that in the original model I used a double square-well model. The primitive model used in this book left out the first well that was adjacent to the hard core; hence, the hard-core part of the potential was untouched and certainly not softened. The important feature of the potential that leads to water-like anomalies is not the *softening* of the hard-core part but the disconnection of the hard-core diameter from the hydrogen-bonding region, i.e. the moving further away of the hydrogen bonding from the hard-core repulsion. Repeated reference to the “core-softened potential mimics the effect of hydrogen bonding” is in fact emphasizing a totally irrelevant feature of the potential and could, therefore, be potentially misleading.

2.6. A Two-Dimensional Model for Water

2.6.1. *Introduction*

Having discussed at great length the 1-D model of water, it is time to proceed one step further towards “realistic” 3-D models of water. This intermediate level is a 2-D model of water that

was published over 30 years ago. I shall refer to this model as the BN2D model.⁵⁴ This was the first model in which the principle discussed in Secs. 2.4 and 2.5, as well as in the preface, was implemented explicitly, i.e. designating a pair potential in such a way that it will produce a low local density component that also has a strong binding energy. The success of this model (as well as the 1-D model discussed in Sec. 2.5) in mimicking the properties of liquid water has boosted further support to the conjecture that this *principle* is more fundamental than the tetrahedral structure⁵⁵ characteristic of 3-D water molecules. (The 1-D model discussed in Sec. 2.5 also showed that *structure*, in itself, is also a non-essential concept in the understanding of liquid water.) This is also the first model for which the joint distribution of binding energy and coordination number was calculated and for which the principle was formulated (see Sec. 2.5.4). In this section, I shall describe the BN2D model and the ideas that guided me in designing this model. In the subsequent section, I shall present a sample of results obtained by both simulation and by application of an integral equation. A more detailed review of the results obtained for this system was published by Dill *et al.* (2005).

⁵⁴The fact that the model resembles the Mercedes-Benz (MB) logo does not justify references to this model as the MB model. It is not the *form* of the particles as depicted in Fig. 2.34 that is important, but the form of the *potential function* described in this section. To the best of my knowledge, Mercedes-Benz did not contribute anything to this potential. As in the case of the 1-D model, the very fact of giving it a new name (and in my view, an inappropriate one) has led to the expected results. Several authors using the BN2D model have given reference and credit to the originator of the *name* MB, rather than to the originator of the *potential*.

⁵⁵It is interesting to recall that in the original publication, Ben-Naim (1971) noted that “the unique properties of liquid water are due to the tetrahedral geometry.” Implementing the 2-D analog of the tetrahedrality principle was the main motivation for the construction of the 2-D model for water-like particles. It was only much later realized that neither the tetrahedrality nor the hexagonality are essential for the unique properties of liquid water.

2.6.2. *The physical model of water-like particles in two dimensions*

Figure 2.34 depicts a few BN2D particles in a two-dimensional box. The implementation of the principle is schematically shown in Fig. 2.35. This figure should be compared with Fig. 2.8.

Each particle is depicted as a disk having three arms emanating from the center and pointing towards the vertices of an equilateral triangle. This is a “reduction” of the tetrahedral model described in Fig. 1.9, where the arms point to the four vertices of a regular tetrahedron.

The intermolecular interaction is a superposition of two functions: a Lennard–Jones type, which depends only on the intermolecular distance R , and a hydrogen bond-like (HB) part, which depends on both the distance and the relative orientations of the two particles. An HB is formed whenever one arm of a particle points to the center of a second particle and aligns with

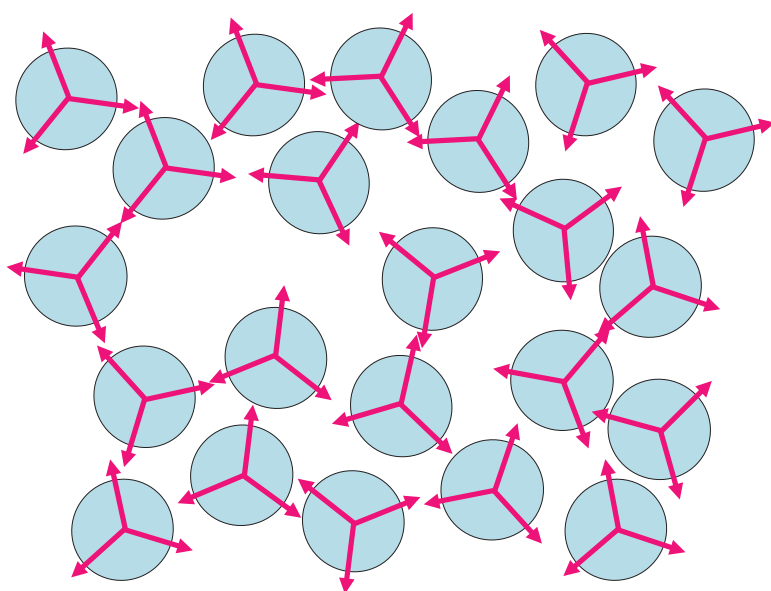


Fig. 2.34 A sample of BN2D particles in two dimensions.

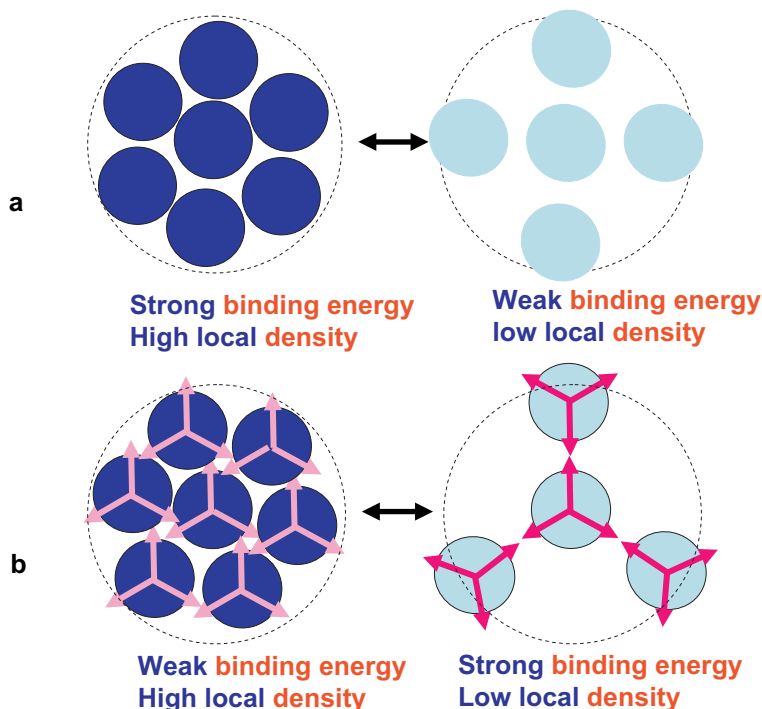


Fig. 2.35 An illustration of the correlation between local density and binding energy in a 2-D system of (a) normal particles and (b) water-like particles.

one arm of the second particle. Figure 2.36 displays a sample of particles in two dimensions in which the arms of each particle are indicated. In this illustration, particles 1 and 2 form an *HB*, since the distance and the orientations are favorable (a precise definition will be presented below). Particles 3 and 4 are correctly oriented to form an *HB* but their separation is too large. On the other hand, particles 5 and 6 are almost at the correct orientation and distance — a case which may be viewed as a bent *HB*. Particles 7, 8, and 9 are successively connected by *HB*s. It is clear that if the *HB* energy were strong enough compared with the thermal energy of the particles, then an extended network of particles, most of which are connected by *HB*s, would form. At a low enough temperature, we may obtain a solid-like network

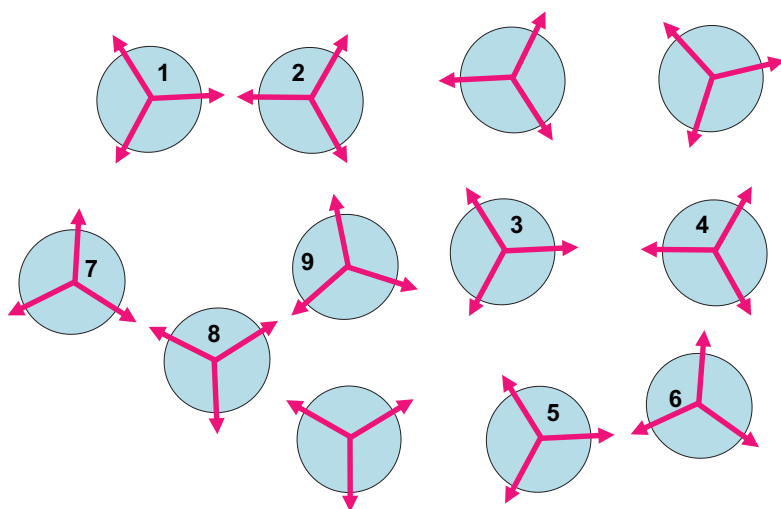


Fig. 2.36 A sample of water-like particles in two dimensions. The circles indicate the Lennard–Jones diameter of the particles. The arrows attached to each particle are unit vectors along which a “hydrogen bond” may be formed. See Sec. 2.6.2.

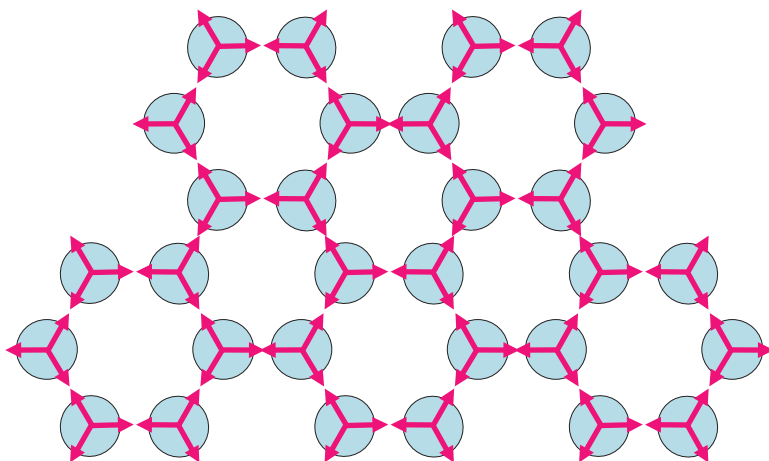


Fig. 2.37 An extended network of hydrogen-bonded particles in two dimensions. In the liquid state, one may encounter aggregates of connected molecules with random size and shape of similar geometry.

such as the ones described in Fig. 2.37. This regular network will to some extent persist in the liquid state as well. Of course, due to thermal agitation we may find clusters of bonded molecules with randomly varying sizes and shapes. Some of the bonds may, in this case, be considered as being bent or broken.⁵⁶ We now describe the analytical form of the pair potential.

Let x, y be the Cartesian axes for the whole system. Let $\mathbf{i}_k$ ($k = 1, 2, 3$) be the unit vector pointing from the center of the particle i ($i = 1, \dots, N$) along the k th arm. The full specification of the location and orientation of particle i is given by vector $\mathbf{X}_i$, comprising the two Cartesian coordinates x_i and y_i , and an angle α_i between the direction of $\mathbf{i}_1$ and the positive direction of the x -axis, i.e.

$$\cos \alpha_1 = (\mathbf{i}_1 \cdot \mathbf{x}) \quad (2.6.1)$$

where $\mathbf{x}$ is a unit vector along the positive direction of the x -axis. Figure 2.38 represents a coordination system for a pair of particles i and j .

The intermolecular potential function for a pair of particles i and j at configuration $(\mathbf{X}_i, \mathbf{X}_j) = (x_i, y_i, \alpha_i, x_j, y_j, \alpha_j)$ has the form

$$U_{ij}(\mathbf{X}_i, \mathbf{X}_j) = U_{LJ}(R_{ij}) + U_{HB}(\mathbf{X}_i, \mathbf{X}_j) \quad (2.6.2)$$

where the Lennard–Jones part of the potential is

$$U_{LJ}(R) = 4\varepsilon_w \left[\left(\frac{\sigma_w}{R} \right)^{12} - \left(\frac{\sigma_w}{R} \right)^6 \right] \quad (2.6.3)$$

⁵⁶In the original publication, Ben-Naim (1971), I had also considered four arms per particle. This case was not studied in detail.

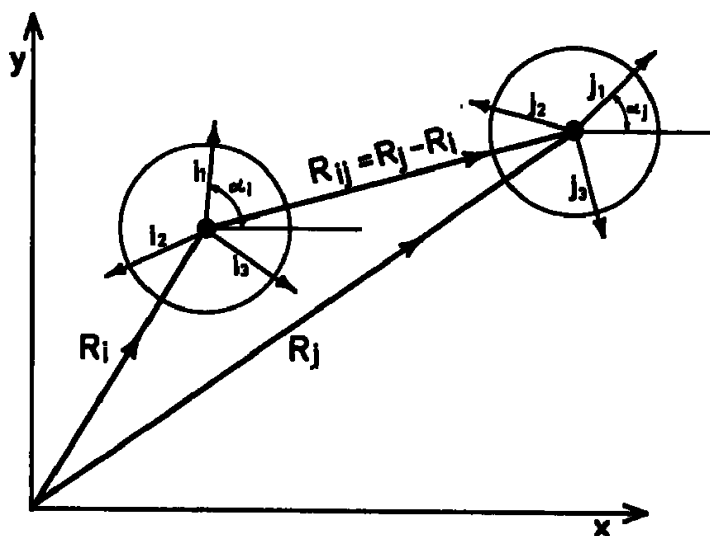


Fig. 2.38 The coordination system for the 2-D model.

and the *HB* part of the potential is defined by

$$U_{HB}(\mathbf{X}_i, \mathbf{X}_j) = \varepsilon_{HB} G_{\sigma'}(R_{ij} - R_H) \times \left[\sum_{k,l=1}^3 G_{\sigma}(\mathbf{i}_k \cdot \mathbf{u}_{ij} - 1) G_{\sigma}(\mathbf{j}_l \cdot \mathbf{u}_{ij} + 1) \right] \quad (2.6.4)$$

Here, ε_{HB} is an energy parameter, the value of which is the maximum attainable *HB* energy. R_H is the characteristic distance at which an *HB* may be formed. G_{σ} is an un-normalized Gaussian function of the form⁵⁷

$$G_{\sigma}(x) = \exp(-x^2/\sigma) \quad (2.6.5)$$

⁵⁷Note that σ_w is used for the diameter of the particles, and σ for the variance or the range of the *HB*.

For some calculations, it is more convenient to choose a step function of the form:

$$G(x) = \begin{cases} 1 & \text{for } |x| < \sigma \\ 0 & \text{for } |x| \geq \sigma \end{cases} \quad (2.6.6)$$

Let $\mathbf{u}_{ij}$ be a unit vector along $\mathbf{R}_{ij}$, i.e.

$$\mathbf{u}_{ij} = \frac{\mathbf{R}_{ij}}{R_{ij}} \quad (2.6.7)$$

where $\mathbf{R}_{ij} = \mathbf{R}_j - \mathbf{R}_i$ and $R_{ij} = |\mathbf{R}_j - \mathbf{R}_i|$.

The sum over k and l in (2.6.4) runs over all the “arms” of particle i and j , respectively. For any given k and l , there is a product of three Gaussians which has the effect of favoring an *HB* formation only if the three conditions are fulfilled simultaneously, namely the distance R_{ij} is close to the characteristic distance R_H , the direction of $\mathbf{i}_k$ lies along the direction of $\mathbf{R}_{ij}$, and the direction of $\mathbf{j}_l$ is along the direction of $-\mathbf{R}_{ij}$. The sum over k and l is over all the configurations for which an arm of the i th molecule is *HB*ed to an arm of the j th molecule. Clearly, if the Gaussian is narrow enough, there can be only one pair of arms that are connected at any given configuration. It is important to choose σ to be small enough so that only a single bond will be formed between any pair of particles and not a double bond. On the other hand, σ should not be too small, otherwise the probability of forming an *HB* will be too small.

The above characterization of the particles, along with the basic pair potential, completes the description of the physical model.

At this stage, it is instructive to digress to an exact definition of the concept of the *structure* as well as the average number of *HB*s in this system. A similar definition has been discussed for the 1-D system in Sec. 2.5 and will be discussed for the 3-D case in Sec. 2.7.

In view of our definition of $U_{HB}(\mathbf{X}_i, \mathbf{X}_j)$ in (2.6.4), we introduce the following definition of the set of configurations:

$$C_{ij}^{HB}(\sigma, \sigma') \leftrightarrow \left\{ \begin{array}{l} -\sigma' < R_{ij} - R_H < \sigma' \\ -\sigma < (\mathbf{i}_k \cdot \mathbf{u}_{ij}) - 1 < \sigma \\ -\sigma < (\mathbf{j}_l \cdot \mathbf{u}_{ij}) + 1 < \sigma \end{array} \right\} \quad (2.6.8)$$

The conditions on the right-hand side of (2.6.8) require that the distance R_{ij} be confined between certain values around R_H and that the orientation of the particles be close to those favoring the formation of a strong bond. The set $C_{ij}^{HB}(\sigma, \sigma')$ comprises all the configurations $(\mathbf{X}_i, \mathbf{X}_j)$ consistent with the right-hand side of (2.6.8). The measure of this set is evidently determined by the values of σ and σ' .

Thus, for any given configuration $(\mathbf{X}_i, \mathbf{X}_j)$, we can tell whether i and j are *HBed* according to the criteria:

$$(\mathbf{X}_i, \mathbf{X}_j) \in C_{ij}^{HB}(\sigma, \sigma') \quad (2.6.9)$$

We can now define the characteristic function

$$B_{HB}(\mathbf{X}_i, \mathbf{X}_j) = \begin{cases} 1 & \text{if } (\mathbf{X}_i, \mathbf{X}_j) \in C_{ij}^{HB}(\sigma, \sigma') \\ 0 & \text{otherwise} \end{cases} \quad (2.6.10)$$

The average value of $B_{HB}(\mathbf{X}_i, \mathbf{X}_j)$ is related to the average number of *HBs* in the system by

$$\langle B_{HB} \rangle = \frac{1}{2} \int d\mathbf{X}_1 \int d\mathbf{X}_2 \rho^{(2)}(\mathbf{X}_1, \mathbf{X}_2) B_{HB}(\mathbf{X}_1, \mathbf{X}_2) \quad (2.6.11)$$

where $\rho^{(2)}(\mathbf{X}_1, \mathbf{X}_2)$ is the pair distribution function. The quantity $\langle B_{HB} \rangle$ may serve as a measure of the degree of *structure* of the system. It is clear that this definition of the structure depends on the definition of the concept of the *HB*, which in turn is dependent on the choice of σ and σ' . A similar definition may be applied in the 3-D case discussed in Sec. 2.7.

It should be noted that in a real water molecule a distinction is made between two pairs of arms; along two directions the

molecule participates as a donor for the *HB*, while along the other two directions it acts as an acceptor. However, since the final outcome of the formation of *HBs* is a symmetrical structure in which four oxygens are placed at the corners of a regular tetrahedron, the distinction between the two pairs of directions may not be essential for the present study. Therefore, in our model, all three directions are considered to be equivalent.

2.6.3. *The application of the Percus–Yevick equation to the BN2D model*

The Percus–Yevick (*PY*) equation for spherical particles in three dimensions was found to be very useful for the study of the pair correlation function.⁵⁸ For the purposes of the present 2-D system, the corresponding *PY* equation may be obtained most directly from the Ornstein–Zernike relation⁵⁹

$$h(\mathbf{X}_1, \mathbf{X}_2) = c(\mathbf{X}_1, \mathbf{X}_2) + (\rho/2\pi) \int c(\mathbf{X}_1, \mathbf{X}_3)h(\mathbf{X}_3, \mathbf{X}_2)d\mathbf{X}_3 \quad (2.6.12)$$

Here, $h(\mathbf{X}_1, \mathbf{X}_2)$ is the total correlation function, defined in terms of the pair correlation function by

$$h(\mathbf{X}_1, \mathbf{X}_2) = g(\mathbf{X}_1, \mathbf{X}_2) - 1 \quad (2.6.13)$$

and $c(\mathbf{X}_1, \mathbf{X}_2)$ is referred to as the direct correlation function which is effectively defined through (2.6.12).⁶⁰ The number density $\rho = N/V$, where V is the volume (area) of the system.

⁵⁸Percus and Yevick (1958), Percus (1962, 1964), Henderson and Davison (1967), Rushbrooke (1968), Munster (1969), Broyles (1960, 1961), and Throop and Bearman (1965, 1966a,b).

⁵⁹See Ben-Naim (2006).

⁶⁰The direct correlation function is not a correlation function like the pair correlation function. The term is derived from the form of Eq. (2.6.12), where the *total* correlation function (h) is viewed as consisting of two parts: the direct (c) and the indirect part, which is the integral on the right-hand side of (2.6.12).

The vector $\mathbf{X}_i$ consists of the three coordinates x_i, y_i, α_i and the integrations in (2.6.12) extend over the following region:

$$\int d\mathbf{X}_3 = \int_V d\mathbf{R}_3 \int_0^{2\pi} d\alpha_3 \quad (2.6.14)$$

i.e. the integration is over the “volume” of the system V and over the whole range of angles $(0, 2\pi)$.

The following notations are introduced:

$$f(\mathbf{X}_1, \mathbf{X}_2) = \exp[-\beta U(\mathbf{X}_1, \mathbf{X}_2)] - 1 \quad (2.6.15)$$

where $\beta = (k_B T)^{-1}$ and k_B is the Boltzmann constant;

$$y(\mathbf{X}_1, \mathbf{X}_2) = g(\mathbf{X}_1, \mathbf{X}_2) \exp[\beta U(\mathbf{X}_1, \mathbf{X}_2)] \quad (2.6.16)$$

The PY equation is obtained by introducing the approximation

$$c(\mathbf{X}_1, \mathbf{X}_2) = y(\mathbf{X}_1, \mathbf{X}_2)f(\mathbf{X}_1, \mathbf{X}_2) \quad (2.6.17)$$

into Eq. (2.6.12) to yield

$$\begin{aligned} y(\mathbf{X}_1, \mathbf{X}_2) = 1 + \frac{\rho}{2\pi} \int y(\mathbf{X}_1, \mathbf{X}_3)f(\mathbf{X}_1, \mathbf{X}_3) \\ \times [y(\mathbf{X}_3, \mathbf{X}_2)f(\mathbf{X}_3, \mathbf{X}_2) + y(\mathbf{X}_3, \mathbf{X}_2) - 1]d\mathbf{X}_3 \end{aligned} \quad (2.6.18)$$

This is an integral equation for the unknown function $y(\mathbf{X}_1, \mathbf{X}_2)$, when $f(\mathbf{X}_1, \mathbf{X}_2)$ is presumed to be a known function.

In this section, we shall not discuss the technical details and the computational procedure; these are discussed in great detail in Ben-Naim (1971, 1972a). We present instead a few results of this model.

Figure 2.39 shows the radial distribution function or the angular average of the pair correlation function for the water-like particles (BN2D) calculated by the PY equation with the

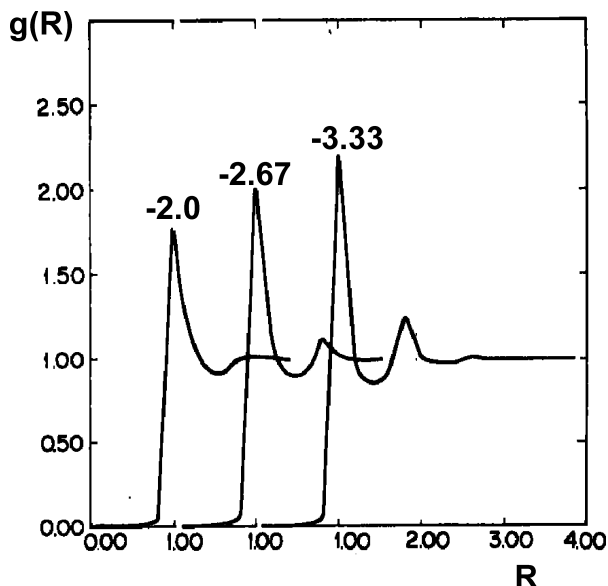


Fig. 2.39 The spatial pair correlation function for water-like particles in two dimensions. (The hydrogen bond energies ε_{HB} are indicated near each curve.)

parameters

$$\begin{aligned} R_H = \sigma = 1.0, \quad \varepsilon/k_B T = 0.1, \\ \varepsilon_{HB}/k_B T = -2.0, -2.67, -3.33 \end{aligned} \quad (2.6.19)$$

The first peak, as expected, is at $R = 1.0$. The second peak is barely discernible for the case $\varepsilon_{HB}/k_B T = -2.0$. However, for $\varepsilon_{HB}/k_B T = -3.33$, it is quite sharp and clear. Recall that for the spherical particles, we observe two peaks at $R = 1.0$ and $R = 2.0$ (see Fig. 1.28 in Chapter 1). These peaks are as expected from a “normal” liquid.⁶¹ Note here that the height of the first peaks increases as the number density $\rho = N/V$ increases (Fig. 2.40b). The increase in the first peak can be

⁶¹For more details, see Ben-Naim (2006).

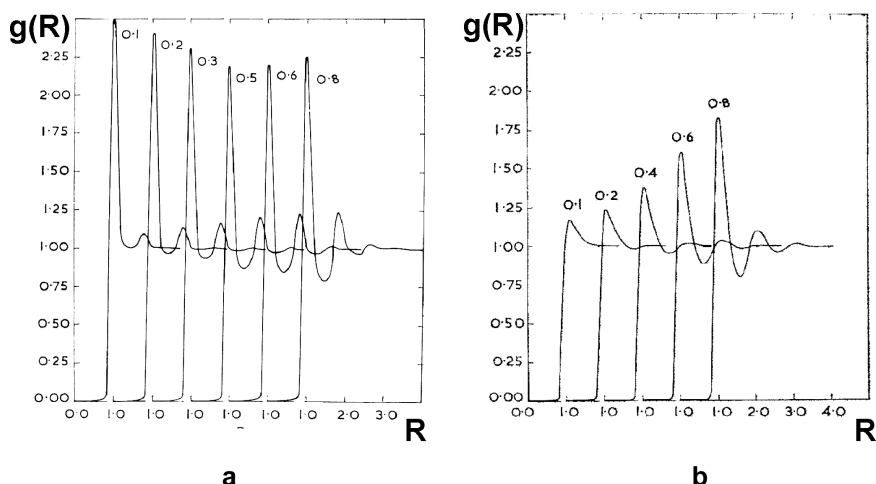


Fig. 2.40 The variation of the pair correlation function with density (as indicated near each curve) for (a) water-like particles and (b) spherical particles.

interpreted also in terms of the coordination number, defined by

$$CN(R_M) = \int_0^{R_M} \rho g(R) 2\pi R dR \quad (2.6.20)$$

where R_M may be conveniently chosen as the location of the first minimum in the *RDF*.

In contrast to the spherical, or the “normal” case, we find that for the water-like particles the height of the first peak decreases as we increase the density up to about $\rho = 0.5$,⁶² then starts to increase (Fig. 2.40a). Also, the second peak is at about $R = \sqrt{3}R_H$. This corresponds to the distance of the second nearest neighbors of *HBed* particles (see Fig. 2.41b). This is the analog of the distance $R = 4.5\text{\AA}$ in liquid water (Fig. 1.29). The angular dependence of the *RDF* was also calculated. Since the *RDF* was calculated only for five values of the orientation angles $\alpha_1 = 0^\circ, 30^\circ, 60^\circ, 90^\circ$, and 120° , we can write the *RDF*

⁶²A similar behavior was observed in the 1-D case (Sec. 2.5). This is also the expected behavior in the 3-D case.

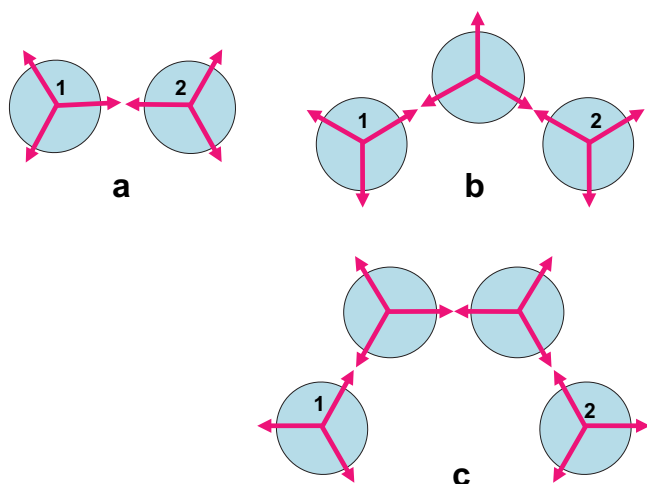


Fig. 2.41 Configurations for the first, second, and third nearest neighbors for the 2-D model.

at each distance R as a 5×5 matrix with elements⁶³

$$g_{kl}(R) = g(R, \alpha_1, \alpha_2) \quad (2.6.21)$$

where

$$\alpha_1 = (k - 1)2\pi/12, \quad \alpha_2 = (l - 1)2\pi/12 \quad (2.6.22)$$

Thus, $k = 1, 2, 3, 4, 5$ corresponds to $\alpha_1 = 0^\circ, 30^\circ, 60^\circ, 90^\circ$, and 120° , and similarly for $l = 1, 2, 3, 4, 5$ and α_2 .

First, let us show the elements of the matrix $g_{kl}(R = 1)$:

$$[g_{kl}(R = 1.0)] = \begin{bmatrix} 1.4 & 0.7 & 19.2 & 0.7 & 1.4 \\ 1.4 & 0.9 & 1.1 & 0.9 & 1.4 \\ 1.5 & 1.0 & 1.0 & 1.0 & 1.5 \\ 1.4 & 0.9 & 1.1 & 0.9 & 1.4 \\ 1.4 & 0.7 & 19.2 & 0.7 & 1.4 \end{bmatrix} \quad (2.6.23)$$

⁶³Since the molecules have three-fold symmetry, it is sufficient to study the orientational dependence of g in the range of $0 \leq \alpha \leq 120$.

Clearly, the largest entries correspond to $\alpha_1 = 0^\circ$ and $\alpha_2 = 60^\circ$, or $\alpha_1 = 120^\circ$ and $\alpha_2 = 60^\circ$. These configurations represent the formation of a direct bond between the two particles (Fig. 2.41a).

The next neighbors occur when a third particle is connected by *HB* to the two particles 1 and 2. The ideal distance for this configuration is $R = \sqrt{3}R_H$, which in our computation falls close to $R = 1.8$. The radial distribution function $g(R)$ shows a second peak at this distance (Fig. 2.39). The full correlation function at $R = 1.8$ is

$$[g_{kl}(R = 1.8)] = \begin{bmatrix} 1.1 & 1.1 & 0.7 & 1.1 & 1.1 \\ 1.2 & 3.0 & 1.0 & 1.0 & 1.2 \\ 1.1 & 0.8 & 0.5 & 0.8 & 1.1 \\ 1.2 & 1.0 & 1.0 & 3.0 & 1.2 \\ 1.1 & 1.1 & 0.7 & 1.1 & 1.1 \end{bmatrix} \quad (2.6.24)$$

The largest entries are for $\alpha_1 = 30^\circ$ and $\alpha_2 = 30^\circ$, or $\alpha_1 = 90^\circ$ and $\alpha_2 = 90^\circ$. These configurations correspond to the case where the two particles are connected through a third particle, as in Fig. 2.41b.

The third neighbor is expected to be at the ideal distance of $R = 2R_H = 2$, for which we get

$$[g_{kl}(R = 2)] = \begin{bmatrix} 1.3 & 1.1 & 0.9 & 1.1 & 1.3 \\ 1.2 & 0.9 & 0.8 & 1.0 & 1.2 \\ 1.4 & 0.8 & 0.7 & 0.8 & 1.4 \\ 1.2 & 1.0 & 0.8 & 0.9 & 1.2 \\ 1.3 & 1.1 & 0.9 & 1.1 & 1.3 \end{bmatrix} \quad (2.6.25)$$

Here, we have a very small preference for the configurations $\alpha_1 = 60^\circ$ and $\alpha_2 = 0^\circ$, or $\alpha_1 = 60^\circ$ and $\alpha_2 = 120^\circ$. These configurations are indeed consistent with the geometry depicted in Fig. 2.41c. Note that we do not get a high peak at $R = 2$. The fact that we do get a peak at $R = 1.8$ and not at $R = 2$

indicates that correlation between particles is propagated mainly through a chain of *HBs* and not by “filling of space” as in the spherical case.

There is one important conclusion that can be drawn from the study of the pair correlation function for 2-D water-like particles which is relevant to the study of liquid water. If strong directional forces or bonds are operative at some selected directions, then the correlation between the two positions of two particles is propagated mainly through a chain of bonds and less by the “filling of space” — a characteristic feature of the mode of packing of simple fluids.⁶⁴

A more detailed study of the pair correlation function of this model was undertaken by Urbic *et al.* (2003). This work was also reviewed by Dill *et al.* (2005).

2.6.4. *Simulated results*

We present here a few results calculated for a system of water-like (BN2D) particles in two dimensions, obtained by the Monte Carlo method. The molecular parameters chosen for this particular illustration are

$$\begin{aligned}\varepsilon_w/k_B T &= 0.5, \quad \sigma_w = 0.7, \quad R_H = 1.0, \\ \varepsilon_{HB}/kT &= -3.0, -5.0, -8.0\end{aligned}\tag{2.6.26}$$

The total number density is $\rho = 0.9$, and the radius of the first coordination sphere was chosen as $R_C = 1.3\sigma_w$. The parameters σ' and σ in (2.65) were chosen to be about 0.015 after some experimentation with the results obtained from the computations. The reasons for the choice of these parameters will not be of concern to us here; for details, see Ben-Naim (1973).

⁶⁴See Ben-Naim (2006).

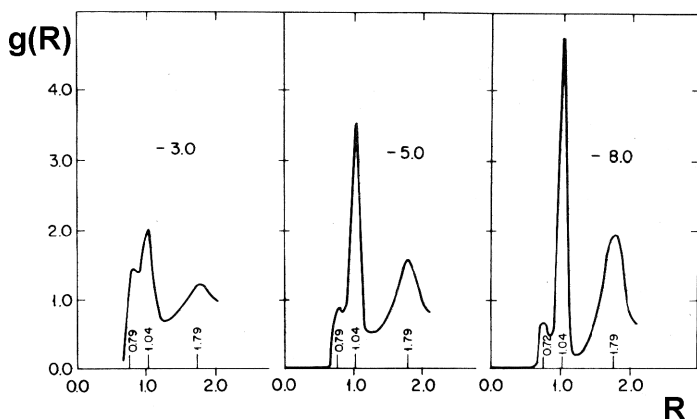


Fig. 2.42 The spatial pair correlation function for a system of water-like particles, with parameters given in (2.6.26). The HB energies $\varepsilon_{HB}/k_B T$ are indicated next to each curve. The locations of the various maxima are indicated on the abscissa.

Note also that the LJ diameter of the particles σ_w was chosen to be smaller than the HB distance R_H . This was done to make the HB ed network more open than the close-packed component. This choice was also found to be useful for the study of aqueous solutions of inert solutes (see Sec. 3.10).

Figure 2.42 shows the radial distribution function for the water-like particles with different HB energies as in (2.6.26). The peak at about $R = 0.8$ is the “normal” peak one would expect for a system of *spherical* particles. As we increase the HB energy, the peak at $R \approx R_H = 1.0$ grows and becomes the dominant feature of the curve. The peak at $R \approx 0.8$ persists, however, even when the HB energy is quite large. The reason is interesting and also has some relevance to the study of liquid water. The choice of the particular density $\rho = 0.9$ was made on the following basis. One has to make a distinction between two limiting densities (similar to that made in the 1-D case in Sec. 2.5). The first is the maximum density of spheres (disks) of diameter $\sigma_w = 0.7$, which is about $\rho_{cp} \approx 2.36$. The second

is the density of the 2-D lattice (Fig. 2.37) of bonded particles, which in our case is $\rho_{\text{lattice}} = 0.77/R_H^2 = 0.77$. Thus, the density $\rho = 0.9$ is such that we are far below the close-packing density and at the same time slightly above the density of the regular lattice (as with liquid water at $t \approx 0^\circ\text{C}$). As a result, some of the particles must find “interstitial” positions in the holes formed by the network of bonded particles. That is, the particles are forced, to a certain extent, to approach each other to within a distance of the order of $R \approx 0.7$.

The second feature of the curves in Fig. 2.42 is the peak at about $R = \sqrt{3}R_H \approx 1.8$, which indicates a large probability of finding pairs of particles bonded through an intermediary particle, as depicted in Fig. 2.41b.

In Fig. 2.43, the distribution functions for the coordination number $x_{CN}(K)$ are plotted for the three cases listed in (2.6.26). The most prominent feature of these curves is the shift to the left of the most probable coordination number as the HB increases. Because of the particular choice of $R_H = 1.0 > \sigma_w = 0.7$, as we increase the strength of the hydrogen bond, more pairs

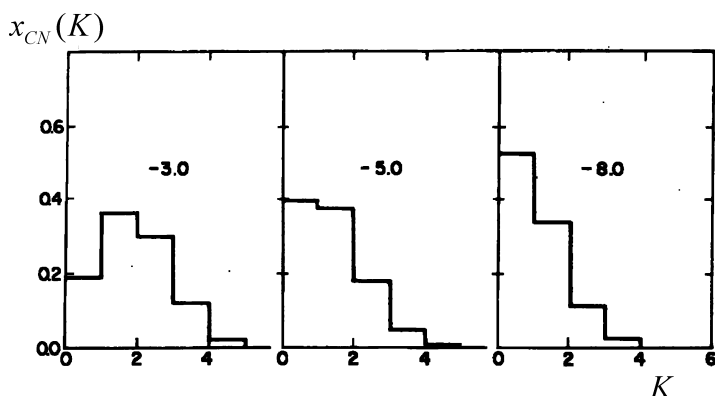


Fig. 2.43 The singlet distribution function $x_{CN}(K)$ for the system of non-spherical particles, with parameters given in (2.6.26). The HB energies $\epsilon_{HB}/k_B T$ are indicated next to each curve.

are forced to attain a distance of $R = R_H$ from each other, and hence, the local density around each particle will, on average, decrease. Hence, at $\varepsilon_{HB}/k_B T = -8.0$, we find that the most probable coordination number is zero. Of course, this specific result depends on the choice of R_C defined here as $R_C = 1.3\sigma_w = 0.9$. The important observation is the shift of the average coordination number to lower values as we increase the strength of the *HB*.

Figure 2.44 shows the distribution function for the binding energy $x_{BE}(\nu)$ for the parameters in (2.6.26). The curves in this figure should be compared with the corresponding curves of $x_{BE}(\nu)$ for simple particles (Figs. 2.3b and 2.44a). The most striking difference between the two sets of curves is the appearance of several well-resolved peaks in the present case, compared with a single peak in the simple spherical case.

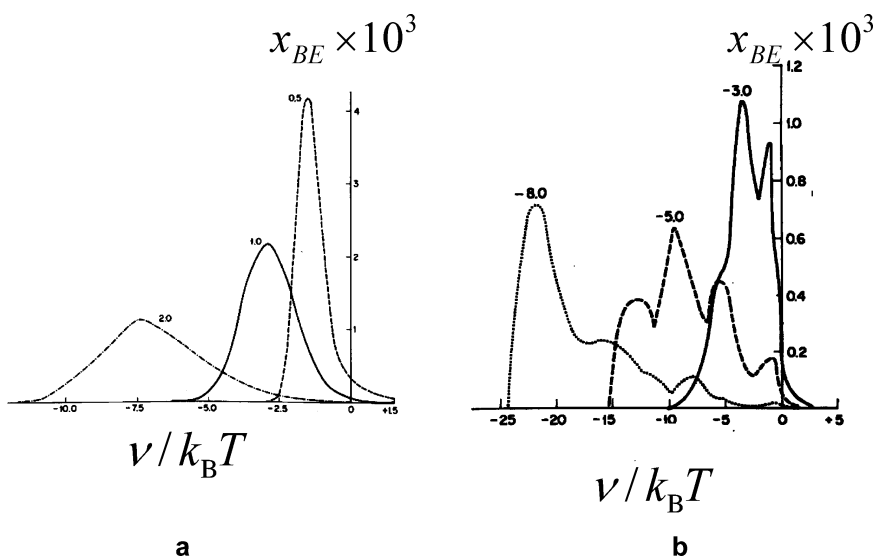


Fig. 2.44 The singlet distribution functions $x_{BE}(\nu)$ for the system of (a) spherical and (b) non-spherical particles, with parameters given in (2.6.26). The *LJ* parameter ε and the *HB* energies $\varepsilon_{HB}/k_B T$ are indicated next to each curve.

For the BN2D particles and at relatively low HB energy ($\varepsilon_{HB}/k_B T = -3.0$), we find essentially two peaks in $x_{BE}(v)$, one corresponding to singly bonded molecules and the second to non-bonded molecules. As we increase the HB energy to $\varepsilon_{HB}/k_B T = -5.0$, we get a clear resolution into four peaks, roughly corresponding to molecules with zero, one, two, and three hydrogen bonds. The form of this curve may suggest a few cut-off points by the use of which we can define four species, and the corresponding mole fractions

$$\begin{aligned} x_3 &= \int_{-\infty}^{v_1^*} x_{BE}(v) dv, & x_2 &= \int_{v_1^*}^{v_2^*} x_{BE}(v) dv \\ x_1 &= \int_{v_2^*}^{v_3^*} x_{BE}(v) dv, & x_0 &= \int_{v_3^*}^{\infty} x_{BE}(v) dv \end{aligned} \quad (2.6.27)$$

v_i^* may be chosen as the minima in the curve of $x_{BE}(v)$ in Fig. 2.44b.

Such a splitting into four quasi-components can serve as a rigorous basis for a mixture-model approach for this liquid. This has direct relevance to the theory of real liquid water.

As the HB energy becomes very large ($\varepsilon_{HB}/k_B T = -8.0$), most of the water-like particles tend to engage in three hydrogen bonds; hence, we get a strong peak at about $v/k_B T \approx -24$, with small peaks corresponding to particles with two, one, and zero bonds.

Figure 2.4b shows the joint distribution constructed by combining the binding energy and coordination number. The values of $x_{CN,BE}(v, K) \Delta v$ are the mole fractions of particles having coordination numbers equal to K and binding energies between v and $v + \Delta v$. This function serves to illustrate the correlation between local density and binding energy. For simple spherical particles in two dimensions, we note that in general high local density is coupled with strong binding energy, which is referred to as the “normal” behavior of a liquid. In water, we expect to

have anomalous coupling of low local density with strong binding energy. This feature is demonstrated by the water-like particles in Fig. 2.5b, where the function $\langle v(K) \rangle / k_B T$ is compared with the corresponding function for the “normal” liquid.⁶⁵

2.6.5. *Further development of the 2-D model*

Dill *et al.* have undertaken an extensive exploration of the BN2D model.⁶⁶ They use both analytical as well as simulation methods to compute a wide range of properties of this model. As expected, the system exhibits a minimum in the temperature dependence of the molar volume, a large value of the heat capacity, and a minimum in the temperature dependence of the compressibility. For more details, the reader is referred to the review article by Dill *et al.* (2005), and the original papers cited here.

Truskett and Dill (2003) extended the calculation of the 2-D model. They found that this model exhibits many of the outstanding properties of liquid water. Truskett and Dill (2003) conclude:

“The success of the model suggests that the unusual properties of water arise from balance between simple centro-symmetrical intermolecular attractions and repulsions, on one hand, and orientation-dependent hydrogen bonds that impose geometrical constraints on the molecular arrangements on the other.”

My view is quite different. The success of this model is due primarily to the *implementation* of the *principle* — as attested by the success of the 1-D model for water.

⁶⁵The unique correlation between local density and binding energy was also found in molecular dynamics simulations by Blumberg *et al.* (1984), and Geiger and Stanley (1982). Interestingly, these authors concluded (belatedly) that the two views of water, the so-called continuous and the MM approach that are “traditionally” considered mutually exclusive, are in fact two different equivalent views of water.

⁶⁶Dill *et al.* (2005).

2.7. Three-Dimensional Models for Water

In this section, we finally arrive at models for water in three dimensions (3-D). As noted in the preface and in Sec. 2.1, present research on the theory of water is dominated by simulations. However, this book is concerned more with the understanding of water behavior rather than on computational methods aiming to achieve better agreement with experimental results. Therefore, most of this chapter will be concerned with some aspects of the theory of water that can potentially enhance our understanding of water. Only a very few results obtained by simulation will be discussed at the end of this section.

2.7.1. *Introduction: A new era of water research*

As discussed in the preface and in Secs. 2.1 and 2.2, earlier models of water assumed that liquid water consisted of mixtures of components, one of which had the characteristic tetrahedral structure of ice. The tetrahedral packing of water molecules was introduced as an *input* into the theory. In 1972, a new era in water research began when a new model of water molecules was constructed in such a way that tetrahedral geometry of the packing of the water molecules could be obtained as an *output* of the theory. The *input* consisted of a pair potential with a propensity to form tetrahedral structure.

These two different points of view were explained in Sec. 2.5 in connection with the primitive and cluster-primitive one-dimensional models for water. In the primitive model single water molecules are defined through their pair potential. The structure formed by these water molecules — clusters of *HBed* molecules — is a *result* of the specific pair potential. On the other hand, in the cluster primitive model, the “structures” — clusters of *HBed* molecules — are *assumed* to be a part of the description of the model, and the *HBs* are now part of the internal description of the clusters.

The same change in approach has occurred in the theory of water. In the older approach, structures or clusters were the building blocks of the model and the *HBs* were part of the internal properties of the clusters. As noted earlier, the roots of this approach can be traced back to Röntgen (1892). The simplest version of these models is Wada's model discussed in Sec. 2.3 and the most sophisticated one was developed by Nemethy and Scheraga (1962a, 1962b, 1962c, 1964). In the new approach, the main protagonist is the single water molecule that, together with the assigned pair potential, is expected to *produce* the clusters, which in the 3-D case are characterized by the tetrahedral structure.

Although there have been several suggestions for the water-water pair potential [such as Rowlinson (1949, 1951), Bjerrum (1951), Watts (1968), and others], none of these were successful in reproducing the tetrahedral packing geometry. The first successful pair potential was that of Ben-Naim and Stillinger (1972). Since then numerous models for 3-D water-like particles have been suggested with ever-increasing efforts to achieve better and better agreement with experimental results.

As will be explained in the next section, the built-in tetrahedrality of the water molecule, though necessary for the success of the 3-D model (but not for the 1-D or the 2-D models), is not sufficient. One should also *design* the pair potential in such a way that the *principle* will be implemented. At the time of constructing the Ben-Naim and Stillinger (*BNS*) potential in the late 1960s, this implementation was achieved by trial and error, whereas for the 2-D and the 1-D potentials as well as for the 3-D potential discussed in Sec. 2.7.4 it was achieved by *design*.

The 3-D models are obviously more realistic than either the 2-D or the 1-D models. However, this closeness to reality should not necessarily mean that the 3-D model is more valuable for understanding water.

For a simple liquid such as argon, a proposed pair potential is judged to be a good one if it leads to a good agreement between calculated quantities and the corresponding measurable quantities. In water even when one gets a perfect agreement between calculated and measurable quantities, it does not follow that the pair potential used in the calculation is the “correct” one. Conversely, even if one has the *correct* pair potential for water, it is doubtful that it will reproduce the properties of water.

The reason for this is simple. The properties of liquid water do not depend only on the pair potential (as is approximately true for the case of simple liquids). Higher-order potentials are very important in the determination of the eventual structure and properties of water.

All one can say from the success of a pair potential in reproducing the correct properties of water is that certain features of the potential function lead to certain characteristic properties of water. Therefore, in my opinion, the excessive endeavor to strive for perfect agreement is not fully justified. The success of any model does not tell us anything about the *real* pair potential and certainly does not add much to our understanding of the outstanding properties of liquid water.

2.7.2. *Effective pair potential for water*

In this section, we discuss the characteristics of an effective pair potential that can be used in a molecular theory of liquid water. As is the case for any liquid, neither theory nor experiment provides us with an analytical form of the entire pair potential as a function of six coordinates. Furthermore, the true pair potential is of no use for the study of liquid water. Therefore, one must resort to an *effective pair potential*. As we have discussed in Sec. 2.2 any effective pair potential must consist of essentially three terms: one corresponding to the strong repulsive

interaction at very short distances (say, $R \leq \sigma$, where σ is the effective hard-core diameter of the molecule); a second corresponding to the long-range interaction; and a third part which we refer to as the hydrogen bond (*HB*) interaction. This part is the most problematic part of the pair potential since it is presumed to produce the combined effect of pair as well as higher-order potentials. We shall use the term *HB* potential to describe this part of the pair potential that is operative in the intermediate range of distances, say, between $2.5 \leq R \leq 3.5 \text{ \AA}$.

A rough estimate of the order of magnitude of the *HB* energy can be obtained from the heat of sublimation of ice, which is about $11.65 \text{ kcal mol}^{-1}$. Each molecule in ice is engaged in four *HBs*, and each *HB* “belongs” to two water molecules. Therefore, one mole of ice has two moles of *HBs*. Assuming that all the energy of sublimation is due to breaking these two moles of *HBs*, we arrive at the estimate of $5.82 \text{ kcal mol}^{-1}$ or about $10k_{\text{B}}T$ at room temperature.

Recognizing the fact that the *HB* occurs only along four directions pointing to the vertices of a regular tetrahedron, we can use the four unit vectors introduced in Chapter 1 (Fig. 1.9) to construct an *HB* potential function. This part is denoted by $U_{\text{HB}}(\mathbf{X}_1, \mathbf{X}_2)$. The full effective pair potential is a superposition of three terms:

$$U(\mathbf{X}_1, \mathbf{X}_2) = U_{\text{LJ}}(R_{12}) + U_{\text{DD}}(\mathbf{X}_1, \mathbf{X}_2) + U_{\text{HB}}(\mathbf{X}_1, \mathbf{X}_2) \quad (2.7.1)$$

Figure 1.10 depicts two water-like molecules at a favorable distance and orientation for the formation of a hydrogen bond. This means that the O-O distance is about $2.76 \text{ \AA}$; that one molecule, serving as a donor, has its O-H direction at about the direction of $\mathbf{R}_{12} = \mathbf{R}_2 - \mathbf{R}_1$, and that the second molecule, serving as an acceptor, has the lone-pair direction along $-\mathbf{R}_{12}$.

We shall now describe only two representative pair potentials: one, based on the Bjerrum model, was the first to reproduce

the radial distribution function of water (see Sec. 2.7.11); the second has some simplified features that make it more convenient for analytical theoretical work.

- (i) The Ben-Naim and Stillinger (BNS) potential based on the Bjerrum model for water

The first example of water-like particles is essentially an extension of Bjerrum's four-point-charge model for the water molecule [Bjerrum (1951), Ben-Naim and Stillinger (1972)]. Figure 2.45 shows this model. It consists of four point charges situated at the vertices of a regular tetrahedron, the center of which is assumed to coincide with the center of the oxygen atom. The point charges are located at $1 \text{ \AA}$ from the center of the tetrahedron. Two charges

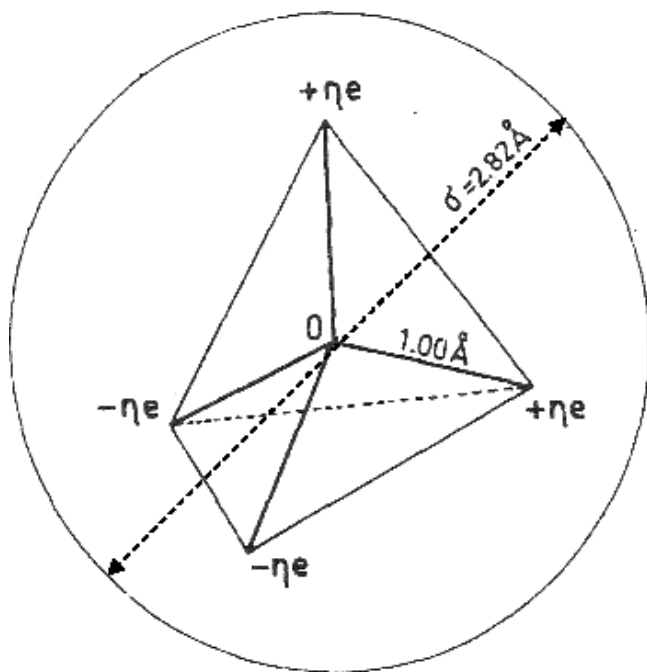


Fig. 2.45 The Bjerrum model for water.

are positive, $+\eta e$ (where e is the magnitude of the electron charge and η is a parameter that is chosen to produce the dipole moment of a water molecule, but is essentially an adjustable parameter), and two charges are negative, $-\eta e$.

The “hydrogen bond” part of the potential in this case consists of 16 Coulombic interactions between the pairs of point charges situated on different molecules, which can be written as

$$U_{HB}(\mathbf{X}_1, \mathbf{X}_2) = (\eta e)^2 \sum_{\alpha_1, \alpha_2=1}^4 (-1)^{\alpha_1+\alpha_2} / d_{\alpha_1\alpha_2}(\mathbf{X}_1, \mathbf{X}_2) \quad (2.7.2)$$

where α_1 and α_2 run over the four point charges of molecules 1 and 2, respectively, in such a way that even and odd values of α_1 correspond to positive and negative charges. $d_{\alpha_1\alpha_2}(\mathbf{X}_1, \mathbf{X}_2)$ is the distance between the charges α_1 and α_2 at the specified configuration of the pair $\mathbf{X}_1, \mathbf{X}_2$.

Clearly, this distribution of the point charges will induce strong interactions along the tetrahedral directions (see Fig. 2.46a). However, to produce an effective pair potential that will be successful, one must add two parts to the Coulombic interactions in (2.7.2).

First, to avoid divergence of the potential function when two charges of opposite signs come very close to each other, one needs a “switching function” $S(R_{12})$, which serves to suppress this possibility by switching off the Coulombic interactions at close distances. The specific function $S(R_{12})$ chosen by Ben-Naim and Stillinger (1972) is

$$S(R_{12}) = \begin{cases} 0 & \text{for } 0 \leq R_{12} \leq R_1 \\ \frac{(R_{12} - R_1)^2(3R_2 - R_1 - 2R_{12})}{(R_2 - R_1)^3} & \text{for } R_1 \leq R_{12} \leq R_2 \\ 1 & \text{for } R_2 \leq R_{12} \leq \infty \end{cases} \quad (2.7.3)$$

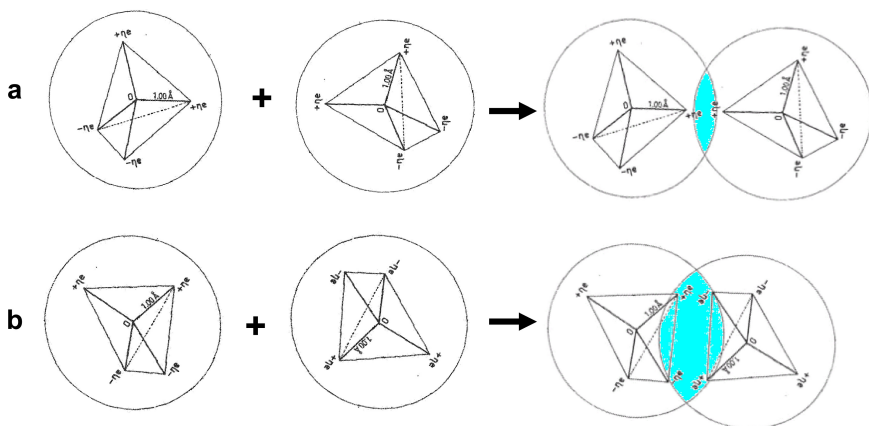


Fig. 2.46 (a) A linear “hydrogen bond” formed by two water-like particles requires penetration into the repulsive region of the pair potential. (b) A double bond requires extensive penetration into the repulsive region; therefore, this configuration is highly improbable.

where R_1 and R_2 as well as η are adjusted so that the minimum of the potential functions is attained at $R_{12} = 2.76 \text{ \AA}$ (at the specific orientation of the pair of molecules referred to below as the symmetric eclipsed one) and that the experimental second virial coefficient $B_2(T)$ is reproduced.

Second, in order to avoid formation of a “double hydrogen bond” between two water molecules (Fig. 2.46b), one needs to imbue the point charges in the repulsive region of the interaction energy in such a way that energy must be invested in order to bring two molecules to form an *HB* (Fig. 2.46a) but the energy cost of forming double *HBs* should be very high, and hence, a configuration such as that depicted in Fig. 2.46b will be highly improbable.

The parameters chosen for this particular model were

$$\eta = 0.19, \quad R_1 = 2.0379 \text{ \AA}, \quad R_2 = 3.1877 \text{ \AA} \quad (2.7.4)$$

Note that the value of $\eta = 0.19$ is slightly larger than the value of $\eta = 0.17$ chosen by Bjerrum to reproduce the dipole

moment of a free water molecule. The combined potential function is thus

$$U(\mathbf{X}_1, \mathbf{X}_2) = U_{LJ}(R_{12}) + S(R_{12})U_{HB}(\mathbf{X}_1, \mathbf{X}_2) \quad (2.7.5)$$

The various ingredients of this potential function are shown schematically in Fig. 2.47 for one particular line of approach for the pair of molecules.

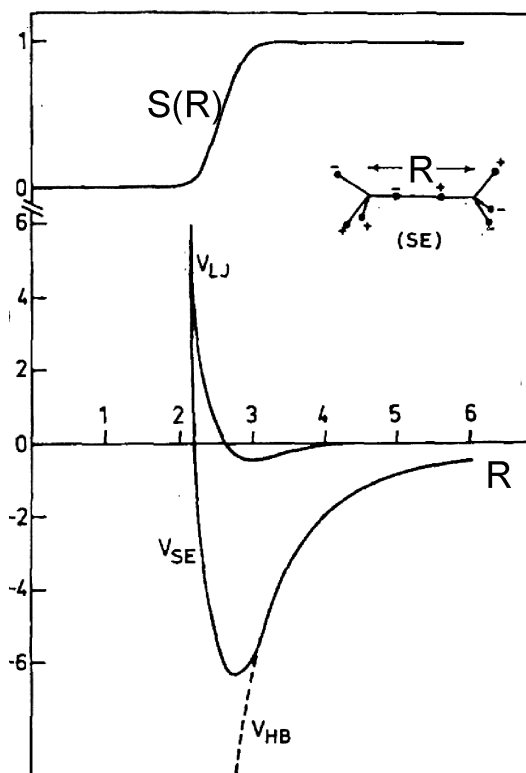


Fig. 2.47 Schematic description of the various ingredients of the BNS potential function based on the Bjerrum model for water; $U_{SE}(R)$ is the full potential function for the symmetric eclipse (SE) approach of two water molecules (plotted in the upper-right part of the figure). Also, the LJ and the HB parts of the potential for this specific orientation are shown. The function $S(R)$ is shown in the upper part of the figure.

We shall describe some results based on this pair potential in Sec. 2.7.10. We next turn to discussing a more general form of an effective pair potential that has some features in common with the Bjerrum model, but has some advantages for an analytical theory of liquid water.

(ii) The primitive BN3D pair potential⁶⁷

As we stated earlier, any effective pair potential must have at least three terms [Eq. (2.7.1)]. Here, we choose a special form of the *HB* part of the potential:

$$U(\mathbf{X}_1, \mathbf{X}_2) = U_{LJ}(R_{12}) + U_{DD}(\mathbf{X}_1, \mathbf{X}_2) + \varepsilon_{HB} G(\mathbf{X}_1, \mathbf{X}_2) \quad (2.7.6)$$

where ε_{HB} is the hydrogen bond energy ($\varepsilon_{HB} \approx -6$ kcal mol⁻¹) and $G(\mathbf{X}_1, \mathbf{X}_2)$ is essentially a geometric function defined as

$$G(\mathbf{X}_1, \mathbf{X}_2) = \begin{cases} 1 & \text{whenever the configuration } (\mathbf{X}_1, \mathbf{X}_2) \\ & \text{is favorable for forming an } HB \\ 0 & \text{otherwise} \end{cases} \quad (2.7.7)$$

and U_{DD} is the dipole-dipole interaction.

The three terms in (2.7.6) correspond to the short-range, long-range and intermediate-range interactions between the water-like particles.

In order to formulate an analytical form for the function $G(\mathbf{X}_1, \mathbf{X}_2)$, it is convenient to think of a water molecule as having four “arms,” i.e. four selected directions along which

⁶⁷The denomination of this potential as BN3D (as well as the corresponding BN2D and BN1D) was not mentioned in the original publication (Ben-Naim, 1974). However, since later publications have used this potential (as well as the BN2D and the BN1D) without giving proper credit to the original publication, I found it necessary to use this denomination as I also did for the BN2D and the BN1D potentials.

they can form *HBs*. These arms are along the four unit vectors introduced in Fig. 1.9. One can define four vectors: two along donor arms $\bar{H}_{i1}$ or $\bar{H}_{i2}$, and two along the acceptor arm $\bar{l}_{i1}$ or $\bar{l}_{i2}$. In terms of these vectors, the function $G(\mathbf{X}_1, \mathbf{X}_2)$ is assumed to have the following general form:

$$G(\mathbf{X}_i, \mathbf{X}_j) = G_{\sigma'}(R_{ij} - R_H) \times \left\{ \sum_{\alpha, \beta=1}^2 G_{\sigma}[(\mathbf{h}_{i\alpha} \cdot \mathbf{u}_{ij}) - 1] G_{\sigma}[(\mathbf{l}_{j\beta} \cdot \mathbf{u}_{ij}) + 1] + \sum_{\alpha, \beta=1}^2 G_{\sigma'}[(\mathbf{l}_{i\alpha} \cdot \mathbf{u}_{ij}) - 1] G_{\sigma}[(\mathbf{h}_{j\beta} \cdot \mathbf{u}_{ij}) + 1] \right\} \quad (2.7.8)$$

where the function $G(x)$ may be chosen either as a step function of the form

$$G_{\sigma'}(x) = \begin{cases} 1 & \text{for } |x| < \sigma \\ 0 & \text{for } |x| \geq \sigma \end{cases} \quad (2.7.9)$$

or as an un-normalized Gaussian function defined by

$$G_{\sigma'}(x) = \exp(-x^2/2\sigma^2) \quad (2.7.10)$$

The function (2.7.8), though cumbersome in appearance, is quite simple in content. Consider first the function $G_{\sigma'}(R_{ij} - R_H)$, where R_H is the intermolecular distance at which we expect a hydrogen bond to be formed. A reasonable choice is $R_H = 2.76 \text{ \AA}$. This function attains its maximal value of unity. It drops to zero [either abruptly (2.7.9) or continuously (2.7.10) for $|R_{ij} - R_H| > \sigma'$]. Next, we stipulate the relative orientation of the pair of molecules. The factor $G_{\sigma}[(\mathbf{h}_{i\alpha} \cdot \mathbf{u}_{ij}) - 1]$ attains its maximum value whenever the unit vector $\bar{H}_{i\alpha}$ (i.e. the donor arm $\bar{H}_{i\alpha}$, $\alpha = 1, 2$, of the i th molecule) is in the direction of the unit vector

$\mathbf{u}_{ij} = \mathbf{R}_{ij}/R_{ij}$. Similarly, $G_\sigma[(\mathbf{l}_{j\beta} \cdot \mathbf{u}_{ij}) + 1]$ attains its maximum value whenever the direction of the acceptor arm $\mathbf{l}_{j\beta}$ is in the direction $-\mathbf{u}_{ij}$. Thus, the product of these three functions attains a value close to unity only if, simultaneously, R_{ij} is about R_H , the direction of $\bar{H}_{i\alpha}$ is about that of $\mathbf{u}_{ij}$, and the direction of $\mathbf{l}_{j\beta}$ is about that of $-\mathbf{u}_{ij}$. Such a configuration is said to be “favorable” for *HB* formation. Clearly, if all of the above three conditions are fulfilled, then the interaction energy is about ε_{HB} . The sum of the various terms in the curly brackets of (2.7.8) arises from the total of eight possible favorable directions for *HB* formation (four when molecule *i* is a donor and four when molecule *i* is an acceptor). The variances σ and σ' are considered as adjustable parameters. Note that of the eight terms in the curly brackets, only one may be appreciably different from zero at any given configuration $\mathbf{X}_i, \mathbf{X}_j$. Clearly, the *HB* part of the potential in (2.7.8) does not suffer from a possible divergence as in the Bjerrum model, and clearly does not allow two bonds to be formed by a pair of water molecules (Fig. 2.48b).

A choice of the square-well function (2.7.9) leads to an on-off definition of an *HB*, i.e. two water molecules are either *HB*ed or not. This simplified view is sometimes convenient in applications. The continuous definition of the *HB* potential using (2.7.10) provides a gradual change from an

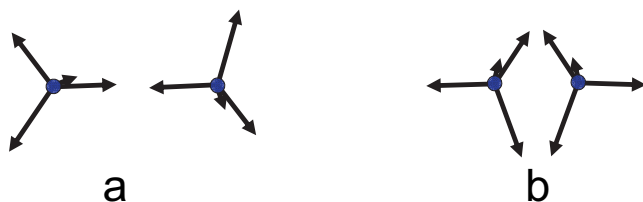


Fig. 2.48 The formation of (a) single *HB*s and (b) of double *HB*s.

*HB*ed to a non-*HB*ed pair of water molecules. This is clearly a more realistic view that can be described as stretching and bending of the hydrogen bond.

Note also that in Eq. (2.7.8) we accounted only for configurations that are favorable for *HB*ing. In a more realistic function, one might add another eight terms to (2.7.8) to account for the electrostatic repulsion whenever two donors or two acceptor arms approach each other. In some of our order-of-magnitude estimates presented in this and in the next chapter, we shall not need any detailed description of the potential function, and we can also ignore the distinction between a donor and an acceptor arm.

For qualitative estimates, we shall simplify the pair potential and instead of (2.7.6) we shall assume the form

$$U(\mathbf{X}_i, \mathbf{X}_j) = U_{HS}(R_{12}) + \varepsilon_{HB} G(\mathbf{X}_i, \mathbf{X}_j) \quad (2.7.11)$$

where the *LJ* part is replaced by the hard-sphere (*HS*) interaction. The dipole-dipole interaction is ignored and the function $G(\mathbf{X}_i, \mathbf{X}_j)$ is simplified so that all the “arms” are considered to be equivalent. Thus, instead of eight terms in (2.7.8) corresponding to the eight pairings of a donor and acceptor, we take 16 terms corresponding to the 16 pairings of one arm on the *i*th molecule with one “arm” on the *j*th molecule. This simplified version of the potential may be referred to as the primitive model for water.⁶⁸

2.7.3. Second virial coefficients of water

The virial coefficients of water are defined as the coefficients in the density expansion of the pressure:

$$\frac{P}{k_B T} = \rho + B_2(T)\rho^2 + B_3(T)\rho^3 + \dots \quad (2.7.12)$$

⁶⁸It should be noted that the identification of the four arms might affect the *counting of configurations*, and hence also the entropy of the system.

The second virial coefficient for non-spherical molecules is given by

$$B_2(T) = -\frac{1}{16\pi^2} \int d\mathbf{X}_2 \{ \exp[-\beta U(\mathbf{X}_1, \mathbf{X}_2)] - 1 \} \quad (2.7.13)$$

The second virial coefficient is a six-fold integral involving the pair potential for two water molecules. The numerical evaluation of such integrals is more difficult than that of the corresponding one-dimensional integral for a system of spherical particles. Furthermore, the integral in (2.7.13), even when evaluated exactly, cannot be expected to be a stringent test of the potential function. Indeed, there can be an infinite number of functions $U(\mathbf{X}_1, \mathbf{X}_2)$ which will lead to the same virial coefficient $B_2(T)$. In Fig. 1.11, we have shown some experimental values of $B_2(T)$. Mas *et al.* (1997) have calculated the second virial coefficient for water for different pair potentials. Most of the calculated results agree with experimental data on the second virial coefficient. They correctly concluded that “in order to conduct simulations of bulk water, one must incorporate three body non-additive effects.”

The curves in Fig. 1.11 were drawn based on the data from Lemmon *et al.* (2007). An empirical equation was suggested by Keyes⁶⁹

$$B_2(T) = \{2.062 - (2.9017 \times 10^3/T) \\ \times \exp[1.7095 \times 10^5/T^2]\} 18 \text{ cm}^3 \text{ mol}^{-1} \quad (2.7.14)$$

Note that in the limit of very high temperatures

$$B_2(T \rightarrow \infty) \approx 37.1 \text{ cm}^3 \text{ mol}^{-1} \quad (2.7.15)$$

⁶⁹Keyes (1958), quoted by Eisenberg and Kauzmann (1969).

Using the primitive pair potential in the form (2.7.11), we can split the integral into two contributions:

$$\begin{aligned}
 B_2(T) &= -\frac{1}{16\pi^2} \int d\mathbf{X}_2 \{ \exp[-\beta U(\mathbf{X}_1, \mathbf{X}_2) - 1] \} \\
 &\approx -\frac{1}{16\pi^2} \left\{ (-1) \int d\mathbf{X}_2 + [\exp(-\beta \varepsilon_{HB}) - 1] \right. \\
 &\quad \left. \int_{HB \text{ region}} \dots \int d\mathbf{X}_2 \right\} \quad (2.7.16)
 \end{aligned}$$

The first term corresponds to the region where $G(\mathbf{X}_1, \mathbf{X}_2) = 0$ and $U_{HS}(R_{12}) \rightarrow \infty$. In this region, the integrand is (-1) , and if we choose $\sigma_w \approx 2.8 \text{ \AA}$ as the effective diameter of the water molecule, we have

$$\frac{1}{16\pi^2} \int d\mathbf{X}_2 = \frac{1}{2} \int_0^{\sigma_w} 4\pi R^2 dR = \frac{4\pi\sigma_w^3}{6} \approx 28 \text{ cm}^3 \text{ mol}^{-1} \quad (2.7.17)$$

This is roughly half of the excluded volume between two spheres of diameter $2.8 \text{ \AA}$. The second part of the integral in (2.7.16) is approximated as follows. We assume that the *HB* interaction is realized only from a small region $\Delta\mathbf{X}$, where the integrand is nearly constant. Since we have eight equivalent regions from which molecule 2 can form an *HB* with molecule 1, we define the *HB* region per arm $\Delta\mathbf{X}$ as⁷⁰

$$8\Delta\mathbf{X} = \int_{HB \text{ region}} \dots \int d\mathbf{X}_2 \quad (2.7.18)$$

Using (2.7.18) and (2.7.17), we can rewrite (2.7.16) as

$$B_2(T) = \frac{4\pi\sigma_w^3}{6} - \frac{8}{2} \{ \exp(-\beta \varepsilon_{HB}) - 1 \} \frac{\Delta\mathbf{X}}{8\pi^2} \quad (2.7.19)$$

⁷⁰ $\Delta\mathbf{X}$ is a "volume" in six-dimensional space.

For some calculations, it is not necessary to specify the range of distances and angles from which an HB can be formed. Instead, one can use the HB region ΔX from which one arm of molecule 1 can form an HB with one arm of molecule 2. The value of ΔX may be estimated from the experimental value of the second virial coefficient. For instance, at $T = 298$ K, the value of B_2 is estimated from (2.7.14)⁷¹:

$$B_2(T = 298 \text{ K}) = -1165 \text{ cm}^3 \text{ mol}^{-1} \quad (2.7.20)$$

Using the value of $28 \text{ cm}^3 \text{ mol}^{-1}$ from (2.7.17), we obtain

$$\frac{\Delta X}{8\pi^2} [\exp(-\beta \varepsilon_{HB}) - 1] = \frac{28 + 1165}{4} \approx 298.25 \text{ cm}^3 \text{ mol}^{-1} \quad (2.7.21)$$

Thus, for any choice of ε_{HB} , we can estimate ΔX . Two estimates of ΔX are

$$\text{for } \varepsilon_{HB} = -6.5 \text{ kcal mol}^{-1}, \quad \Delta X \approx 0.43 \text{ cm}^3 \text{ mol}^{-1} \quad (2.7.22)$$

$$\text{for } \varepsilon_{HB} = -7.5 \text{ kcal mol}^{-1}, \quad \Delta X \approx 0.87 \text{ cm}^3 \text{ mol}^{-1} \quad (2.7.23)$$

Clearly, the stronger we choose the HB energy, the smaller the HB region necessary to fit the experimental value of the second virial coefficient.

The above estimates of ΔX were made based on the second virial coefficient for water. Besides the uncertainty of extrapolating to low temperature, these values are relevant to the interaction between exactly *two real* water molecules. When we need to treat the water in the liquid state, we cannot rely on these estimates but use ΔX as an adjustable parameter.

⁷¹Note that this estimate is very uncertain. The analytical function (2.7.14) represents the experimental values of B_2 in the range 323–733 K. Around room temperature, $B_2(T)$ is a very steep function of T .

2.7.4. *Definition of the structure of water*

The concept of the structure of water (SOW) is ubiquitous in the literature on water and aqueous solutions. In most cases, the concept of the SOW is discussed in a very qualitative way. For instance, Eisenberg and Kauzmann (1969) start from the concept of “structure” as applied to the crystal ice I_h , then proceed to describe the structure of liquid water. Most of the discussion is descriptive and no quantitative definition of the SOW is offered.

In the theory of liquids, the structure is usually defined in terms of the molecular distribution function.⁷² This definition, though quantitative, is not satisfactory when applied to liquid water. What is needed is a *number* that measures the extent of the structure of water, as is currently understood, with the help of which one can compare the structures of the liquid in two different states.

As we have noted in Sec. 1.4, the height of the second peak of the pair correlation function is also used as the signature of the structure of water. Indeed, in most cases where we expect the structure of water to be reduced (say, by increasing the temperature or adding an electrolyte), we observe a diminishing of the height of the second peak. However, this quantity is strictly a measure of the relative concentration of pairs of water molecules at a distance of about 4.5 Å, which is also the distance of the second nearest neighbors in ice I_h . It does not measure the degree of structure as currently understood in the literature. We present here one possible definition that is based on the form of the pair potential as discussed in Sec. 2.7.2, which conforms to what is expected from a measure of the SOW and one that can be computed by any simulation technique.

⁷²See, for instance, Fletcher (1970).

Using the definition of the pair potential in the form

$$U(\mathbf{X}_1, \mathbf{X}_2) = U_{LJ}(R_{12}) + \varepsilon_{HB}G(\mathbf{X}_1, \mathbf{X}_2) \quad (2.7.24)$$

we define the following function:

$$\psi_i(\mathbf{X}^N) = \sum_{\substack{j=1 \\ j \neq i}}^N G(\mathbf{X}_i, \mathbf{X}_j) \quad (2.7.25)$$

For each configuration $\mathbf{X}^N$ of the N water molecules, we choose one particular molecule, say, the i th one. Since $G(\mathbf{X}_i, \mathbf{X}_j)$ is unity whenever molecule j is in a favorable configuration to form an *HB* with i , the sum on the right-hand side of (2.7.25) *counts* all the water molecules that are *HB*ed to i at a specific configuration of the entire system. Since we have chosen σ in Eq. (2.7.8) to be small enough so that two water molecules can form at most one *HB* between them, the value of $\psi_i(\mathbf{X}^N)$ can roughly change between zero and four. [In the case of the discrete definition of *HB* (2.7.9), G can be either zero or one, and hence, ψ_i can take only the discrete values of 0, 1, 2, 3, 4. For the continuous definition (2.7.10), G changes continuously from zero to one; therefore, ψ_i can also take any value between 0 and 4.]

We now define the average value of $\psi(\mathbf{X}^N)$ in, say, the T, V, N ensemble as⁷³

$$\langle \psi \rangle = \int d\mathbf{X}^N P(\mathbf{X}^N) \psi_1(\mathbf{X}^N) \quad (2.7.26)$$

This is the average number of *HB*s formed by a specific water molecule (say, molecule numbered 1) in a system of pure water

⁷³A similar average can be defined also in the T, P, N ensemble (see Sec. 2.7.7). Note also that $\langle \psi \rangle$ is the average number of *HB*s that a specific molecule, say 1, forms. Since all molecules are equivalent, it does not matter which one we choose.

at T, V, N . The quantity $\langle\psi\rangle$ is related to the total average number of HB s in the system, which we denote by $\langle N_{HB}\rangle$. This is defined as

$$\begin{aligned}\langle N_{HB}\rangle &= \frac{1}{2} \int d\mathbf{X}^N P(\mathbf{X}^N) \sum_{i=1}^N \sum_{\substack{j=1 \\ i \neq j}}^N G(\mathbf{X}_i, \mathbf{X}_j) \\ &= \frac{1}{2} \int d\mathbf{X}_1 d\mathbf{X}_2 \rho^{(2)}(\mathbf{X}_1, \mathbf{X}_2) G(\mathbf{X}_1, \mathbf{X}_2).\end{aligned}\quad (2.7.27)$$

Since the sum over all i and j (with $i \neq j$) counts the number of all different pairs of molecules, the integral is the average number of pairs of molecules, the configuration of which is within the favorable range for forming an HB . The factor $\frac{1}{2}$ is included because the sum in the integrand counts each pair twice.

The second form on the right-hand side of (2.7.27) converts the average into an integral over the pair distribution function. The relation between $\langle N_{HB}\rangle$ and $\langle\psi\rangle$ is obtained from (2.7.25), (2.7.26), and (2.7.27), i.e.

$$\begin{aligned}\langle N_{HB}\rangle &= \frac{1}{2} \int d\mathbf{X}^N P(\mathbf{X}^N) \sum_{i=1}^N \sum_{\substack{j=1 \\ i \neq j}}^N G(\mathbf{X}_i, \mathbf{X}_j) \\ &= \frac{1}{2} N \int d\mathbf{X}^N P(\mathbf{X}^N) \psi_1(\mathbf{X}^N) \\ &= \frac{1}{2} N \langle\psi\rangle\end{aligned}\quad (2.7.28)$$

Thus, either $\langle\psi\rangle$ or $\langle N_{HB}\rangle$ can serve as a definition of the SOW . Clearly, this definition conforms with our intuitive expectation of a measure of the SOW . If $\langle\psi\rangle \approx 4$, each molecule is on average HB ed to four other molecules, as in ice I_h .⁷⁴ This is a

⁷⁴Note that $\langle\psi\rangle = 4$ does not mean that the structure is the same as in ice. All it says is that most of the molecules are engaged in four HB s.

highly structured state. On the other hand, $\langle \psi \rangle \approx 0$ corresponds to the lowest structured state.

We can use the definition of $\psi(\mathbf{X}^N)$ in (2.7.25) to construct an exact mixture-model approach to liquid water. In Sec. 2.3, we showed that any quasi-component distribution function can be used for constructing a mixture model for any liquid. Specifically, for water, we construct the following mixture model. First, we define the counting function

$$N_n(\mathbf{X}^N) = \sum_{i=1}^N \delta[\psi_i(\mathbf{X}^N) - n] \quad (2.7.29)$$

where δ can be either a Kronecker delta or a Dirac delta function depending on whether we choose the discrete or the continuous definition function of the *HB* [i.e. either (2.7.9) or (2.7.10)]. $N_n(\mathbf{X}^N)$ is the number of molecules which form n *HBs* when the system is in a specific configuration $\mathbf{X}^N$. The average number of such molecules is

$$\begin{aligned} \langle N_n \rangle &= \int d\mathbf{X}^N P(\mathbf{X}^N) \sum_{i=1}^N \delta[\psi_i(\mathbf{X}^N) - n] \\ &= N \int d\mathbf{X}^N P(\mathbf{X}^N) \delta[\psi_1(\mathbf{X}^N) - n] \end{aligned} \quad (2.7.30)$$

From (2.7.30), we can define the mole fraction x_n corresponding to $\langle N_n \rangle$, i.e.

$$x_n = \frac{\langle N_n \rangle}{N} \quad (2.7.31)$$

The average number of *HBs* in the system is thus

$$\begin{aligned} \frac{N}{2} \sum_{n=0}^4 n x_n &= \frac{N}{2} \int d\mathbf{X}^N P(\mathbf{X}^N) \sum_{n=0}^4 n \delta[\psi_1(\mathbf{X}^N) - n] \\ &= \frac{N}{2} \int d\mathbf{X}^N P(\mathbf{X}^N) \psi_1(\mathbf{X}^N) = \langle N_{HB} \rangle \end{aligned} \quad (2.7.32)$$

which is the same as $\langle N_{HB} \rangle$ in (2.7.27). We shall discuss in Sec. 2.7.7 a method of estimating x_n , and hence $\langle N_{HB} \rangle$. Clearly, the mole fractions x_n as well as the averages $\langle \psi \rangle$ and $\langle N_{HB} \rangle$ can be computed by any simulation technique applied to liquid water.

2.7.5. *An approximate method of calculating the structure of water*

Having defined the concept of the SOW in Sec. 2.7.4, we next ask how we can measure this structure. The following is an approximate relation between the solvation Gibbs energy of water and the quantity $\langle \psi \rangle$, or equivalently $\langle N_{HB} \rangle$, in pure water. This approximation is based on the assumption that H_2O and D_2O may each be represented by a molecular model with a pair potential of the form (2.7.6). The two liquids are assumed to have the same pair potential except for a difference in the HB energy ε_{HB} , which we denote by ε_D and ε_H for D_2O and H_2O , respectively. In other words, we assume that the geometry and the LJ parts of the interaction are the same for H_2O and D_2O ; only the strength of the HB energies are different.

Starting with the expression for the solvation Gibbs energy of water in pure water (see Sec. 1.6)

$$\Delta G_w^* = -k_B T \ln \langle \exp(-\beta B_w) \rangle_0 \quad (2.7.33)$$

where B_w is the binding energy of an added water molecule at a configuration $\mathbf{X}_0$ to a system of N water molecules at a fixed configuration $\mathbf{X}^N = \mathbf{X}_1, \dots, \mathbf{X}_N$. The average in (2.7.33) is over all configurations of the N water molecules in the T, P, N ensemble:

$$B_w \equiv U(\mathbf{X}_0, \mathbf{X}_1, \dots, \mathbf{X}_N) - U(\mathbf{X}_1, \dots, \mathbf{X}_N) \quad (2.7.34)$$

We differentiate ΔG_w^* with respect to ε_{HB} at constant T, P, N to obtain

$$\begin{aligned}
 \left(\frac{\partial \Delta G_w^*}{\partial \varepsilon_{HB}} \right)_{T,P,N} &= -k_B T \frac{\partial}{\partial \varepsilon_{HB}} \left\{ \ln \frac{\int dV \exp[-\beta PV] \int d\mathbf{X}^N \exp[-\beta U_N - \beta B_w]}{\int dV \exp[-\beta PV] \int d\mathbf{X}^N \exp[-\beta U_N]} \right\} \\
 &= \frac{1}{2} \int dV \exp[-\beta PV] \int d\mathbf{X}^N P(\mathbf{X}^N / \mathbf{X}_0) \sum_{i=0}^N \sum_{\substack{j=0 \\ j \neq i}}^N G(i, j) \\
 &\quad - \frac{1}{2} \int dV \exp[-\beta PV] \int d\mathbf{X}^N P(\mathbf{X}^N) \sum_{i=1}^N \sum_{\substack{j=1 \\ j \neq i}}^N G(i, j) \\
 &= \langle N_{HB} \rangle_w^{(N+1)} - \langle N_{HB} \rangle_0^{(N)} \quad (2.7.35)
 \end{aligned}$$

Note that in the last form on the right-hand side of (2.7.35) we have two different averages in the T, P, N ensemble. The first is the *conditional* average number of HBs in a system of $N + 1$ water molecules, given that one water molecule is at a fixed configuration $\mathbf{X}_0$. The second is the average number of HBs of a system of N water molecules. The latter is the same as in (2.7.27) except that the average is taken in the T, P, N ensemble. The subscripts 0 and w in these averages indicate that the averages are taken with respect to the distributions $P(V, \mathbf{X}_N)$ and $P(V, \mathbf{X}_N / \mathbf{X}_0)$, respectively.

Clearly, if we release the constraint on the added water molecule to be at specific configuration $\mathbf{X}_0$, the average number of HBs should not change. Therefore, the difference on the right-hand side of (2.7.35) may be written as

$$\begin{aligned}
 \left(\frac{\partial \Delta G_w^*}{\partial \varepsilon_{HB}} \right)_{T,P,N} &= \langle N_{HB} \rangle_0^{(N+1)} - \langle N_{HB} \rangle_0^{(N)} \\
 &= \frac{(N+1)}{2} \langle \psi \rangle_0 - \frac{N}{2} \langle \psi \rangle_0 \\
 &= \frac{1}{2} \langle \psi \rangle_0 \quad (2.7.36)
 \end{aligned}$$

Thus, the derivative of ΔG_w^* with respect to the parameter ε_{HB} is a measure of the structure of water (see Sec. 2.7.4).

We can now use (2.7.36) to estimate the structure of water. The assumption is made that $(\varepsilon_D - \varepsilon_H)$ is small enough so that we can expand ΔG_w^* to first order in $\varepsilon_D - \varepsilon_H$ to obtain

$$\Delta G_{D_2O}^* - \Delta G_{H_2O}^* \approx \frac{1}{2} \langle \psi \rangle_0 (\varepsilon_D - \varepsilon_H) \quad (2.7.37)$$

This relation may be used to estimate the extent of structure $\langle \psi \rangle_0$ from experimental data on the solvation Gibbs energies, and from $\varepsilon_D - \varepsilon_H$.

As an example of the application of (2.7.37), we use the solvation Gibbs energies of H_2O and D_2O in their own liquids, at 25°C (see Sec. 1.6):

$$\Delta G_{D_2O}^* - \Delta G_{H_2O}^* = -6.405 + 6.32 = -0.085 \text{ kcal mol}^{-1}$$

and taking $\varepsilon_D - \varepsilon_H \approx -0.22 \text{ kcal mol}^{-1}$ (based on the difference in the enthalpies of sublimation of light and heavy ice), we obtain

$$\langle \psi \rangle \approx 0.77 \quad (2.7.38)$$

This is too low a value for the average number of HB s formed by a specific water molecule. It is not clear whether this is a result of the simplifying assumptions made in the model or due to the inadequacy of the first-order expansion used in Eq. (2.7.37). We shall see in the next section that $\langle \psi \rangle$ is closer to four, indicating a higher degree of structure.

Another useful result may be obtained by differentiating $\langle N_{HB} \rangle$ in (2.7.28) with respect to ε_{HB} . The result is

$$\begin{aligned} \left(\frac{\partial \langle N_{HB} \rangle}{\partial (-\varepsilon_{HB})} \right) &= \beta [\langle N_{HB}^2 \rangle - \langle N_{HB} \rangle^2] \\ &= \beta (\langle (N_{HB} - \langle N_{HB} \rangle)^2 \rangle) \geq 0 \end{aligned} \quad (2.7.39)$$

Note that since $\varepsilon_{HB} < 0$, $-\varepsilon_{HB}$ is positive. The result (2.3.39) means that the stronger the HB energy (larger $-\varepsilon_{HB}$), the larger the structure of the water. (Here, the derivative is taken in either the T, P, N or the T, V, N ensemble.) This is consistent with the intuitive expectation that as we increase the strength of the HB we also increase the structure of the system. It is also consistent with the conclusion of Kuharski and Rossky (1985) based on the theoretical quantum mechanical study of the structures of liquids H_2O and D_2O .

2.7.6. Solvation of water in pure water

Again, we start with the Gibbs energy of solvation of water in liquid water⁷⁵:

$$\Delta G_w^* = -k_B T \ln \langle \exp(-\beta B_w) \rangle_0 \quad (2.7.40)$$

where B_w is the total interaction energy of a single water molecule with all other molecules of the system at some specific configuration $\mathbf{X}_1, \dots, \mathbf{X}_N$. As in Sec. 2.7.5, we assume that the pair potential has the general form (2.7.24).

The experimental values of the solvation Gibbs energies were given in Sec. 1.6. These values were determined from the equilibrium densities of water in the liquid and gaseous states. The statistical mechanical expression for the solvation Gibbs energy is given in (2.7.40).

We shall now estimate the conditional solvation Gibbs or Helmholtz energy per arm of a water molecule. This quantity is useful in various applications in the theory of aqueous solutions. Since $P\Delta V_w^*$, where ΔV_w^* is the solvation volume, is usually negligible compared with ΔG_w^* , we shall actually compute the solvation Helmholtz energy and assume that $\Delta G_w^* \approx \Delta A_w^*$.

⁷⁵For details, see Sec. 1.6 and Ben-Naim (2006).

We start from the pair potential (2.7.24), which we write as

$$\begin{aligned} U(\mathbf{X}_i, \mathbf{X}_j) &= U_{LJ}(R_{ij}) + \varepsilon_{HB} G(\mathbf{X}_i, \mathbf{X}_j) \\ &= U_{LJ} + U_{HB} \end{aligned} \quad (2.7.41)$$

where U_{LJ} is the Lennard–Jones part, and U_{HB} is the HB part of the interaction potential.

The total binding energy of the newly added water molecule at $\mathbf{X}_0$ is rewritten as

$$\begin{aligned} B_w &= \sum_{i=1}^N U(\mathbf{X}_0, \mathbf{X}_i) \\ &= \sum_{i=1}^N U_{LJ}(R_{0,i}) + \sum_{i=1}^N U_{HB}(\mathbf{X}_0, \mathbf{X}_i) \\ &= B_w^{LJ} + B_w^{HB} \end{aligned} \quad (2.7.42)$$

We can further split the HB binding energy of the water molecules as a sum of the four arms:

$$B_w^{HB} = \sum_{l=1}^4 B_l^{HB} \quad (2.7.43)$$

With (2.7.42) we can rewrite the solvation Helmholtz energy of water in liquid water as

$$\begin{aligned} \Delta A_w^* &= -k_B T \ln \langle \exp[-\beta B_w] \rangle_0 \\ &= -k_B T \ln \langle \exp[-\beta (B_w^{LJ} + B_w^{HB})] \rangle_0 \\ &= -k_B T \ln \langle \exp[-\beta B_w^{LJ}] \rangle_0 - k_B T \ln \langle \exp[-\beta B_w^{HB}] \rangle_{LJ} \\ &= \Delta A_{LJ}^* + \Delta A_{HB/LJ}^* \end{aligned} \quad (2.7.44)$$

In (2.7.44), the solvation process of the added water molecule at $\mathbf{X}_0$ is split into two steps. We first solvate the Lennard–Jones part. The corresponding solvation Helmholtz

energy is ΔA_{LJ}^* . The second step involves the “turning on” of the HB part, given that the LJ has already been turned on. Note that the first term in (2.7.44) is an average with the distribution $P(\mathbf{X}^N)$, whereas the second is a conditional average with the distribution $P(\mathbf{X}^N/\mathbf{X}_0^{LJ})$, which is the probability density of finding the configuration $\mathbf{X}^N$ of the entire system given that an LJ particle was placed at $\mathbf{X}_0$ (in fact, since the LJ particle is spherical we can just place it at a point $\mathbf{R}_0$).

The next step is to rewrite the second term on the right-hand side of (2.7.44) as a sum of four terms. We use (2.7.43) to rewrite (2.7.44) as

$$\Delta A_w^* = \Delta A_{LJ}^* - k_B T \ln \left\langle \exp \left(-\beta \sum_{l=1}^4 B_l^{HB} \right) \right\rangle_{LJ} \quad (2.7.45)$$

The assumption is now made that the conditional average on the right-hand side of (2.7.45) may be factored into a product of four averages, each of which pertains to the binding energy of one specific arm, i.e.

$$\left\langle \exp \left(-\beta \sum_{l=1}^4 B_l^{HB} \right) \right\rangle_{LJ} = \prod_{l=1}^4 \langle \exp(-\beta B_l^{HB}) \rangle_{LJ} \quad (2.7.46)$$

The factorization of the average in (2.7.46) involves the assumption that the conditional solvation Helmholtz energies of the four arms of the water molecule are independent.⁷⁶

Substituting (2.7.46) into (2.7.45), we rewrite the solvation Helmholtz energy of a water molecule in pure water as

$$\Delta A_w^* = \Delta A_{Ne}^* + \sum_{l=1}^4 \Delta A^{*HB}(l/LJ) \quad (2.7.47)$$

⁷⁶Originally, this assumption was made on intuitive grounds (Ben-Naim, 1992). Recently, it was examined by Predota *et al.* (2003) by a simulation method. It was concluded that this is indeed a plausible approximation.

where we have identified the LJ part of the solvation Helmholtz energy ΔA_{LJ}^* with the solvation Helmholtz energy of a neon atom in water. This is equivalent to the statement that solvation of the LJ part of the interaction energy of the *added* water molecule in pure water is equivalent to the solvation of a real neon atom.

The second term on the right-hand side of (2.7.47) is the conditional solvation Helmholtz energy for the process of turning on the four arms of the water molecule. Strictly, we have to distinguish between the two donor arms and the two acceptor arms (Sec. 2.7.2). However, for all our purposes we can disregard this distinction and assume that this term is simply four times the conditional solvation Helmholtz energy of one arm, which we designate as the arm α . Hence, we write

$$\Delta A_w^* = \Delta A_{Ne}^* + 4\Delta A^{*HB}(\alpha/LJ) \quad (2.7.48)$$

The conditional Helmholtz energy of solvation of one arm may be determined either by using experimental values of ΔA_w^* and ΔA_{Ne}^* or by theoretical calculation.

The experimental value of the conditional solvation Helmholtz (or Gibbs) energy per arm of H_2O at $25^\circ C$ can be obtained from the experimental values of the solvation Helmholtz energy of water and neon, i.e.

$$\Delta A^{*HB}(\alpha/LJ) = \frac{\Delta A_w^* - \Delta A_{Ne}^*}{4} \approx -2.25 \text{ kcal mol}^{-1} \quad (2.7.49)$$

The corresponding value for D_2O is

$$\Delta A^{*HB}(\alpha/LJ) \approx -2.26 \text{ kcal mol}^{-1} \quad (2.7.50)$$

It is of interest to note that had we used the same calculation for the solvation Helmholtz energy per arm for H_2S and H_2Se in water, the corresponding values would be much smaller. Thus,

for H_2S we have

$$\Delta A^{*HB}(\alpha/LJ) = \frac{\Delta A_{H_2S}^* - \Delta A_{Ar}^*}{4} \approx -0.64 \text{ kcal mol}^{-1} \quad (2.7.51)$$

and for H_2Se we find

$$\Delta A^{*HB}(\alpha/LJ) = \frac{\Delta A_{H_2Se}^* - \Delta A_{Kr}^*}{4} \approx -0.52 \text{ kcal mol}^{-1} \quad (2.7.52)$$

We now proceed to an approximate theoretical estimate of $\Delta A^{*HB}(\alpha/LJ)$ for water in water. We start from the definition of this quantity in (2.7.47) and (2.7.46):

$$\begin{aligned} \exp[-\beta \Delta A^{*HB}(\alpha/LJ)] &= \langle \exp(-\beta B_{\alpha}^{HB}) \rangle_{LJ} \\ &= \int d\mathbf{X}^N P(\mathbf{X}^N/LJ) \exp(-\beta B_{\alpha}^{HB}) \end{aligned} \quad (2.7.53)$$

Here, B_{α}^{HB} is the binding energy of one arm (α) to the entire system of N water molecules at some specific configuration $\mathbf{X}^N$. The average in (2.7.53) is taken with respect to the conditional distribution $P(\mathbf{X}^N/LJ)$, i.e. the distribution of the configuration $\mathbf{X}^N$, given an LJ particle at some fixed position, say, $\mathbf{R}_0$.

The range of integration over all the configurations of the N water molecules may be divided into two regions as follows:

$$\int d\mathbf{X}^N P(\mathbf{X}^N/LJ) \exp(-\beta B_{\alpha}^{HB}) = \int_{\substack{\text{one } w \\ \text{HBed to } \alpha}} + \int_{\substack{\text{no } w \\ \text{HBed to } \alpha}} \quad (2.7.54)$$

The first integral on the right-hand side of (2.7.54) is over all configurational space for which at least one water molecule (w) is HB ed to the arm (α). Since at most one water molecule can form an HB to a single arm at any time, this is the same as the

region from which *exactly* one water molecule is *HB*ed to the arm. Furthermore, since there are N equivalent water molecules, we can rewrite this term as

$$\begin{aligned} \int_{\substack{\text{one } w \\ \text{HBed to } \alpha}} &= \sum_{i=1}^N \int_{\substack{\text{ith } w \\ \text{HBed to } \alpha}} \\ &= N \int_{\substack{\text{molecule 1} \\ \text{HBed to } \alpha}} d\mathbf{X}^N P(\mathbf{X}^N/LJ) \exp[-\beta U^{HB}(\alpha, \mathbf{X}_1)] \end{aligned} \quad (2.7.55)$$

In (2.7.55), we write the first integral on the right-hand side of (2.7.54) as a sum of N integrals. Note that the added water molecule was assigned the index zero. Therefore, the region of integration over all configurations $\mathbf{X}^N$ such that *one* molecule is *HB*ed to arm α is the sum of the regions in which a specific water molecule i is *HB*ed to the arm α . Clearly, there are N such terms, all of equal magnitude. Therefore, we choose one water molecule, say, number 1, and take N times the integral over all configurational space for which molecule 1 is *HB*ed to α . Furthermore, since the arm α can form only one *HB* at a time, the binding energy B_{α}^{HB} is simply $U^{HB}(\alpha, \mathbf{X}_1)$, i.e. the *HB* part of the potential between the arm α and the specific water molecule at $\mathbf{X}_1$.

The second integral on the right-hand side of (2.7.54) can now be written as

$$\int_{\substack{\text{no } w \\ \text{HBed to } \alpha}} d\mathbf{X}^N P(\mathbf{X}^N/LJ) = 1 - \sum_{i=1}^N \int_{\substack{\text{ith } w \\ \text{HBed to } \alpha}} d\mathbf{X}^N P(\mathbf{X}^N/LJ) \quad (2.7.56)$$

Since this integral is over all configurational space for which *no* water molecule is *HB*ed to the arm α , B_{α}^{HB} is zero in the entire range of these configurations. What remains on the left-hand side of (2.7.56) is an integral over the probability distribution function $P(\mathbf{X}^N/LJ)$. This integral is simply the probability of finding the configuration of all the water molecules such that no water

molecule can form an *HB* with the arm α , given that the *LJ* particle is at some fixed position. It should be noted that the *HB* part of the potential was defined in terms of the geometrical function $G(\mathbf{X}_i, \mathbf{X}_j)$. When we refer to water molecules forming an *HB* with the arm α , we mean that a water molecule is in a favorable configuration such that it can form an *HB* with the arm α .

The left-hand side of (2.7.56) is the probability of an event. Therefore, it can be written as one minus the probability of the complementary event, i.e. that at least one water molecule is *HB*ed to α . The latter is further written as a sum of probabilities, i.e. either water numbered 1 is *HB*ed to α , or water numbered 2 is *HB*ed to α , etc. Combining (2.7.54) and (2.7.55) with (2.7.56), we can rewrite (2.7.53) as

$$\begin{aligned} & \exp[-\beta \Delta A^{*HB}(\alpha/LJ)] \\ &= 1 + N \int_{\substack{\text{molecule 1} \\ \text{HBed to } \alpha}} d\mathbf{X}^N \{ \exp[-\beta U^{HB}(\alpha, \mathbf{X}_1)] - 1 \} P(\mathbf{X}^N/LJ) \\ &= 1 + \int d\mathbf{X}_1 \{ \exp[-\beta U^{HB}(\alpha, \mathbf{X}_1)] - 1 \} \rho_w(\mathbf{X}_1/LJ) \quad (2.7.57) \end{aligned}$$

In the last form on the right-hand side of (2.7.57), we used the definition of the conditional density of water molecules at $\mathbf{X}_1$ given an *LJ* particle at the center of our coordinate system. Note also that since $U^{HB}(\alpha, \mathbf{X}_1)$ is zero except for a very small configurational space, the integrand in (2.7.57) is zero beyond this region; therefore, we have removed the restriction on the range of the integration.

The conditional density can be written as

$$\rho_w(\mathbf{X}_1/LJ) = \frac{1}{8\pi^2} \rho_w g_{w,LJ}(\mathbf{X}_1, LJ) \quad (2.7.58)$$

The average correlation function of water around an *LJ* particle at a distance of about 2.8 Å is estimated to be about two. Assuming now that the *HB* function is discrete (see Sec. 2.7.2),

we can rewrite the integral on the left-hand side of (2.7.57) as

$$\begin{aligned} & \exp[-\beta \Delta A^{*HB}(\alpha/LJ)] \\ &= 1 + [\exp(-\beta \varepsilon_{HB}) - 1] \frac{2(2\Delta X)\rho_w}{8\pi^2} \end{aligned} \quad (2.7.59)$$

Here, ρ_w is the number density of water and ΔX is the configurational range for the formation of *one* HB between two water molecules (see Sec. 2.7.3). Since one arm can form two different HBs with one water molecule, we have two such regions, i.e. $2\Delta X$.

One can use any specific model potential function to estimate the right-hand side of (2.7.59). Fortunately, since the combination $[\exp(-\beta \varepsilon_{HB}) - 1]\Delta X/8\pi^2$ has already been estimated from the second virial coefficient,⁷⁷ we need not know the values of each factor. Using the value of $298.25 \text{ cm}^3 \text{ mol}^{-1}$ given in (2.7.21), we estimate for $T = 298 \text{ K}$, the solvation Helmholtz energy per arm as

$$\begin{aligned} \Delta A^{*HB}(\alpha/LJ) &\approx -k_B T \ln(1 + 298 \times 4 \times 5.55 \times 10^{-2}) \\ &= -2.49 \text{ kcal mol}^{-1} \end{aligned} \quad (2.7.60)$$

where $\rho_w = 5.55 \times 10^{-2} \text{ mol cm}^{-3}$ is the number density of water at 25°C . This result is in good agreement with the experimental value given in (2.7.49). Note that in this calculation, we used the value of $g_{w,LJ} \approx 2$, which is probably too large. With a smaller value, we could have improved somewhat the agreement between the theoretical value (2.7.60) and the experimental value (2.7.49).

2.7.7. *Distribution of species of water molecules*

In Sec. 2.3, we have seen that any quasi-component distribution function can be used as a basis for constructing an exact

⁷⁷Note that the estimate of ΔX from the second virial coefficient is relevant to the actual pair potential between two water molecules. Here, we are using an effective and not the true pair potential.

mixture model for any liquid. We now develop a mixture-model approach which is particularly suitable for liquid water. A variety of approximate versions of such mixture-model approaches have been used in the development of theories of water and aqueous solutions.

The classification of water molecules according to the number of *HBs* in which they participate is the same as discussed in Sec. 2.3. Here, we shall be interested in the distribution of these species. Let ρ_w be the total number density of water molecules and ρ_n be the number density of water molecules participating in exactly n *HBs*. We shall refer to these as the n -species or n -molecule, or an n -cule for short. The mole fraction of such species is $x_n = \rho_n / \rho_w$. The chemical potential of the n th species is written as⁷⁸

$$\mu_n = \mu_n^* + k_B T \ln \rho_n \Lambda^3 \quad (2.7.61)$$

where μ_n^* is the pseudo-chemical potential of the n th species. Since our species are all water molecules being engaged in different number of *HBs*, they must have the same internal degrees of freedom; both the momentum and the internal *PF* of a single molecule are common to all species.

At equilibrium, we have the condition

$$\mu_w = \mu_0 = \mu_1 = \mu_2 = \mu_3 = \mu_4 \quad (2.7.62)$$

The pseudo-chemical potential μ_n^* defined in (2.7.61) is the change in the Helmholtz (or Gibbs) energy in placing one n -molecule at a fixed position in the liquid at T, V, N (or T, P, N) constants, i.e.

$$\begin{aligned} \mu_n^* &= A(T, V, N; \text{one } n\text{-species at } \mathbf{R}_0) - A(T, V, N) \\ &= -k_B T \ln \frac{Q(T, V, N; \text{one } n\text{-species at } \mathbf{R}_0)}{Q(T, V, N)} \end{aligned} \quad (2.7.63)$$

⁷⁸For details, see Ben-Naim (2006).

Because of the condition of equilibrium (2.7.62), we can write the chemical potential of the water molecule as

$$\begin{aligned}\mu_w &= \mu_w^* + k_B T \ln \rho_w \Lambda^3 \\ &= \mu_n^* + k_B T \ln \rho_n \Lambda^3\end{aligned}\quad (2.7.64)$$

Note that the chemical potential of each species is equal to μ_w . However, the pseudo-chemical potentials are different for each species. Since Λ^3 is the same for all species we can rewrite (2.7.64) as

$$\rho_n \Lambda^3 = \exp[\beta(\mu_w - \mu_n^*)] \quad (2.7.65)$$

Summing over n , we get

$$\rho_w \Lambda^3 = \sum_{n=0}^4 \rho_n \Lambda^3 = \exp[\beta \mu_w] \sum_{n=0}^4 \exp[-\beta \mu_n^*] \quad (2.7.66)$$

or equivalently

$$\exp[-\beta \mu_w^*] = \sum_{n=0}^4 \exp[-\beta \mu_n^*] \quad (2.7.67)$$

This relation is the same as the relationships between the pseudo-chemical potentials of different isomers in chemical equilibrium.⁷⁹ The interpretation of (2.7.67) is quite simple. In view of (2.7.63), we can translate (2.7.67) into

$$\begin{aligned}& \frac{Q(T, V, N; \text{one water at } \mathbf{R}_0)}{Q(T, V, N)} \\ &= \sum_{n=0}^4 \frac{Q(T, V, N; \text{one } n\text{-species at } \mathbf{R}_0)}{Q(T, V, N)}\end{aligned}\quad (2.7.68)$$

Thus, the partition function of a system with one additional *water* molecule at $\mathbf{R}_0$ is simply the sum over all the *states* of this

⁷⁹See Ben-Naim (2006).

molecule, which in our case are the five different n -species of the water molecules.

Next, write the analog of (2.7.67) and (2.7.68) for each species. For each single n -species at $\mathbf{R}_0$, we can distinguish different sub-species. For instance, for the 1-species we can write the analog of (2.7.67) as

$$\exp[-\beta\mu_1^*] = \sum_{l=1}^4 \exp[-\beta\mu_{one\ specific\ l\ arm}^*] \quad (2.7.69)$$

and the analog of (2.7.68)

$$\begin{aligned} Q(T, V, N; one\ 1-species\ at\ \mathbf{R}_0) \\ = \sum_{l=1}^4 Q(T, V, N; one\ specific\ arm\ (l)\ turned\ on) \end{aligned} \quad (2.7.70)$$

Note that the state of one 1-species (i.e. a one-arm forming *HB*) at $\mathbf{R}_0$ comprises four states according to which *specific* arm is forming the *HB*. This is shown schematically in Fig. 2.49a.

Similarly, for the 2-species we can write (Fig. 2.49b)

$$\exp[-\beta\mu_2^*] = \sum_{\substack{l_1=1 \\ l_1 \neq l_2}}^4 \sum_{l_2=1}^4 \exp[-\beta\mu_{two\ specific\ l_1\ and\ l_2\ arms}^*] \quad (2.7.71)$$

and a similar expression for the 3-species (Fig. 2.49c).

This looks a little complicated but basically it is very simple. When placing a water molecule at $\mathbf{R}_0$, we distinguish between the n -species according to the *number* of arms that are engaged in *HBs*. When placing an n -species at $\mathbf{R}_0$, we can further distinguish between particles according to which *specific* arms are engaged in *HBs*.

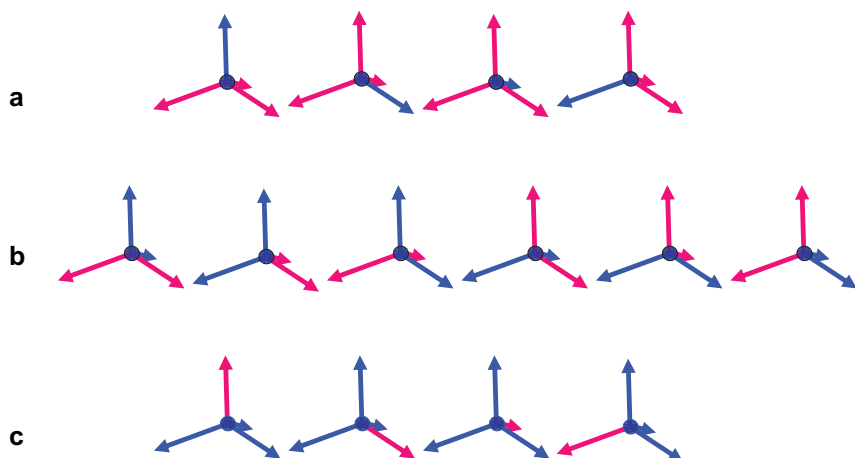


Fig. 2.49 (a) The four possible states of a 1-species. (b) The six possible states of a 2-species. (c) The four possible states of a 3-species. The blue arrow indicates a “turned on” arm.

Thus, the general expression for the pseudo-chemical potential of the water molecule is

$$\begin{aligned} \exp[-\beta\mu_w^*] &= \frac{Q(T, V, N; \text{one } w \text{ at } \mathbf{R}_0)}{Q(T, V, N)} \\ &= \frac{\sum_{n=0}^4 \binom{4}{n} Q(T, V, N; \text{one } w \text{ at } \mathbf{R}_0 \text{ with } n \text{ specific arms HBed})}{Q(T, V, N)} \end{aligned} \quad (2.7.72)$$

We now write the chemical potential of the 0-species as

$$\begin{aligned} \mu_0 &= \mu_0^* + k_B T \ln \rho_0 \Lambda^3 \\ &= -k_B T \ln \langle \exp[-\beta B_0] \rangle_0 + k_B T \ln \rho_0 \Lambda^3 q_w^{-1} \\ &= \Delta A_{Ne}^* + k_B T \ln \rho_0 \Lambda^3 q_w^{-1} \end{aligned} \quad (2.7.73)$$

where ΔA_{Ne}^* is the solvation Helmholtz energy of the neon atom in water. Similarly, using the same approximation as in

(2.7.47) we can write the solvation Helmholtz energy of the water molecule with n *specific* arms engaged in HBs as

$$\begin{aligned}\Delta A^*(n \text{ specific arms HBed}) \\ &= \Delta A_{Ne}^* + n\Delta A^{*HB}(\text{one specific arm/LJ}) \\ &= \Delta A_{Ne}^* + n\Delta A^*(1, HB/LJ)\end{aligned}\quad (2.7.74)$$

where $\Delta A^{*HB}(1, HB/LJ)$ is the conditional solvation Helmholtz energy of one specific arm being HBed given that the LJ part has been solvated.

Combining (2.7.72), (2.7.67), and (2.7.74), we have

$$\begin{aligned}\exp[-\beta\mu_w^*] &= \sum_{n=0}^4 \binom{4}{n} q_w \\ &\quad \times \exp[-\beta\Delta A_{Ne}^* - \beta n\Delta A^{*HB}(1, HB/LJ)]\end{aligned}\quad (2.7.75)$$

From the equilibrium condition (2.7.62) and (2.7.61), it follows that

$$\mu_w^* - \mu_n^* = k_B T \ln \left(\frac{\rho_n}{\rho_w} \right)_{eq} = k_B T \ln x_n \quad (2.7.76)$$

where x_n is the average mole fraction of water molecules engaged in exactly n HBs.

Defining

$$Y = \exp[-\beta\Delta A^{*HB}(1, HB/LJ)] \quad (2.7.77)$$

we can rewrite (2.7.75) as

$$\begin{aligned}\exp[-\beta\mu_w^*] &= q_w \exp[-\beta\Delta A_{Ne}^*] \sum_{n=0}^4 \binom{4}{n} Y^n \\ &= q_w \exp[-\beta\Delta A_{Ne}^*] (1 + Y)^4\end{aligned}\quad (2.7.78)$$

and similarly

$$\exp[-\beta\mu_n^*] = q_w \exp[-\beta\Delta A_{Ne}^*] \binom{4}{n} Y^n \quad (2.7.79)$$

Hence, from (2.7.76), (2.7.78), and (2.7.79), we get

$$x_n = \frac{\binom{4}{n} Y^n}{(1 + Y)^4} \quad (2.7.80)$$

with the normalization condition

$$\sum_n x_n = 1 \quad (2.7.81)$$

Note that x_n is the mole fraction of the n -species, i.e. water molecules that are engaged in HB s. In the definition of Y in (2.7.77), we have a *specific* arm engaged in HB .

The average number of HB s formed by a water molecule is

$$\langle \psi \rangle = \sum_{n=0}^4 n x_n = \frac{\sum n \binom{n}{4} Y^n}{(1 + Y)^4} = \frac{4Y}{1 + Y} \quad (2.7.82)$$

We recall from (2.7.49) the experimental value of $\Delta A^{*HB}(1, HB/LJ)$, which is the conditional solvation Helmholtz energy per arm of a water molecule. From this we can calculate Y in (2.7.77) and from (2.7.80) we can compute the distribution of the various species as well as the average quantity $\langle \psi \rangle$. These values are shown for H_2O and D_2O at $25^\circ C$ and 1 atm in Table 2.1.

In this approximation, we find that most of the water molecules are in the $n = 4$ state. The value of $\langle \psi \rangle$ is probably too high. It should be noted that each of the mole fractions x_n as well as $\langle \psi \rangle$ may be calculated by simulation methods.

Table 2.1. Values of the mole fractions of the various species of water molecule and the average structure computed from Eqs. (2.7.80) and (2.7.82) for H₂O and D₂O at 25°C

	H ₂ O	D ₂ O
x_0	2.49×10^{-7}	2.36×10^{-7}
x_1	4.37×10^{-5}	4.18×10^{-5}
x_2	2.87×10^{-3}	2.79×10^{-3}
x_3	8.36×10^{-2}	8.24×10^{-2}
x_4	0.913	0.915
$\langle \psi \rangle$	3.909	3.913

2.7.8. Application of the Percus–Yevick equation

An approximate version of the Percus–Yevick (PY) equation has been applied for the pair potential based on the Bjerrum model [Ben-Naim (1970)]. The pair correlation function is written in the form

$$g(\mathbf{X}_1, \mathbf{X}_2) = y(\mathbf{X}_1, \mathbf{X}_2) \exp[-\beta U(\mathbf{X}_1, \mathbf{X}_2)] \quad (2.7.83)$$

Assume that all of the angle dependence of g is borne by the pair potential U , whereas the function y is assumed to depend on the distance $R = |\mathbf{R}_2 - \mathbf{R}_1|$ only. This assumption was partially justified in a two-dimensional system (Ben-Naim, 1972c, 1972d), but now it is clear that this is not a good approximation.⁸⁰ As was stated in the original article, “The angle-dependent pair potential was chosen in such a way that the characteristic tetrahedral geometry for the relative orientation of two water molecules is favored.” As I have pointed out several times in this book, achieving the tetrahedral structure was

⁸⁰This approximation is probably valid in the region of distances around the first peak of the pair correlation function. It will certainly fail for distances near the second peak. See Chapter 4 for details.

one of the main goals of the theoretical effort in this field. It was only much later realized that the tetrahedral geometry, though a dominant feature of the structure of water, does not harbor the clues to the understanding of the properties of water. We present here one result of the application of the *PY* equation for liquid water.

Consider the pair potential given in Sec. 2.7.2, which we now write as

$$U(\mathbf{X}_1, \mathbf{X}_2; \lambda) = U_{LJ}(R_{12}) + \lambda S(R_{12}) U_{HB}(\mathbf{X}_1, \mathbf{X}_2) \quad (2.7.84)$$

where $\lambda(0 \leq \lambda \leq 1)$ is a coupling parameter. The process of solving the *PY* integral equation begins with $\lambda = 0$. The result provides the pair correlation function for the Lennard–Jones potential $U_{LJ}(R_{12})$. Next, the value of λ is increased, as a result of which the contribution due to the *HB* potential increases. Figure 2.50 shows one interesting feature of the coupling of the *HB* part of the pair potential. The dotted line is the solution for the Lennard–Jones potential (i.e. $\lambda = 0$). The other three curves show the response of the function $g(R)$ to increasing the value of $\lambda(0 \leq \lambda \leq 0.3)$. Note a shift of the second peak leftward from the initial value of $5.6 \text{ \AA}$ to the final value of $4.8 \text{ \AA}$ (at $\lambda \approx 0.3$). [The latter should be compared with the value of $4.5 \text{ \AA}$ in the experimental curve of $g(R)$.] This result indicates that as one couples the *HB* part of the pair potential, the tendency to form a tetrahedral geometry increases, and therefore the characteristic peak at about $4.5 \text{ \AA}$ is developed. Other features of the radial distribution function obtained from these computations are not in agreement with the experimental results. For instance, the average coordination number obtained for the case $\lambda \approx 0.3$ was about 7.4, compared with the experimental value of about 4.4.

It is possible that the *PY* integral equation, though very successful for simple fluids, is inadequate for a system of particles interacting with very strong attractive forces. In addition, the solution of the full *PY* equation is still unfeasible for

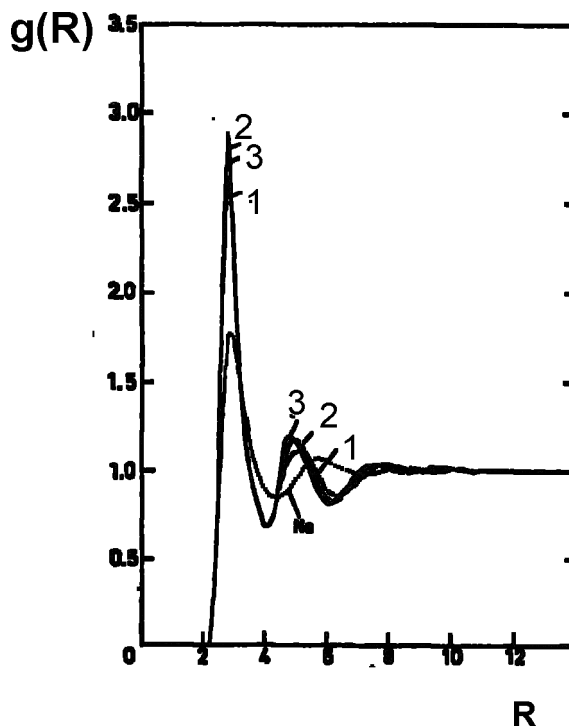


Fig. 2.50 The response of the radial distribution function $g(R)$ to increasing λ in Eq. (2.7.84). The dotted curve corresponds to $\lambda = 0$. Curves 1, 2, and 3 correspond to different stages in the increasing values of λ ($0 \leq \lambda \leq 0.3$).

non-spherical particles, and only an approximate version of this equation has been applied in this work. [For more details, see Ben-Naim (1970).]

To the best of the author's knowledge, not much work has been done on using integral equation methods to study water. Perhaps one exception is the work by Pettitt and Rossky (1982).

2.7.9. Application of cluster expansion to water

Dahl and Andersen (1983b) and Andersen (1974) used an approximate cluster theory of liquids to calculate some of the outstanding properties of water. The input pair potential used in the theory is essentially the BN3D potential described

in Sec. 2.7.2. Instead of a square-well potential described in Sec. 2.7.2, they used a double square-well potential characterized by two energies. With this highly simplified model, they were able to show that a system of such particles has a minimum in the temperature dependence of the volume (as well as the gradual disappearance of the minimum at high pressures), a minimum in the compressibility as a function of temperature, and a minimum in the heat capacity. They also calculated the average numbers of hydrogen bonds in a system of such particles. In this particular model two kinds of hydrogen bonds were defined, the strong and the weak, corresponding to the two energies ε_2 and ε_1 of the double square-well potential function.

In my opinion, the success of this theory in reproducing some of the outstanding properties of water is essentially a success of the pair potential, described in Sec. 2.7.2. It clearly demonstrates that the charge distribution is not a necessity for the manifestation of the anomalous properties of water. What is important is the implementation of the *principle* in the pair potential. In the 3-D case the implementation of the principle leads to tetrahedral geometry. But as we have seen in Secs. 2.5 and 2.6, tetrahedral geometry in itself is not necessary for understanding the characteristic properties of liquid water.

Once again we note that the success of this model in reproducing some of the properties of liquid water does not teach us anything new about the molecular reasons for these properties nor does it tell us anything about the “reality” of the potential function used in these calculations. It does show, however, that implementation of the *principle* is essential for the manifestation of water-like behavior.

2.7.10. *Simulated results*

In the past 30 years, simulations of the properties of water have become dominant in the field of the study of liquid water.

As I have discussed in Sec. 2.2, simulations are closer to experiment than to theory. The main theoretical element in the simulation is the construction of the pair potential.⁸¹ The pair potential is judged to be successful if it correctly reproduces the experimental behavior of liquid water. Recently, Sanz *et al.* (2004) and Vega *et al.* (2005) have suggested that the prediction of the phase diagram of water should be a stringent test for any model for water.

As I have discussed in Sec. 2.7.1, a model that produces better agreement between calculated and experimental results does not necessarily mean that it is closer to describing real water molecules. All one can say is that a system of water-like particles show the characteristic behavior of real liquid water and nothing more.

In this section, we present only a few results obtained by simulation methods. We shall not describe any of the technical details of the calculations.

(i) Monte Carlo simulations

The Monte Carlo (MC) method, used to simulate the properties of liquids, was developed by Metropolis *et al.* (1953). Without going into any detail, it should be pointed out that there are two important features of this MC method that make it extremely useful for the study of the liquid state. One is the use of periodic boundary conditions, a feature that helps to minimize the surface effects that are likely to be substantial in such a small sample of particles. The second involves the way the sample of configurations are selected. In the authors' words: "Instead of choosing configurations randomly, then weighing them with $\exp[-\beta E]$, we choose configurations with probability $\exp[-\beta E]$ and weight them evenly."

⁸¹Also, the methodology of the simulation technique itself, which was developed for the study of liquids in general, is an important theoretical achievement.

The first simulation of liquid water was reported by Barker and Watts (1969). The potential function they used was that used earlier by Rowlinson (1951).⁸² The Monte Carlo method was applied to 64 water-like particles at 25°C.

The average energy and heat capacity computed for this system were $-8.36 \text{ kcal mol}^{-1}$ and $20.5 \text{ cal mol}^{-1} \text{ deg}$, respectively. The agreement was judged to be satisfactory. Figure 2.51 shows

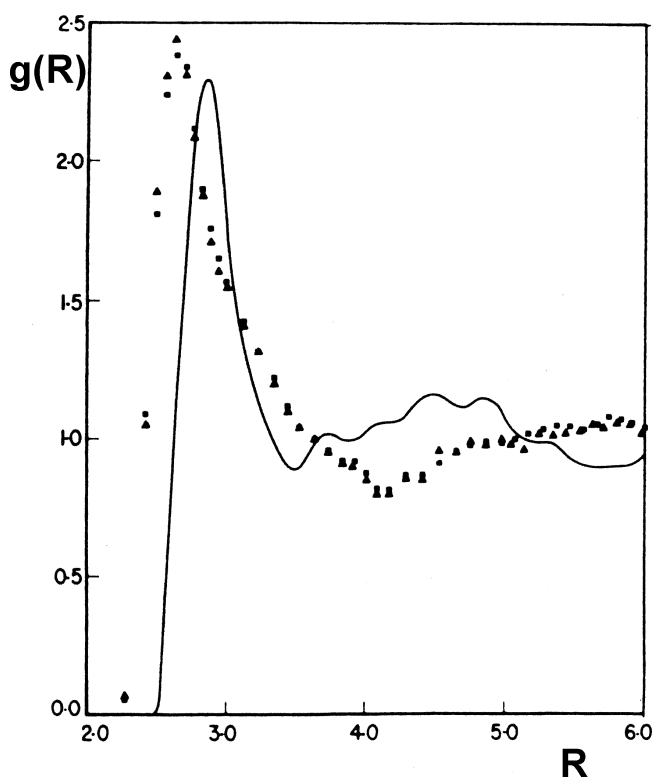


Fig. 2.51 Comparison between the experimental radial distribution function for water at 25°C (full curve) and the corresponding results from Monte Carlo computations (triangles and squares). [Redrawn with changes from Barker and Watts (1969).]

⁸²Rowlinson (1951) used a modified Stockmayer potential to calculate the second virial coefficient for water [see Ben-Naim (1974), page 247, Table 6.1.]

the computed radial distribution function and the experimental curve obtained by Narten *et al.* (1967). Here, agreement with the experimental results is quite poor. First, the average coordination number (computed for $0 \leq R \leq 3.5 \text{ \AA}$) was found to be 6.4, compared with the experimental value of about 4.4. More importantly, however, the location of the second peak of $g(R)$ was at $5.8 \text{ \AA}$, far larger than the expected value of $4.5 \text{ \AA}$ in the pair correlation function for real water.

At the time of the publication of Barker and Watts results, it was not clear whether the failure to obtain the correct *RDF* was due to the inadequate pair potential or to the approximation made in the calculations. Now it is clear that the main reason for the failure was the inadequacy of the Rowlinson potential. The same potential that gave reasonably good agreement with the second virial coefficient and the heat capacity could not produce enough “structure” to mimic the local environment around a water molecule.⁸³ As we have discussed in Secs. 2.7.2 and 2.7.3, one can easily obtain the virial coefficient, the energy, and the heat capacity of water. All of these depend on the strength of the intermolecular interactions but not on the ability of the potential to produce the correct local tetrahedral environment around a water molecule. As we have discussed in Sec. 2.5, in the early 1970s when the first successful pair potential was published, the tetrahedral structure of water was both the main guidance in the construction of the pair potential as well as the main goal of the theoretical effort. It was only later, after the success of the 1-D and 2-D models for water, that it was recognized that the tetrahedrality, although a prevailing feature of the structure of water, is not in itself the molecular reason for the anomalous thermodynamic properties of water.

⁸³In the 3-D case, the correct location of the second peak of the *RDF* is a result of the tetrahedrality of the packing of the water molecules.

It is of interest to quote a passage of my earlier book (Ben-Naim, 1974) on this matter:

“It is difficult to trace the origin of these discrepancies between the computed and the experimental radial distribution function. It is possible that the pair potential does not produce enough preference for the tetrahedral geometry (hence, the coordination number and the location of the second peak do not show the characteristic values as in water), or that the numerical procedure was not run with a sufficient number of particles and configurations.”

Swaminathan and Beveridge (1977) also calculated the distribution of coordination number (CN) and binding energy (BE) (Fig. 2.52).⁸⁴ The distribution $x_{CN}(K)$ shows as expected a clear preference for a coordination number for four. The distribution of binding energy shows a single maximum at about $\nu = -17.7 \text{ kcal mol}^{-1}$. These authors also calculated the combined distribution $x_{CN,BE}(\nu, K)$. They found that for $K > 4$ the

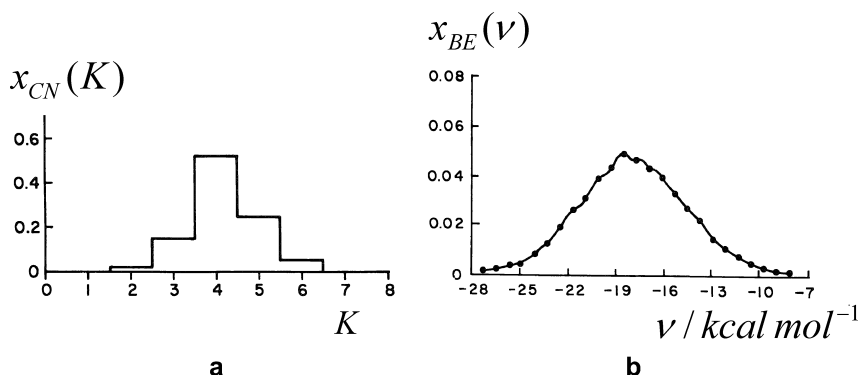


Fig. 2.52 The distribution for coordination number and for binding energy. [Redrawn from Swaminathan and Beveridge (1977).]

⁸⁴In this MC simulation, the authors used the MCY pair potential developed by Matsuoka *et al.* (1976).

binding energies are displaced towards lower energies whereas for $K < 4$ they are towards higher energies. This is very similar to what was found for the 2-D models for water in Sec. 2.6.

In connection with this distribution we note that some authors have interpreted the unimodal distribution $x_{BE}(v)$ as evidence against the *validity* of the *MM* approach. As we have discussed in Sec. 2.3, the *MM* approach does not rely on evidence from either experiment or theoretical calculations. The fact that the distribution $x_{BE}(v)$, or any other distribution, is continuous and unimodal only means that there is no clear-cut resolution into several peaks corresponding to the various species (as we have seen in the 2-D model). The *species* can be defined for any distribution independently of its form (except in the extreme case of a delta function).

Hirata and Rossky (1981) also calculated the distribution of binding energy and found essentially a unimodal distribution. Other simulations using the Monte Carlo methods have been reported by many authors.⁸⁵

Very recently, Bizjak *et al.* (2007) published an article entitled: “The three-dimensional Mercedes-Benz model of water.” In both the abstract and in the introduction these authors write: “In the present work, we developed the 3-dimensional analog of the *MB* model.” Lamentably, this statement is misleading in two senses. First, the authors *did not develop* the 3-dimensional model (referred to in Sec. 2.7.2 as the BN3D model). This model was developed in 1974 and not in 2007.⁸⁶ Second, the BN2D

⁸⁵Sarkisov *et al.* (1974), Jorgensen and Madura (1985), Jorgensen *et al.* (1983), and Jorgensen (1982).

⁸⁶The case of the BN3D model is more than “mere” plagiarism. It is an utmost chutzpa to copy a potential from a book published in 1974, give reference to that book, but claim credit as if they themselves *have developed* the BN3D potential. Naturally, subsequent articles gave credit to those who *copied* the BN3D potential rather than acknowledging the rightful author who developed the BN3D potential (see also footnote 54, page 210). For instance, a recent article posted on arXiv reported on some developments of the “MB approach” which does not exist.

model was suggested as a simplified version of the BN3D model and not the other way around as claimed by the author. As I have discussed in Sec. 2.6, the denomination of the BN2D model as the *MB* model is inappropriate for the 2-D case. It is *a fortiori* inappropriate to refer to the BN3D as the “3-D MB model for water”!

Having set the record straight, I am pleased to see that the BN3D model has been successful in reproducing some of the outstanding properties of liquid water. These results lend further support to the contention that the *principle* that was a built-in feature of the BN3D model is indeed essential for the manifestation of the anomalous properties of water. I expect that this model will also be successful in the study of aqueous solutions. For non-ionic solutes I believe that this model will be useful as it is. For ionic solutes, perhaps it will be necessary to add a point electric dipole as suggested in Sec. 2.7.2 [see Eq. (2.7.6)], or even a polarization term for the ion-water interaction.

(ii) Molecular dynamics simulation

The molecular dynamic (MD) method used in simulating the properties of liquids was developed by Alder and Wainwright (1959). It is conceptually simpler than the MC method in the sense that one actually follows the evolution of the system with time by solving the equation of motion of some 10^3 particles and by calculating the time averaged quantities. However, its implementation is more complex than the MC method.

This method was successfully applied for simple liquids. It was applied to liquid water only after the development of the *BNS* pair potential.⁸⁷ Rahman and Stillinger carried out an extensive MD simulation of water-like particles based on the *BNS* potential.⁸⁸ They applied the molecular dynamics method for a system of 216 particles interacting via the effective pair

⁸⁷Ben-Naim and Stillinger (1972).

⁸⁸Rahman and Stillinger (1971, 1973), and Stillinger and Rahman (1972).

potential based on the Bjerrum model, referred to as the *BNS* potential. The molecular dynamics method has an important advantage over the Monte Carlo method: whereas the latter is devised for computing average quantities for a system in equilibrium only, in the former it is possible to compute transport properties as well.

The sample of 216 particles was studied at a number density of $\rho = 3.344 \times 10^{22} \text{ cm}^{-3} = 0.03344 \text{ \AA}^{-3}$. The typical time increment was chosen to be $\Delta t \approx 4.6 \times 10^{-16} \text{ sec}$, and altogether about 10^4 steps were taken. (Half of that time was considered as the time required for the system to “age” and the averages were computed from the subsequent period of $5 \times 10^3 \Delta t$.) The temperature was computed from the average kinetic energy of the molecules. (Note that in molecular dynamics the temperature is inferred from the average kinetic energy after the equilibrium distribution of the kinetic energy has been established.) The average potential energy corresponding to the system at a temperature of 34.3°C was found to be $-9.184 \text{ kcal mol}^{-1}$, which compares nicely with the experimental value of -9.84 . A less satisfactory value was obtained for the heat capacity. The average contribution to the heat capacity due to intermolecular interactions was estimated between the temperatures -8.2 and 34.3°C to be $21.4 \text{ cal mol}^{-1} \text{ K}^{-1}$. This should be compared with the experimental value of about $12 \text{ cal mol}^{-1} \text{ K}^{-1}$ for water. (The latter is obtained from a total heat capacity C_V of about $18 \text{ cal mol}^{-1} \text{ K}^{-1}$ in this range of temperatures minus the contribution due to translation and rotation, which is about $3R \approx 6 \text{ cal mol}^{-1} \text{ K}^{-1}$). As in the other simulation techniques, it is difficult to trace the exact source of this discrepancy, whether from shortcomings of the model or from inaccuracy of the computations.

Rahman and Stillinger have carried out a very thorough investigation of the pair correlation function and its temperature dependence. Figure 2.53 shows the function $g_{\text{OO}}(R)$ for three temperatures (corresponding to -8.2°C , 34.3°C , and 314.8°C).

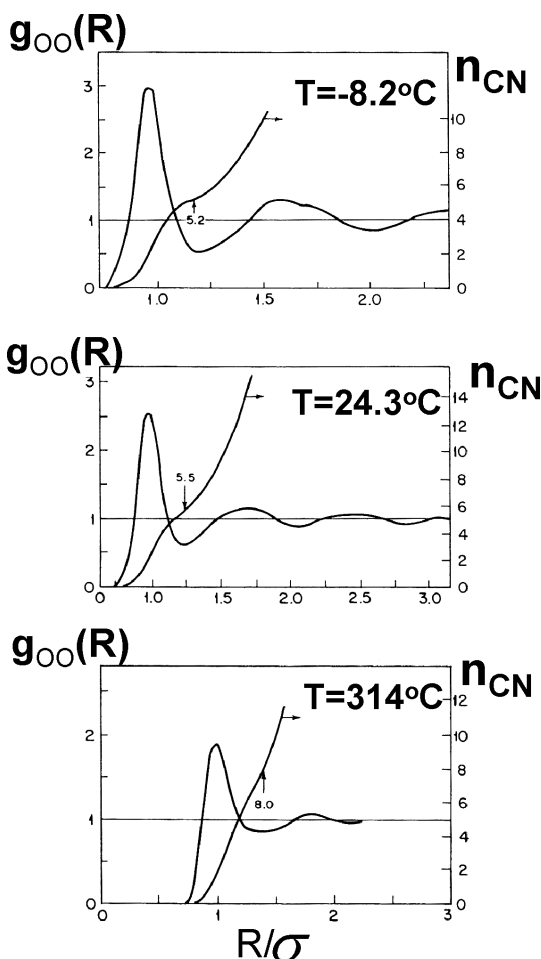


Fig. 2.53 The function $g_{OO}(R)$ for three different temperatures, as indicated next to each curve, computed by the method of molecular dynamics. The monotonically increasing curves give the “running coordination number” n_{CN} . [Redrawn with changes from Stillinger and Rahman (1971, 1972).]

All of the features of the radial distribution function were simulated by the model particles. There is a sharp peak at $R^* = R/\sigma = 0.975$, corresponding to $R = 2.75 \text{ \AA}$ (with $\sigma = 2.82 \text{ \AA}$). The second peak occurs at $R^* = 1.69$, corresponding to $R = 4.76 \text{ \AA}$, which is a little above the experimental value of about

$R = 4.6 \text{ \AA}$. Also, the average coordination number computed up to the first minimum (following the first maximum) is 5.5, which is somewhat higher than the experimental value of about 4.4.

The temperature dependence of the radial distribution function $g_{OO}(r)$ obtained from these computations was also in qualitative agreement with the experimental results. We note especially that at the highest temperature ($T = 314.8^\circ\text{C}$), the second peak of $g_{OO}(r)$ decreases appreciably and a clear-cut shift to the right is observed, indicating a destruction of the characteristic tetrahedral geometry of the packing in liquid water. One feature that further supports this conclusion is the average coordination numbers, computed up to the first minima, which were 5.2, 5.5, and 8.0 at the three temperatures, respectively.

In their second paper, Stillinger and Rahman (1972) concluded: "There is evidence in our results that the interaction used is too tetrahedral, i.e. the hydrogen bonding is too directional." They also interpreted the large heat capacity (C_V) obtained in the simulation with the statement that the "structural order in our model breaks up more rapidly than it should."

Clearly, these statements show that tetrahedral structure was at the very center of any theoretical discussion of the molecular properties of water. In my opinion, following the discussion in Sec. 2.3, the high heat capacity obtained (almost double the expected value) is not a result of too much tetrahedrality in the model but simply a result of the spread in the binding energy. In the language of the mixture-model approach, we can say that this model provides two components having comparable concentrations but differing considerably in their energies. The large heat capacity is a result of the "melting" of the low energy component into the high energy components. This effect could occur with either too much or too little tetrahedrality.

In later publications, Rahman and Stillinger (1973, 1974) used a slightly modified *BNS* potential which was designated the

ST2⁸⁹ potential in order to obtain better agreement between the simulated and experimental results. In my opinion, the efforts to pursue this goal by Rahman and Stillinger and by many others that followed are not fully justified. As I have noted several times in this book, a better agreement between the computed and experimental results does not tell us anything about the “correct” or the “real” pair potential for water, nor does it explain any of the outstanding properties of water. All it says is that with such and such a feature of the pair potential, (the input) one obtains such and such properties similar to water (the output). Not much more than that.

It is appropriate to quote a conclusion from Ben-Naim and Stillinger (1972): “Although the Monte Carlo simulation of real water will very likely play an important role in future developments, it certainly must not be considered as an utterly definitive and complete source of knowledge. It is, after all, only a refined (and highly magnified!) sort of experiment on water, and for the most part will only tell us “what,” not “why.” The Monte Carlo results will eventually require explanations based on analytical theory, in the same way that the integral equation formalism for $g^{(2)}$ nowadays affords explanations for simple fluids (like argon).” Clearly, this conclusion applies equally to the MD simulation. Since this book’s main concern is the question of “why,” I shall not further discuss simulated results. The interested reader should consult the original publications and the reviews mentioned in Sec. 2.2.

⁸⁹A minor change in the parameters does not justify a new designation. It is also misleading. Since there exists no ST1 potential, the unwary reader might think that the predecessor of the ST2 is the ST1, not the BNS, which of course is not true. It is not uncommon to see statements such as: “effective water-water pair potential devised by Stillinger and Rahman and designated as ST2” (Nemethy *et al.*, 1981). With all due respect to the work of Stillinger and Rahman, they did not *devise* the ST2 potential; they only *modified* the BNS potential that was devised by Ben-Naim and Stillinger.

CHAPTER 3

Water with One Simple Solute

Personal Introduction

The study of thermodynamic properties of aqueous solutions of inert gases was the subject of my PhD thesis. In the early 1960s, not much was known about these systems. Experimental data were very scarce and inaccurate. Theory was highly speculative. Nevertheless, I chose this subject mainly for one reason: I was fascinated by the “hearsay” that inert solute dissolved in water lowers the entropy of the system. Lowering the entropy meant increasing the structure of water. But why? How can inert solutes cause an increase in structure and lower the entropy? That was quite a mystery. I say it was “hearsay” because the experimental data on solubilities of inert solutes was very inaccurate. The entropy of solution was determined from the temperature dependence of the solubility. That renders the uncertainty of the values of the entropy of solution even larger than the uncertainty of the solubilities themselves. At that time I was not aware of the fact that the so-called standard entropy of solution was itself an uncertain measure of the entropy of solvation.

I started my work on these systems almost all by myself without any guidance nor supervision from an expert in the field. It was known that inert solutes such as argon were sparingly soluble in water. In order to measure the entropy of solution, one needed very accurate values of the solubility of the inert gases. These were very difficult to obtain. All the experimental

methods known at that time were inadequate, and so I had to design a new method for measuring the solubilities of inert gases in water.¹ At that time, there were two theories that attempted to explain the thermodynamics of these solutions: Eley's theory based on a lattice model for water and Frank and Evan's idea of iceberg formation. None of these were satisfactory. Eley's model was not only based on a lattice model for water, but it also had an additional restriction on the number of "holes" a solute can occupy in this lattice. On the other hand, Frank and Evans postulated that when an inert solute is inserted in water, icebergs are formed around it. This idea became very popular. Although there was no proof nor any molecular explanation for the iceberg formation, the idea of iceberg formation was used to explain the anomalous entropy and enthalpy of solvation. As it occurs quite often in science, a fancy term for a phenomenon ends up being the explanation of that phenomenon. At that time, the concept of entropy was closely associated with disorder. Therefore, a decrease in entropy was synonymous with an increase in order, which is the same as an increase in structure. Thus, the statement that the negative entropy of solution of argon in water is a result of iceberg formation is tantamount to saying that argon increases the structure of water, which is the same as saying that argon increases the "order" in water. The conjecture that argon forms icebergs does not explain anything unless one can explain why argon forms icebergs. Answering this question is not a trivial matter.

In my work on aqueous solutions of inert gases, I have reformulated the "iceberg-formation" idea. Instead of claiming that argon forms icebergs, I started from the assumption that structure, any structure for that matter, is already there in the pure liquid. Argon does not form any new structure but rather only

¹Ben-Naim and Baer (1963).

shifts an existing equilibrium towards the more structured form. This reformulation of the problem still leaves unanswered the question of why argon shifts the equilibrium towards the more structured form. Unanswered indeed but answerable as will be discussed in Sec. 3.7.

The non-trivial answer to this question was given only after I finished my PhD thesis. Before grappling with this theoretical question, I had to solve the more mundane and practical problem of how to measure accurately the solubility of argon in water. It was only after solving this problem, which was far from easy, that I was able to turn to the theoretical interpretation of the thermodynamics of argon in water. The experimental method used to measure solubilities of gases in liquids is described in Ben-Naim and Baer (1963). The method contains an interesting trick that I am proud of even after 40 years. The reader is urged to have a look at the original paper to see how a notoriously difficult experimental problem was solved. Over the years I have visited many laboratories where this method was used to measure solubilities of inert gases in liquids.

In the course of studying aqueous solution of inert solutes, I found that there are discrepancies between various measures of the so-called standard entropy of solution. In some cases different “standard” quantities yielded results of opposite signs. This led me into the search of a genuine, reliable and, of course, measurable quantity that I shall refer to as the solvation quantity — dropping altogether the “standard” adjective from the original term. This was described in great detail in a recent monograph and will be briefly discussed in Sec. 3.3. The idea of structural changes in the solvent and their effect on thermodynamic quantities of solvation are described in Sec. 3.7. Originally, I used a simple mixture-model approach to show that any structural changes in the water induced by the solute can affect the entropy and the enthalpy of solvation but not

the Gibbs energy of solvation. This statement, which is related to the exact entropy-enthalpy compensation theorem, was later proved in the most general terms, not relying on the concept of the structure of water (see Sec. 3.4). This conclusion was not easily accepted. At that time the structural changes induced by a solute were used to explain the low solubility of inert solutes in water. Some authors even criticized this conclusion as being in conflict with the Second Law of Thermodynamics. Yet others who embraced the conclusion have reproduced and re-published it under different notations and different terms.

For a long time the concept of the structure of water and structural changes in the solvent were discussed in the literature in very qualitative terms. There was no molecular definition nor a quantitative measure of the structure of water. No-one has estimated how much structural changes are induced by the solute. A possible definition of the structure of water was discussed in Chapter 2, and an approximate way to obtain a measure of the structure of water was discussed in Sec. 2.7. In Sec. 3.7, I shall present a similar measure of the structural changes induced by a solute based on the isotope effect on the Gibbs energy of solvation.

3.1. Introduction and Some Historical Notes

The study of very dilute solutions of simple solutes such as argon, methane, and the like is of interest for various reasons. First, these solutions reveal some anomalous properties in comparison with non-aqueous solutions and therefore present an attractive challenge to chemists, physicists, and biochemists. Second, aqueous solutions of a simple solute may be viewed as pure water subjected to a weak “external” field of force. Therefore, the study of such systems can contribute to our understanding of pure liquid water itself. Finally, and most

importantly, understanding the thermodynamics of these systems at a molecular level is a first step in the study of the role of water in biochemical systems.

The theoretical understanding of dilute aqueous solutions has lagged behind that for pure water. However, because of their interest and importance, there has been significant progress in the understanding of these systems. Some of the outstanding properties of aqueous solutions of inert molecules were known in the 1930s. These will be reviewed in Sec. 3.2.

The first molecular interpretation was attempted by Eley (1939, 1944). Eley assumed that the process of solution can be viewed as a two-step process: first, the creation of a cavity that can accommodate the solute, and second, the introduction of the solute into this cavity. Thus, schematically, the process is depicted in Fig. 3.1. For each thermodynamic quantity of solution,² say the standard enthalpy and entropy, one can write

$$\Delta H_s^0 = \Delta H^C + \Delta H^{\text{int}} \quad (3.1.1)$$

$$\Delta S_s^0 = \Delta S^C + \Delta S^{\text{int}} \quad (3.1.2)$$

where the superscripts *C* and *int* stand for “cavity” and “interaction,” respectively.

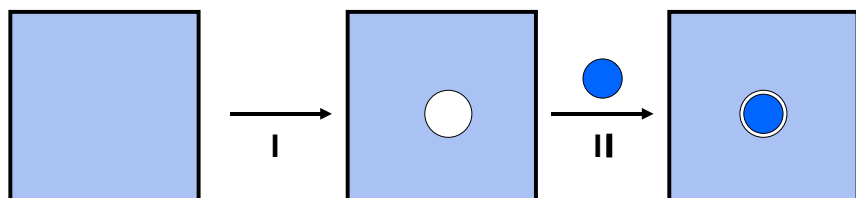


Fig. 3.1 The two steps in Eley's process of solvation: (I) creation of a cavity and (II) insertion of a solute into the cavity.

²I use here the terms standard entropy and enthalpy of solution, as were common at that time. Today, these terms are replaced by the entropy and enthalpy of *solvation*. See also Sec. 3.3.

It should be noted that the general idea of splitting any thermodynamic quantity of solution into two terms as in (3.1.1) and (3.1.2) can be formally made exact.³ However, Eley also used a lattice model for water and assumed that water contained a fixed number of cavities, or holes. He was able to give a qualitative interpretation of the difference in ΔH_s^0 and ΔS_s^0 for an inert solute s in water and in other liquids. Today, the lattice type of model used by Eley and the assumption of a fixed number of holes are not acceptable.

The next significant attempt to interpret the large negative values of the enthalpies and the entropies of solution of inert gases in water was published by Frank and Evans in 1945. Frank and Evans (1945) proposed a radically new idea. Instead of a lattice model (with a fixed number of holes and hence a fixed *structure* of water, as implied by Eley's model), they postulated that the large negative enthalpy and entropy of solution was a result of the formation of "icebergs" around the solutes. In the 1930s and 1940s, the entropy of a system was viewed as a measure of the molecular *structure*, or the *order* in the system. If icebergs were formed by the insertion of a solute, then the negative values of ΔS_s^0 and ΔH_s^0 could be interpreted in terms of an increase in the *structure* (or the order) in water. However, Frank and Evans left the main question unanswered: why would an inert atom, such as argon, form an iceberg around it? Without such an explanation, Frank and Evans' suggestion of iceberg formation is reduced to sheer tautology. It is merely a rephrasing of the fact that entropy decreases in terms of the increment in the structure or in the order of water.⁴

Frank and Evans made an interesting comparison between the entropy of solution of KCl and the entropy of solution of

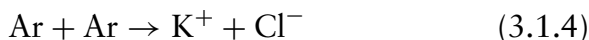
³See Ben-Naim (2006).

⁴In later publications, the "iceberg" idea was modified: the inert solute built a "cage-like" structure of hydrogen-bonded molecules around it. This still leaves unanswered the question as to why the net structure of water increases.

two moles of argon in water⁵:

$$\begin{aligned}\Delta S^0(\text{KCl}) &= -51.9 \text{ cal mol}^{-1} \text{K}^{-1} \\ \Delta S^0(2\text{Ar}) &= -60.4 \text{ cal mol}^{-1} \text{K}^{-1}\end{aligned}\tag{3.1.3}$$

The argon atom and the ions K^+ , and Cl^- are isoelectronic; each has 18 electrons. Disregarding the difference in the radii of Ar, K^+ , and Cl^- , we can write the following schematic process:



From these data, one can conclude that the entropy change in the “reaction” (3.1.4) is

$$-51.9 + 60.4 = 8.5 \text{ cal mol}^{-1} \text{K}^{-1} \tag{3.1.5}$$

This is quite a puzzling result. We know that the ions produce a very strong electric field near their surface which forces the water molecules to orient their dipole moments towards the charge of the ion. Hence, this is a plausible interpretation of the large negative entropy of solvation of ions (note that we do not have the solvation entropy of the single ions but the sum of the solvation entropies of both ions). The puzzling finding in Eq. (3.1.5) is that the solvation entropy of two argon atoms is even *more negative* than the solvation entropy of the two ions. In other words, if we discharge the ions (or transfer an electron from Cl^- to K^+ and obtain the neutral Cl and K, which are approximated as Ar and Ar), we get a *negative* quantity. Why?

This result is clearly counterintuitive. A large negative entropy of solvation is perceived as a result of an ordering effect. It is easy to understand that the strong electric field produced by

⁵We shall disregard the specific standard states used by Frank and Evans. The qualitative argument presented here is independent of the choice of standard states.

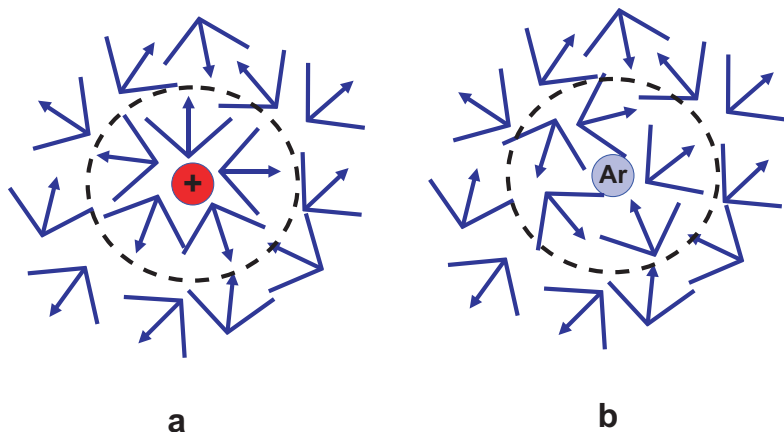


Fig. 3.2 (a) Ordering of water molecules around a positive charge. The arrows indicate the direction of the dipole moment of the water molecules. (b) What is the “order” of water around an inert solute Ar?

ions causes the ordering of water molecules (Fig. 3.2a), but what “field” is produced by argon that causes an even larger ordering effect? For as long as one does not provide an explanation as to why argon would increase the structure of water, the mystery of the origin of the large negative entropy of solvation of inert gases remains unsolved.

The idea of iceberg formation has captured the imagination of many scientists. In spite of its speculative nature, and in spite of the fact that it does not explain anything, the iceberg formation idea became very popular. In many publications, the formation of icebergs has been used as an argument for explaining not only the entropy and the enthalpy of solvation but also the solubility and the partial molar heat capacity of inert solutes in water. We shall discuss these aspects in the succeeding sections of this chapter.

A reformulation of the problem of structural changes induced by a solute that eventually led to a molecular understanding of the entropy of solution was suggested by Ben-Naim

(1965b, 1974). Instead of creating a new structural form, such as icebergs, it was assumed that pure water contains some degree of structure. Within the mixture model of water, the *structure* is simply defined as the concentration of the more structured component. Instead of the formation of icebergs, one can formulate the problem in terms of *shifting* an existing equilibrium between species towards the one which is more structured. This reformulation, though leading to the same result, is different from the idea of building up a *new* structure. It still leaves two unanswered questions: first, What is the structure of water? and second, Why should this structure be enhanced by an inert solute such as argon? We have discussed the answer to the first question in Sec. 2.7. In Sec. 3.7, we shall deal with the second question. We shall also see in Sec. 3.7 that the structural shift induced by an inert solute can explain the large negative entropy and enthalpy of solvation but not the large Gibbs energy of solvation.

3.2. Survey of Some Properties of Simple Aqueous Solutions

In this section, we survey some of the outstanding properties of aqueous solutions of simple non-polar solutes such as argon, methane, and the like. [For an extensive review, see Battino and Clever (1966), Wilhelm and Battino (1973), Wilhelm (1977), and Franks, Volume II 1973a.] The solubility of such solutes, as measured by the Ostwald absorption coefficient, is markedly smaller in water than in a typical organic liquid. (By “typical” or “normal” organic liquids, we mean alkanes, alkanols, benzene and its simple derivatives, etc.)

The Ostwald absorption coefficient is defined as the ratio of the number densities of a solute s in the liquid (l) and the gaseous

(g) phases at equilibrium, i.e.⁶

$$\gamma_s = \left(\frac{\rho_s^l}{\rho_s^g} \right)_{eq} \quad (3.2.1)$$

The solvation Gibbs energy of a solute s in a liquid l is defined as the change in Gibbs energy for the process of transferring one solute s from a fixed position in an ideal gas phase (ig) into a fixed position in the liquid (l) (Fig. 3.3a). The process is carried out at a fixed temperature T and pressure P . For more details, see Sec. 3.3 and Ben-Naim (2006).

The solvation Gibbs energy of s in l is directly related to γ_s through⁷

$$\Delta G_s^* = k_B T \ln \left(\frac{\rho_s^{ig}}{\rho_s^l} \right)_{eq} = -k_B T \ln \gamma_s \quad (3.2.2)$$

Thus, the statement of a low solubility, in terms of γ_s , is equivalent to a relatively large and positive value of the solvation Gibbs energy, say, of argon in water, as compared with other organic solvents. In Fig. 3.4, we plot the solvation Gibbs energies of argon and xenon in a series of linear alkanols as a function of n , where n is the number of carbon atoms in the n -alcohol molecule. $n = 1$ corresponds to methanol and $n = 0$ corresponds to a hypothetical alcohol with zero carbon atoms, or a hypothetical liquid “water.” We see that the values of ΔG_s^*

⁶There exists a variety of other “units” by which solubility data may be reported; these and the inter-conversion formulas are discussed in the literature [Hildebrand and Scott (1950), Friend and Adler (1957), Himmelblau (1959), and Battino and Clever (1966)]. In this chapter, we adhere to the application of the Ostwald absorption coefficient as a measure of the solubility.

⁷Strictly, the quantity in (3.2.2) is the *difference* in the solvation Gibbs energy of s in the two phases. However, in practice, the gaseous phase is considered to be an ideal gas; hence, the quantity defined in (3.2.2) is practically the same as the solvation Gibbs energy in water.

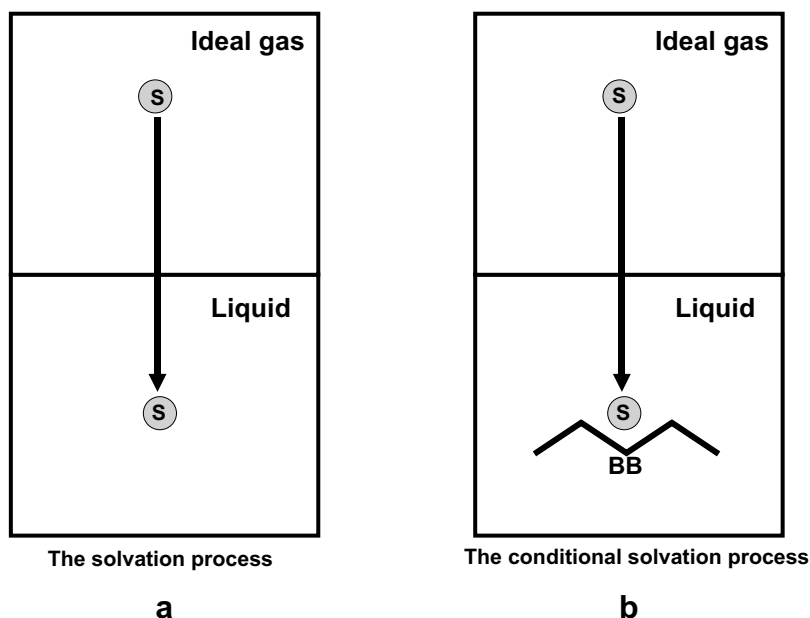


Fig. 3.3 The process of (a) solvation and (b) conditional solvation of a solute s in a liquid next to a backbone (BB).

change very little as a function of n . If we attempt to extrapolate the value of ΔG_s^* for the hypothetical “water” by taking the limit $n \rightarrow 0$, we find that these values (indicated by arrows in Fig. 3.4) are much lower than the experimental values. Thus, a distinctly abrupt change in ΔG_s^* is observed when we pass from the series of n -alkanols to real liquid water. In other words, water, though formally belonging to this homologous series with $n = 0$, has unusual properties and cannot be viewed as one of the members of the homologue series of n -alkanols (compare this with the findings in Sec. 1.6, Fig. 1.40).

Figure 3.5 shows the solvation Gibbs energy of methane in mixtures of water and ethanol at three temperatures. Note also that the change of the Gibbs energy of solvation as a function of the mole fraction of the co-solvent is not monotonic, especially

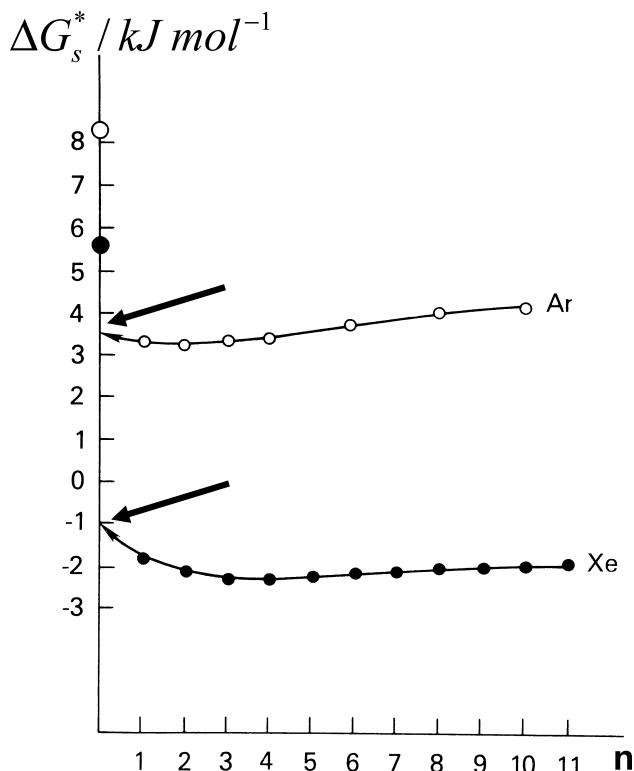


Fig. 3.4 Solvation Gibbs energies of argon (open circles) and xenon (full circles) in linear alcohols. n is the number of carbon atoms in the n -alkanols. The arrows indicate the extrapolated values for $n = 0$. The corresponding experimental values of ΔG_s^* of argon and xenon in water are shown as open and full circles at $n = 0$.

in the water-rich region.⁸ Similar results are available for argon in water methanol, water dioxane,⁹ and water ethylene glycol.¹⁰ The solvation thermodynamic quantities of several gases in water alcohol mixtures were published by Cargill (1993) and

⁸Ben-Naim and Baer (1964).

⁹Ben-Naim and Moran (1965).

¹⁰Ben-Naim (1968).

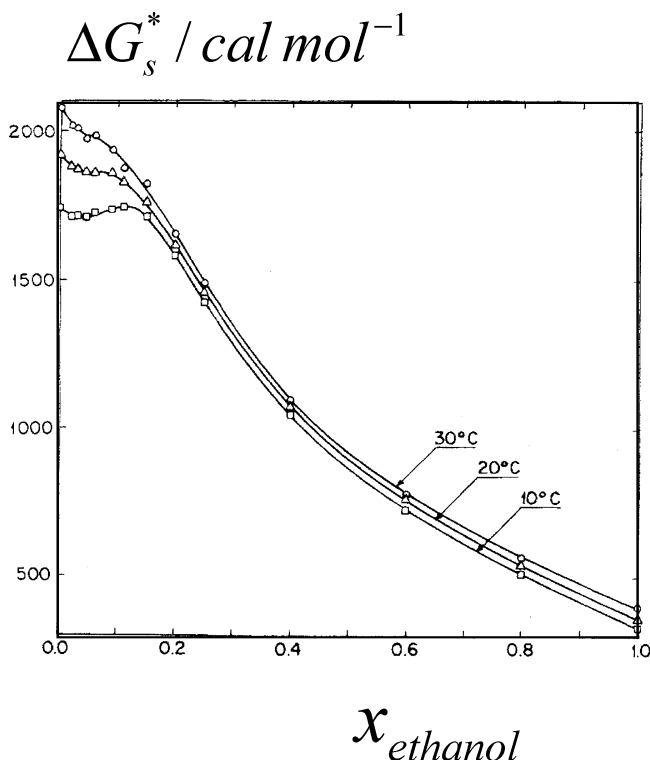


Fig. 3.5 Solvation Gibbs energy of methane in mixtures of water and ethanol at three temperatures (based on data from Yaacobi and Ben-Naim (1973)).

by Cargill and Morrison (1975). See also the review by Battino and Clever (1966).

We note that the low solubility of argon in water is outstanding compared to “normal” solvents, but it is not *unique* to water. The solubility of argon in ethylene glycol, for example, is also very low and of the same order of magnitude as in water (Fig. 3.6). As we shall see in the succeeding sections of this chapter, the solubility, or equivalently the solvation Gibbs energy, depends mainly on the strength of the intermolecular interactions between solute-solvent and solvent-solvent molecules, and

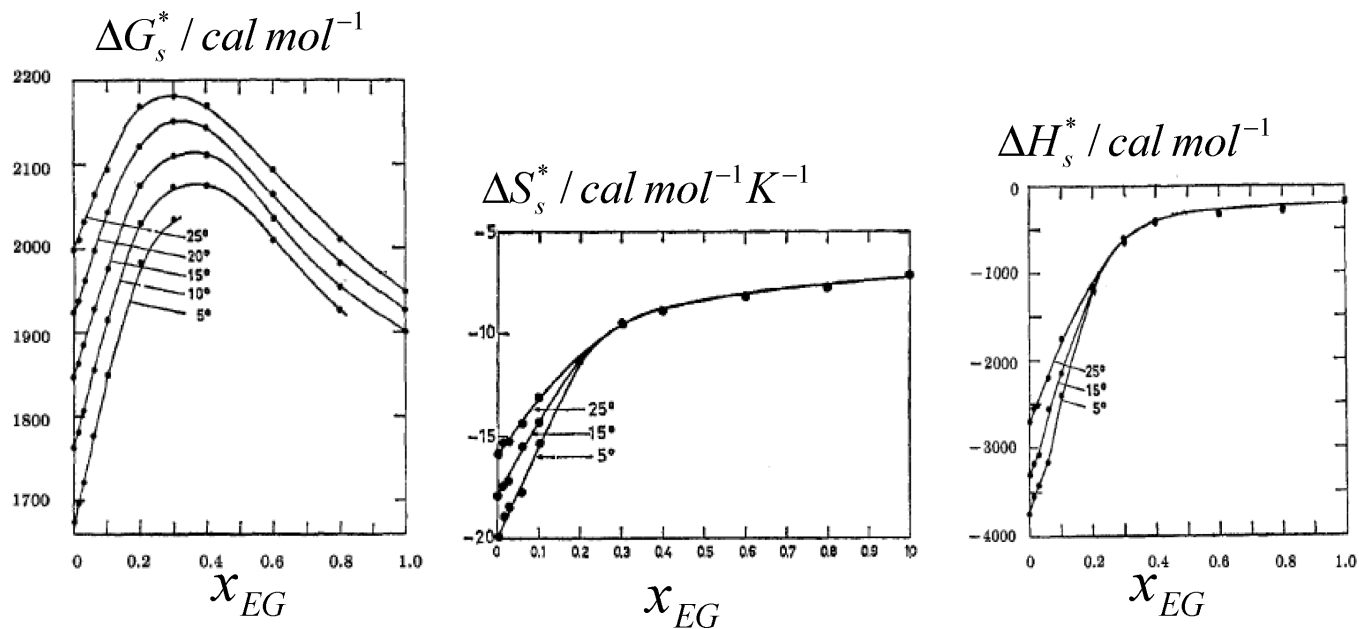


Fig. 3.6 Solvation thermodynamic quantities of argon in mixtures of water and ethylene glycol (based on data from Ben-Naim (1968)).

is not a result of the unique correlation between local density and binding energy. This is an important finding that we shall further discuss in several places in this chapter.

Table 3.1 shows some values of the Ostwald absorption coefficient γ of argon in water and in some liquids. It should be noted that the solubility as measured by γ is about an order of magnitude smaller in water compared with other solvents. Note, however, that the solubility of argon in ethylene glycol at 25°C is about 0.035, almost the same as in water [see Ben-Naim (1968)].

Table 3.1. Ostwald Absorption Coefficient γ for Argon in Water and in Some Organic Liquids at Two Temperatures^a

Solvent	15°C	25°C
Benzene	0.232	0.240
Cyclohexane	0.330	0.334
<i>n</i> -Hexane	0.474	0.472
<i>n</i> -Heptane	0.411	0.415
<i>n</i> -Octane	0.355	0.367
3-Methylheptane	0.360	0.377
2,3-Dimethylhexane	0.381	0.377
2,4-Dimethylhexane	0.400	0.400
<i>n</i> -Nonane	0.340	0.338
<i>n</i> -Decane	0.315	0.311
<i>n</i> -Dodecane	0.271	0.275
<i>n</i> -Tetradecane	0.247	0.250
Fluorobenzene	0.291	0.298
Chlorobenzene	0.202	0.204
Bromobenzene	0.153	0.157
Iodobenzene	0.104	0.109
Toluene	0.240	0.249
Nitrobenzene	0.100	0.105
Water	0.0396	0.0341

^aData taken from Clever *et al.* (1957), Saylor and Battino (1958), and Ben-Naim (1965b).

Table 3.2. Values of the Solvation Gibbs Energy, Entropy, Enthalpy, and Heat Capacity of Methane in Water and in Some Non-Aqueous Solvents at Two Temperatures^a

Solvent	<i>t</i> [°C]	ΔG_s^* [cal mol ⁻¹]	ΔS_s^* [cal mol ⁻¹ K ⁻¹]	ΔH_s^* [cal mol ⁻¹]	$\Delta C_{P,s}^*$ [cal mol ⁻¹ K ⁻¹]
Water	10	1747	-18.3	-3430	{ 53
	25	2000	-15.5	-2610	
Heavy water (D ₂ O)	10	1703	-19.2	-3740	{ 52
	25	1971	-16.5	-2940	
Methanol	10	343	-2.6	-390	{ -21
	25	390	-3.7	-710	
Ethanol	10	330	-3.2	-670	{ -5
	25	380	-3.5	-650	
1-Propanol	10	345	-4.3	-880	{ 25
	25	400	-3.0	-500	
1-Butanol	10	369	-2.8	-420	{ -33
	25	430	-4.5	-910	
1-Pentanol	10	399	-3.3	-530	{ -7
	25	450	-3.6	-630	
1,4-Dioxane	10	538	-0.8	+310	{ -6
	25	553	-1.1	+220	
Cyclohexane	10	154	-1.9	-390	{ 11
	25	179	-1.4	-230	

^aData from Yaacobi and Ben-Naim (1974).

Table 3.2 presents some thermodynamic data for the solvation of methane in water and in non-aqueous solvents. The most outstanding feature is the relatively large negative entropy and enthalpy of solvation of methane in water. Also, the solvation heat capacity is much larger in water than in other liquids.

In Fig. 3.7, we show the entropy and the enthalpy of solvation of methane as a function of the mole fraction of ethanol. Note that the anomalously large and negative entropy and enthalpy of solvation are confined to the water-rich region of the water-ethanol mixtures.

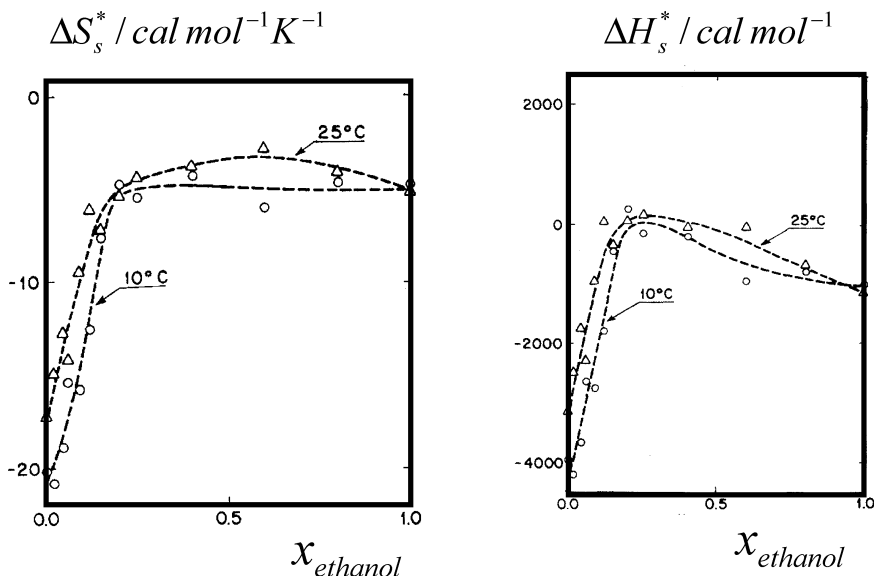


Fig. 3.7 Solvation entropies and enthalpies of methane in mixtures of water and ethanol at two temperatures (based on data from Yaacobi and Ben-Naim (1973)).

Figure 3.8 presents some data on the solvation Gibbs energy of various hydrocarbon molecules in water. For each homologous series, ΔG_s^* is linear in n , the number of carbon atoms, except for the smallest member of the series. The linearity of the solvation Gibbs energy as a function of n has inspired some people to assume that $\Delta G_n^*/n$ is the Gibbs energy of solvation per methylene group. This assumption is known as group additivity. In Chapter 4, we shall discuss this behavior in terms of the hydrophobic interaction between simple non-polar solutes. Denoting by ΔG_n^* the Gibbs energy of solvation of a molecule with chain length n , we may define

$$\delta G(n + \text{CH}_3 \rightarrow n + 1) = \Delta G_{n+1}^* - \Delta G_n^* - \Delta G_{\text{CH}_3}^* \quad (3.2.3)$$

where δG is the indirect work required to bring a methyl group from infinite separation from a hydrocarbon of size n to form

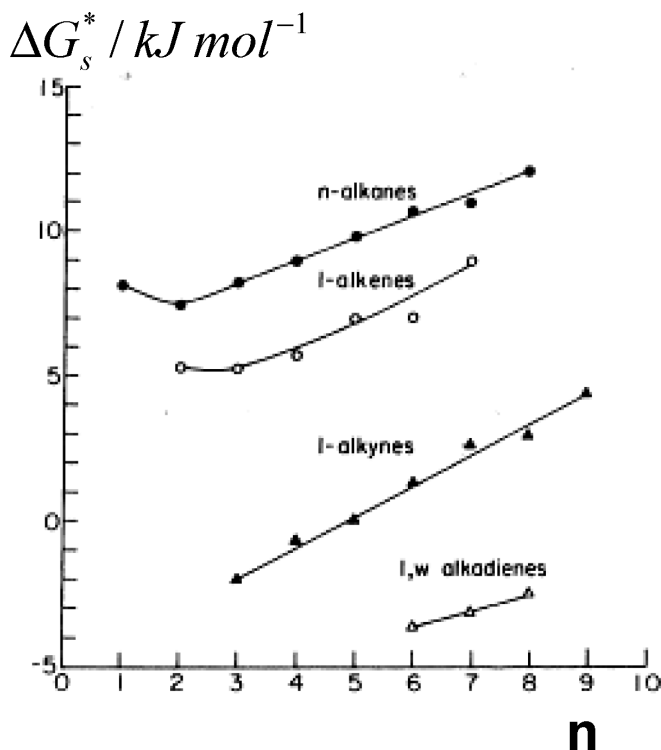


Fig. 3.8 Gibbs energy of solvation of some hydrocarbons in water as a function of n , the number of carbon atoms in the hydrocarbon. All values at 25°C.

a hydrocarbon of size $n + 1$. Since all of the quantities on the right-hand side of Eq. (3.2.3) pertain to the same solvent, the approximate constancy of the slopes of the curves in Fig. 3.8 is essentially a reflection of the fact that δG is constant, almost independent of n and of the functional group of a particular homologous series. Thus, the linearity of ΔG_s^* with s is better described as *bond additivity* rather than *group additivity*.

The low solubility of hydrocarbons in water has led to the concept of *hydrophobic* solute; methane molecules, given the opportunity to distribute between water and, say, ethanol, will prefer the latter. The term “phobia” is not really

appropriate; phobia means fear, not dislike. Nevertheless, the term hydrophobic is commonly used to express the “dislike” of a solute towards water, as compared to the other solvent. Solutes that are very soluble in water are referred to as hydrophilic solutes.¹¹

The second striking difference between aqueous and non-aqueous solutions is the temperature dependence of the solvation Gibbs energy. This is manifested in the relatively large entropy of solvation of the inert gases in water as compared with other liquids. In Fig. 3.9, we plot values of ΔH_s^* and $T\Delta S_s^*$ for xenon in a series of n -alkanols. Again, we see that there is a very small variation in the values of ΔH_s^* and $T\Delta S_s^*$ as

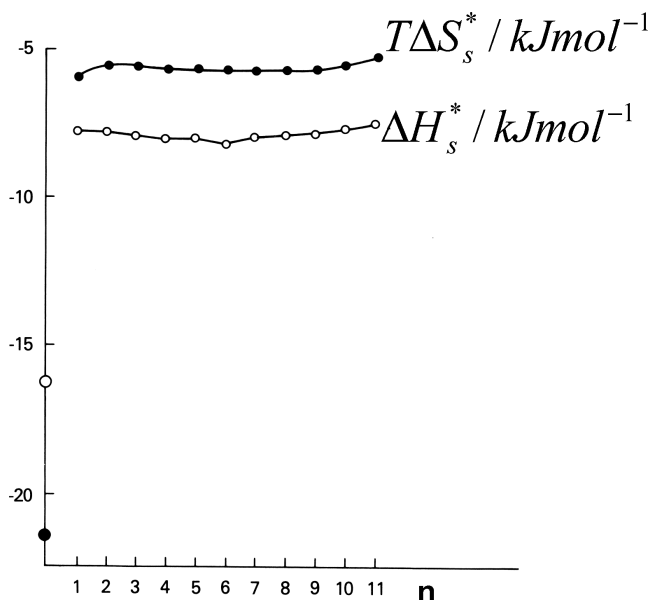


Fig. 3.9 ΔH_s^* and $T\Delta S_s^*$ for xenon in water and in different n -alkanols. n is the number of carbon atoms in the alkanol. All values at 20°C and 1 atm.

¹¹Strictly speaking, the term hydrophobia is not the antonym of hydrophilia. This pair are not antonyms like the pair philanthrope and misanthrope.

we change n . The corresponding values of ΔH_s^* and $T\Delta S_s^*$ in water are markedly *lower* than the values that one would have obtained by extrapolating to $n = 0$, indicating that these quantities are anomalously large and negative in water. We shall see in Sec. 3.7 that these properties are intimately related to the *principle*, i.e. the unique correlation between local density and binding energy. It should be noted that ΔG_s^* and ΔH_s^* may be viewed as the two “components” of the temperature dependence of ΔG_s^* . We write

$$\frac{\partial \Delta G_s^*}{\partial T} = -\Delta S_s^* = \frac{\Delta G_s^*}{T} - \frac{\Delta H_s^*}{T} \quad (3.2.4)$$

Thus, the *total* temperature dependence of the solvation Gibbs energy is equal to the sum of $\Delta G_s^*/T$ and $-\Delta H_s^*/T$. Both ΔG_s^* and $-\Delta H_s^*$ are positive. This means that both contribute to the positive temperature dependence of ΔG_s^* .

Figures 3.6 and 3.7 show how the entropy and the enthalpy of solvation change when we add a co-solvent to water. Note that in both cases there is a steep increase in the values of ΔH_s^* and ΔS_s^* in the water-rich region, then almost leveling off in the co-solvent rich region. This is true for both water ethanol as well as to water ethylene glycol. This finding indicates again that the anomalous entropy and the enthalpy of solvation have different sources to the solvation Gibbs energy.

The third unusual property of aqueous solutions of inert gas molecules is the relatively large partial molar heat capacity of the solute in water. This is equivalent to a large heat capacity of the solvation of the inert gases in water. The partial molar heat capacity of a solute s in mixtures of s and water is defined by

$$C_{P,s} = \left(\frac{\partial \bar{H}_s}{\partial T} \right)_{P, N_s, N_w} \quad (3.2.5)$$

The heat capacity of solvation of s is defined by

$$\Delta C_{P,s}^* = \left(\frac{\partial \Delta H_s^*}{\partial T} \right)_{P, N_s, N_w} \quad (3.2.6)$$

For simple solutes such as argon, the partial molar heat capacity of s in an ideal gas phase is due to the translational degrees of freedom only, and this does not change upon transferring of s from an ideal gas into the liquid. Therefore, whatever excess value of either $C_{P,s}$ or $\Delta C_{P,s}^*$ is ascribed to the structural changes induced by the addition of the solute to water.

In Table 3.2, we present some values of $\Delta C_{P,s}^*$ in water and in a few other “normal” liquids. It is clear that in water the values of $\Delta C_{P,s}^*$ are outstandingly large and positive. As can be seen from Figs. 3.5 and 3.6, the temperature dependence of ΔH_s^* is much larger in water than in “normal” liquids including in mixtures of water and co-solvent in the co-solvent rich compositions.

The last quantity we shall discuss here is the solvation volume. The volume of solvation of a solute s is defined as

$$\Delta V_s^* = \left(\frac{\partial \Delta G_s^*}{\partial P} \right)_T \quad (3.2.7)$$

Table 3.3 shows some values of ΔV_s^* for methane and ethane in some liquids at 25°C. These values are somewhat smaller in water as compared with the other liquids for which the relevant data are available.

The solvation Gibbs energy of small inert molecules such as neon and argon in D₂O is smaller than in H₂O. For larger inert molecules, krypton and xenon, ΔG_s^* in D₂O is larger than in H₂O. Tables 3.4, 3.5, and Fig. 3.10 present some relevant data.¹² As can be seen from Fig. 3.10, the Gibbs energy of

¹²For a more extensive discussion of the solubility of gases in H₂O and D₂O, see Scharlin and Battino (1992).

Table 3.3. Solvation Volumes ΔV_s^* ($\text{cm}^3\text{mol}^{-1}$) for Methane and Ethane at Infinite Dilution in Some Solvents at 25°C

Solvent	Methane	Ethane
Water	36.17	50.07
Carbon tetrachloride	49.06	63.36
<i>n</i> -Hexane	56.03	65.33
Benzene	54.61	70.61

Table 3.4. Values of ΔG_s^* and ΔH_s^* for Neon, Argon, Krypton, and Xenon in H_2O and D_2O at 25°C

		ΔG_s^* (kJ mol^{-1})	ΔS_s^* ($\text{JK}^{-1} \text{mol}^{-1}$)	ΔH_s^* (kJ mol^{-1})
Neon	H_2O	11.19	-45.4	-2.3
	D_2O	10.99	-43.6	-2.0
Argon	H_2O	8.40	-65.1	-11.0
	D_2O	8.15	-68.5	-12.26
Krypton	H_2O	6.94	-70.5	-14.1
	D_2O	6.99	-68.4	-13.4
Xenon	H_2O	5.62	-81.9	-18.8
	D_2O	5.64	-70.9	-15.5

transferring argon from H_2O to D_2O , or to mixtures of H_2O and D_2O is always negative. In Table 3.5, we also show some values of $\Delta\Delta G_s^*$, $\Delta\Delta S_s^*$, and $\Delta\Delta H_s^*$ for transferring argon from H_2O to mixtures of H_2O and D_2O . Note that in all cases the solubility of argon in D_2O or in mixtures of H_2O and D_2O is larger than the solubility in H_2O . These findings are somewhat unexpected. We shall discuss this topic in Sec. 3.7.

Table 3.5. Thermodynamic Quantities of Transferring Argon from H₂O to Mixtures of H₂O and D₂O at 20°C

D ₂ O	$\Delta\Delta G_s^*$ (cal mol ⁻¹)	$\Delta\Delta S_s^*$ (cal mol ⁻¹ K ⁻¹)	$\Delta\Delta H_s^*$ (cal mol ⁻¹)
$x_{D_2O} = 0.03$	-3.5	-0.25	-77
$x_{D_2O} = 0.5$	-24.0	-0.5	-170
$x_{D_2O} = 0.9$	-42.0	-0.8	-276
$x_{D_2O} = 1.0$	-49.8	-0.77	-275

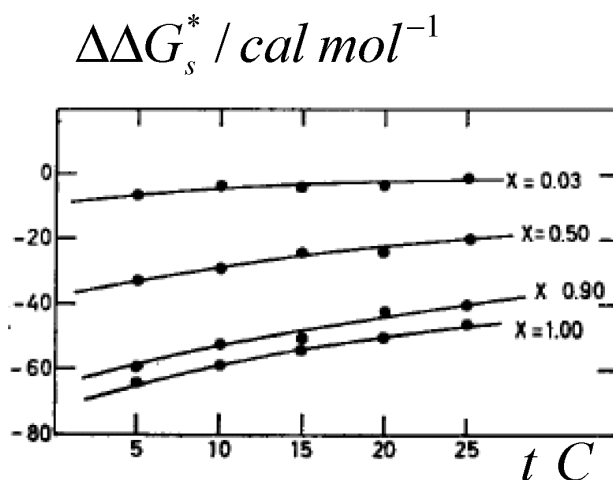
**Fig. 3.10** Gibbs energy change in transferring argon from H₂O to mixtures of H₂O and D₂O as a function of temperature.

Table 3.6 includes some information on the partial molar volumes of argon, methane, and ethane in water and in non-aqueous solvents.

3.3. Solvation and Conditional Solvation

Before plunging into the theoretical interpretation of the solvation thermodynamic quantities, we first need to define the

Table 3.6. Partial Molar Volume (cm^3/mole) of Argon, Methane, and Ethane in Water, Benzene, and Carbon Tetrachloride at 25°C^a

Solvent	Ar	CH_4	C_2H_6
Water	32	37	41
Benzene	43	52	73
Carbon tetrachloride	44	52	61

^aData from Horiuti (1931), Hildebrand and Scott (1950), Namiot (1961), and Smith and Walkley (1962).

quantities we are going to work with and discuss the methods of calculating these quantities from measurable quantities.

In the past, there were a few quantities referred to as “standard Gibbs energy of solutions.” These quantities were defined in terms of transferring a solute from one phase to another at some specified standard states. Different authors reported results on standard Gibbs energy of solutions using different *standard* states (or different scales of concentrations). This rendered comparison between different sources of data sometimes difficult, sometimes impossible. It was not uncommon to find tables of values of ΔG_s° or ΔS_s° without specifying the relevant standard states used in the definition — clearly rendering these data meaningless.¹³ An interesting though extreme example is the following. Arnett and McKelvey (1969) found that the Gibbs energies of transferring propane from H_2O to D_2O have different *signs* if calculated using mole fraction or molality scale. They referred to this finding as a “shocking example.”

In this book, I shall use the concepts of *solvation* and the corresponding thermodynamics of solvation as defined below.

¹³The superscript “o” indicates that the quantity is a “standard” thermodynamic quantity.

Other quantities of solvation and their relations with the solvation thermodynamic quantities were discussed at great length in Ben-Naim (2006).

3.3.1. *Definition of the solvation process*

The solvation process is defined as the process of transferring a single molecule from a fixed position in an ideal gas phase to a fixed position in a liquid (Fig. 3.3a). In most cases we carry out the solvation process at constant temperature T and pressure P . However, for some theoretical work it is more convenient to work in the T, V, N ensemble instead of the T, P, N ensemble.

The theoretical expression for the Gibbs energy of solvation is obtained from the following considerations. The chemical potential of a molecule of type s , in a phase l can be written as

$$\mu_s^l = \mu_s^{*l} + k_B T \ln \rho_s^l \Lambda_s^3 \quad (3.3.1)$$

where $\rho_s^l = N_s^l/V^l$ is the average density of s in the system, Λ_s^3 is the momentum partition function or the de Broglie wavelength of the molecule s , and μ_s^{*l} is the pseudo-chemical potential (PCP). The chemical potential (per particle) is the change in the Gibbs energy associated with the addition of one particle s into the system, keeping T, P constant. The PCP is the change in the Gibbs energy associated with the process of adding one particle s to a fixed position, say $\mathbf{R}_0$, keeping T and P constant. Since all points (in the macroscopic system) are equivalent, it does not matter where we place the particle. Therefore, we omit $\mathbf{R}_0$ from the notation μ_s^{*l} . The difference between μ_s^l and μ_s^{*l} is schematically depicted in Fig. 3.11, which shows the process of adding one solute s to the system and one solute s added to a fixed position. The second term on the right-hand side of (3.3.1) must be negative for classical systems.¹⁴

¹⁴See, for example, Hill (1960).

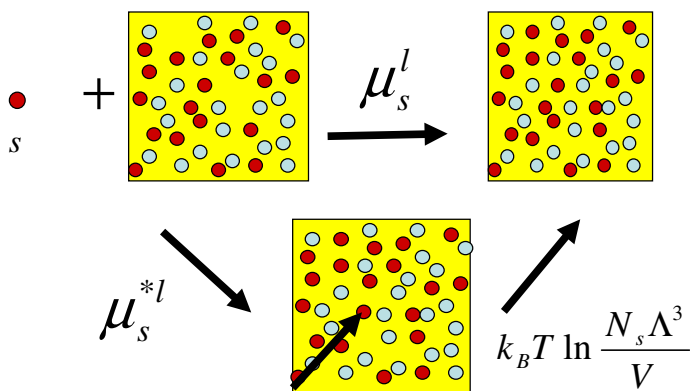


Fig. 3.11 The chemical potential and the pseudo-chemical potential. μ_s^l is the change in Gibbs energy when adding one particle to the system. μ_s^{*l} is the change in the Gibbs energy when adding one solute s at a fixed point. $k_B T \ln (N_s \Lambda^3 / V)$ is the change in free energy for the release of the particle from a fixed point.

From the definition of the solvation process, it follows that the change in the solvation Gibbs energy associated with the solvation process is

$$\Delta \mu_s^* = \Delta G_s^*(ig \rightarrow l) = \mu_s^{*l} - \mu_s^{*ig} \quad (3.3.2)$$

In Fig. 3.3, we also show the process that we shall refer to as the conditional solvation process. The definition of the two processes is the same except that in the conditional process we transfer s to a fixed point in a liquid adjacent to some molecule referred to as the backbone (BB). Clearly, if the backbone perturbs the distribution of solvent molecules around it, the conditional solvation thermodynamic quantities will be different from the corresponding solvation quantities.

3.3.2. *Hydrophobic and hydrophilic solutes*

The terms hydrophobic ($H\phi O$) and hydrophilic ($H\phi I$) solutes have been used in the literature with a variety of meanings.

We shall introduce here a simple definition in terms of the partition coefficients of a given solute between two solvents.¹⁵ Qualitatively, having two immiscible solvents, water w and some reference solvent α , we add a solute s and ask how it is distributed between the two liquids. The simplest measure of this distribution is the ratio of the number densities of s in the two phases at equilibrium. This is related to the difference in the solvation Gibbs energies of s in the two phases; thus

$$\eta_s = \left(\frac{\rho_s^w}{\rho_s^\alpha} \right)_{eq} = \exp[-\beta(\Delta G_s^{*w} - \Delta G_s^{*\alpha})] \quad (3.3.3)$$

where ΔG_s^{*w} and $\Delta G_s^{*\alpha}$ are the solvation Gibbs energies in w and α , respectively. If we choose the two phases α and w to have the same volumes, then the term on the left-hand side of (3.3.3) gives the ratio of the number of solute molecules in the two phases.

Clearly, the larger the ratio η_s , the larger the relative affinity of s for the two phases. Since we are interested in the relative affinities of various solutes towards water, we can choose a constant reference solvent α and measure the ratio η_s for various solutes. The simplest reference “solvent” is an ideal gas, for which $\Delta G_s^{*ig} = 0$ and η_s in (3.3.3) reduces to the Ostwald coefficient (3.2.1):

$$\gamma_s = \left(\frac{\rho_s^w}{\rho_s^{ig}} \right)_{eq} = \exp(-\beta \Delta G_s^{*w}) \quad (3.3.4)$$

Having various solutes, we can construct a hydrophobicity (or hydrophilicity) scale according to the value of γ_s , or equivalently, according to the value ΔG_s^* . Within this definition,

¹⁵This is the simplest, not the most important definition. Nowadays, there are about 40 different so-called “hydrophobicity scales” (Cornette *et al.*, 1987). Most of them are irrelevant to the problem of protein folding (Ben-Naim, 1990a).

argon is more hydrophobic (or less hydrophilic) than krypton at, say, 25°C. Thus, the more positive ΔG_s^* , the more hydrophobic the solute; the more negative ΔG_s^* , the more hydrophilic the solute. One can conveniently choose $\Delta G_s^* = 0$ as the dividing line between $H\phi O$ and $H\phi I$ solutes, but this is not necessary. What is important is the relative hydrophobicity, or the difference between the solvation Gibbs energies of two solutes in the *same* solvent. In the above definition, the same solvent is water. Clearly, the concept can be extended to any solvent or mixture of solvents.

One important extension of the concept of hydrophobicity is useful in the study of solvent effects on biochemical processes. This is the relative hydrophobicity of groups such as methyl, ethyl, hydroxyl, etc., attached to a polymer. Formally, we can define the same quantity ΔG_s^* as before, but now the solvent is not pure water but the molecules of solvent next to the polymer. This extension of the concept of the hydrophobicity of groups or radicals leads naturally to the concept of the *conditional* solvation Gibbs energy. Thus, instead of ΔG_s^* , the work required to transfer s from a fixed position in the gaseous phase to a fixed position in water, we now need to transfer the group s to a fixed position adjacent to some molecule, which could be a small molecule or a protein. We shall refer to this as the backbone (*BB*) (Fig. 3.3b). Clearly, because of the effect of the polymer on its immediate environment, the conditional solvation Gibbs energy will be, in general, different from the solvation Gibbs energy. This is similar to the difference in Gibbs energies in any two solvents. Therefore, a hydrophobicity scale based on the solvation Gibbs energy might be very different from a hydrophobicity scale based on conditional solvation Gibbs energy.

For groups or radicals such as methyl, ethyl, etc., we cannot measure the partition coefficient analog to γ_s . We shall not need these quantities in this book. It should be emphasized, however,

that the conditional solvation Gibbs energies are more important quantities than the solvation quantities in the study of the solvent effect in biochemical processes.¹⁶

3.3.3. *Why do we need solvation quantities?*

In this book, we are mainly interested in the understanding of the outstanding properties of water and aqueous solutions. To this end, the solvation quantities provide valuable information on the strength of the interaction of the solute with the solvent and on the effect of the solute on the “structure” of water. These topics will be discussed in subsequent sections of this chapter.

In practice, solvation quantities are important mainly for two reasons. First, the solvation Gibbs energy determines the solubility of a given solute. Suppose we have a pure phase, say, pure solid or liquid s . If s is brought to equilibrium with water l , then we have the condition of equilibrium

$$\mu_s^s = \mu_s^l = \mu_s^{*l}(\rho_{s,eq}^l) + k_B T \ln \rho_{s,eq}^l \Lambda_s^3 \quad (3.3.5)$$

For simplicity, suppose the pure phase of s remains pure, or nearly pure, at equilibrium with l (i.e. we neglect the solubility of the water in the pure s). In this case, μ_s^s is constant. The equilibrium density of s in l is determined by Eq. (3.3.5). In general, the dependence of μ_s^{*l} on ρ_s is very complicated and one cannot easily determine ρ_s from this equation. However, if the solubility is very low, then we know that μ_s^{*l} becomes independent of ρ_s , and (3.3.5) is simplified to

$$\mu_s^s = \mu_s^{*l} + k_B T \ln \rho_{s,eq}^l \Lambda_s^3 \quad (3.3.6)$$

Now suppose that the pure s has a low vapor pressure so that the vapor of s at equilibrium with pure s is an ideal gas.

¹⁶See Ben-Naim (1992).

In this case

$$\mu_s^s = \mu_s^{ig} = \mu_s^{*ig} + k_B T \ln \rho_s^{ig} \Lambda_s^3 \quad (3.3.7)$$

From (3.3.6) and (3.3.7) we get

$$\Delta\mu_s^* = \mu_s^{*l} - \mu_s^{*ig} = -k_B T \ln \left(\frac{\rho_{s,eq}^l}{\rho_{s,eq}^{ig}} \right) \quad (3.3.8)$$

Thus, from the solvation Gibbs energy and the vapor pressure of the pure s , we can calculate the solubility of s in l .

The second important application of solvation quantities is to determine the equilibrium constant of a chemical reaction in a liquid phase. In the early days of physical chemistry, theoretical studies of the equilibrium constant of chemical reactions were confined to the gaseous phase, specifically to the ideal gas phase. Statistical mechanics was very successful when applied to these systems. However, much of the experimental work was carried out in solutions, for which theory could do very little. It was clear, however, that both the equilibrium constant and the rate constant of a chemical reaction were affected by the solvent.

Consider a simple conversion reaction, say, of two isomers A and B :



If the energy levels of A and B are known, one can calculate the equilibrium constant of this reaction as

$$K^{ig} = \left(\frac{\rho_B}{\rho_A} \right)_{eq}^{ig} = \frac{q_B}{q_A} = \exp[-\beta \Delta G^{\circ g}(A \rightarrow B)] \quad (3.3.10)$$

where q_A and q_B are the internal partition functions of single A and B molecules, respectively (measured relative to the same reference zero energy). $\Delta G^{\circ g}$ is the standard Gibbs energy of the reaction (3.3.9).

In a solution, the equilibrium constant for the same reaction is given by

$$K^l = \frac{q_B}{q_A} \exp[-\beta(\Delta\mu_B^{*l} - \Delta\mu_A^{*l})] \quad (3.3.11)$$

where $\Delta\mu_A^{*l}$ and $\Delta\mu_B^{*l}$ are the solvation Gibbs energies of the solutes A and B, respectively. Although it is difficult to calculate the solvation Gibbs energies, one can determine these quantities experimentally and thereby get an estimate of the equilibrium constant for the reaction in the liquid phase. The general relationship between the standard Gibbs energy of the reaction and the solvation Gibbs energy is depicted in Fig. 3.12:

$$\begin{aligned} K^l &= \exp[-\beta\Delta G^{ol}(A \rightarrow B)] \\ &= \exp[-\beta\Delta G^{og}(A \rightarrow B)] \exp[-\beta(\Delta\mu_B^{*l} - \Delta\mu_A^{*l})] \\ &= K^{ig} \exp[-\beta(\Delta\mu_B^{*l} - \Delta\mu_A^{*l})] \end{aligned} \quad (3.3.12)$$

or equivalently

$$\Delta G^{ol}(A \rightarrow B) - \Delta G^{og}(A \rightarrow B) = \Delta\mu_B^{*l} - \Delta\mu_A^{*l} \quad (3.3.13)$$

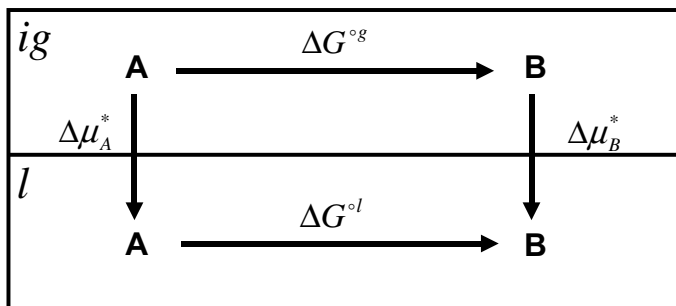


Fig. 3.12 A cyclic process relating the standard Gibbs energies of the reaction $A \rightarrow B$ in two phases ig and l to the solvation Gibbs energies of A and B.

3.4. Statistical Mechanical Expressions for the Solvation Thermodynamic Quantities

In this section, we derive some general statistical mechanical expressions for the thermodynamic quantities of solvation which are independent of any assumptions about the model. We shall later examine special cases of these relations for either a molecular model for water (in terms of a model pair potential) or for a specific mixture-model view of liquid water.

For simplicity, we assume that we have a very dilute system of a solute s in water. By very dilute, we mean that the ideal dilute limiting behavior is attained. Formally, it is sufficient to treat a system containing just one solute s in a solvent containing N water molecules. For convenience, we use the T, V, N ensemble, but similar expressions can be obtained in the T, P, N ensemble (where the Gibbs energy and the enthalpy of solvation replace the Helmholtz energy and the energy of solvation discussed here within the T, V, N ensemble). The Helmholtz energy of solvation of s in the T, V, N ensemble is¹⁷

$$\Delta A_s^* = -k_B T \ln \langle \exp(-\beta B_s) \rangle_0 \quad (3.4.1)$$

where

$$\begin{aligned} \langle \exp(-\beta B_s) \rangle_0 &= \frac{\int d\mathbf{X}^N \exp[-\beta U_N(\mathbf{X}^N) - \beta B_s(\mathbf{R}_s, \mathbf{X}^N)]}{\int d\mathbf{X}^N \exp[-\beta U_N(\mathbf{X}^N)]} \\ &= \int d\mathbf{X}^N P(\mathbf{X}^N) \exp[-\beta B_s(\mathbf{R}_s, \mathbf{X}^N)] \end{aligned} \quad (3.4.2)$$

where B_s is defined by

$$\begin{aligned} B_s(\mathbf{R}_s, \mathbf{X}^N) &= U_{N+1}(\mathbf{R}_s, \mathbf{X}_1, \dots, \mathbf{X}_N) - U_N(\mathbf{X}_1, \dots, \mathbf{X}_N) \\ &= \sum_{i=1}^N U(\mathbf{R}_s, \mathbf{X}_i) \end{aligned} \quad (3.4.3)$$

¹⁷For details, see Ben-Naim (1992, 2006).

Equation (3.4.1) follows directly from the definition of the process of solvation (see also Appendix G). The expression for the solvation, Gibbs or Helmholtz energy in terms of the process of inserting a particle at a fixed position is quite old, probably due to Kirkwood (1935) and later used in the scaled particle theory [see Sec. 3.8 and also Hill (1960) and Widom (1963, 1982)].

The quantity $B_s(\mathbf{R}_s, \mathbf{X}^N)$ is the total binding energy of s to all the N water molecules at a specific configuration $\mathbf{X}^N$. The solute s is presumed to be at some fixed position $\mathbf{R}_s$. We shall always assume pairwise additivity of the interactions, hence the second form on the right-hand side of Eq. (3.4.3). We note also that the average $\langle \cdot \rangle_0$ is taken with the probability distribution of the N water molecules of *pure* liquid water, i.e. in the absence of a solute s at $\mathbf{R}_s$. The subscript zero serves to distinguish this average from the conditional average introduced below.

The quantity $P(\mathbf{X}^N)$ in (3.4.2) is the probability density distribution for the configurations of the solvent molecules:

$$P(\mathbf{X}^N) = \frac{\exp[-\beta U_N(\mathbf{X}_1, \dots, \mathbf{X}_N)]}{\int d\mathbf{X}^N \exp[-\beta U_N(\mathbf{X}_1, \dots, \mathbf{X}_N)]} \quad (3.4.4)$$

Note that, in general, when the solvent is composed of many components, we need to take an average over all molecules in the system except the one placed at $\mathbf{R}_s$.

The solvation entropy of s is obtained by taking the derivative of Eq. (3.4.1) with respect to T , i.e.¹⁸

$$\begin{aligned} \Delta S_s^* &= - \left(\frac{\partial \Delta G_s^*}{\partial T} \right)_{V,N} \\ &= k_B \ln \langle \exp(-\beta B_s) \rangle_0 \\ &\quad + \frac{1}{T} (\langle B_s \rangle_s + \langle U_N \rangle_s - \langle U_N \rangle_0) \end{aligned} \quad (3.4.5)$$

¹⁸For details, see Ben-Naim (1992, 2006).

where the symbol $\langle \cdot \rangle_s$ signifies a conditional average over all configurations of the solvent molecules, given a solute s at a fixed position $\mathbf{R}_s$; that is, we use the conditional distribution defined by

$$P(\mathbf{X}^N/\mathbf{R}_s) = \frac{\exp[-\beta U_N(\mathbf{X}^N) - \beta B_s(\mathbf{R}_s, \mathbf{X}^N)]}{\int d\mathbf{X}^N \exp[-\beta U_N(\mathbf{X}^N) - \beta B_s(\mathbf{R}_s, \mathbf{X}^N)]}. \quad (3.4.6)$$

The solvation energy is obtained from Eqs. (3.4.1) and (3.4.5) in the form

$$\Delta E_s^* = \Delta A_s^* + T \Delta S_s^* = \langle B_s \rangle_s + \langle U_N \rangle_s - \langle U_N \rangle_0 \quad (3.4.7)$$

As noted before for all the systems of interest in this book, there is not much difference between the values of ΔG_s^* and ΔA_s^* , and between ΔH_s^* and ΔE_s^* . The expressions (3.4.1), (3.4.5), and (3.4.7) are very general and apply to any solute in any solvent. We present the results in the T, P, N ensemble as follows:

$$\Delta G_s^* = -k_B T \ln \langle \exp[-\beta B_s] \rangle_0 \quad (3.4.8)$$

$$\begin{aligned} \Delta S_s^* &= k_B \ln \langle \exp[-\beta B_s] \rangle_0 + \frac{1}{T} [\langle B_s \rangle_s + \langle U_N \rangle_s - \langle U_N \rangle_0] \\ &\quad + \frac{P}{T} [\langle V \rangle_s - \langle V \rangle_0] \end{aligned} \quad (3.4.9)$$

$$\begin{aligned} \Delta H_s^* &= \Delta G_s^* + T \Delta S_s^* \\ &= \langle B_s \rangle_s + \langle U_N \rangle_s - \langle U_N \rangle_0 + P [\langle V \rangle_s - \langle V \rangle_0] \\ &= \Delta E_s^* + P \Delta V_s^* \end{aligned} \quad (3.4.10)$$

Note that in (3.4.8)–(3.4.10) all the averages are taken in the T, P, N ensemble. We shall continue our discussion below using the results (3.4.1), (3.4.5), and (3.4.7), which are simpler to analyze. The same conclusions apply to Eqs. (3.4.8)–(3.4.10).

The most important thing to note is that there is a fundamental difference between ΔA_s^* (or ΔG_s^*) on the one hand, and ΔS_s^* and ΔE_s^* (or ΔH_s^*) on the other.

The solvation Gibbs energy depends on the distribution of configurations of the *pure* water, i.e. the solvent *before* the insertion of the solute s . On the other hand, both ΔE_s^* and ΔS_s^* depends on the *conditional* distribution (3.4.6). These results are valid for any solute in any solvent. In particular, for simple solutes in water several important conclusions may be derived from this observation.

The solvation energy as presented in Eq. (3.4.7) has a very simple interpretation. It consists of an average binding energy of s to the system and a change in the average total interaction energy among all the N water molecules induced by the solvation process.¹⁹ For any solvent, this change in the total potential energy may be re-interpreted as a “structural change” induced by the solute s on the solvent.²⁰

From (3.4.1), we see that ΔA_s^* [as well as ΔG_s^* in (3.4.8)] does not depend on the effect of the solute on the average interaction among the solvent molecules. The quantity ΔA_s^* is an average of the function $\exp[-\beta B_s]$, which is a measure of the strength of the interaction of s with the solvent.²¹ Therefore, whatever the effect of the solute on the average interaction energy among the solvent molecules is, it might affect both ΔE_s^* and ΔS_s^* but not ΔA_s^* . Below, we shall recast this conclusion in terms of structural changes. We stress again that this interpretation in terms of structure and structural changes is useful but not essential.

¹⁹We have seen in Chapter 2 that if the solute s is the same as the solvent, then ΔE_s^* is equal to the average binding energy of s .

²⁰As is clear from the discussion above, the term “structural changes” is convenient but not essential.

²¹Sometimes, this average is referred to as an average free energy of interaction. This is not an appropriate term. Free energy applies to either a state of a system or to a process, but not to interaction.

If the solubility of s is very low, then ΔG_s^* determines the solubility. It follows that the solubility of s in this case is independent of the effect of s on the total interaction energy among the solvent molecules.

Read the following exercise carefully. It contains a dangerous pitfall.

Exercise E.3.1.

E.3.1 Consider the following argument:

- (i) The large negative entropy of solvation of argon in water is due to the enhancement of the structure of water.
- (ii) $\Delta G_s^* = \Delta H_s^* - T\Delta S_s^*$ is large and positive (i.e. low solubility of s) due to the dominant term $-T\Delta S_s^*$.
- (iii) It follows from (i) and (ii) that the enhancement of the structure of water is also responsible for the large positive value of ΔG_s^* .

Does (iii) follow from (i) and (ii)?

This argument has appeared frequently in the literature. We shall rephrase the same argument within the *MM* approach in Sec. 3.5.

The second conclusion is that whatever the effect of s on $\langle U_N \rangle$ is, the contribution of $\langle U_N \rangle_s - \langle U_N \rangle_0$ to ΔE_s^* is the same as the contribution to $T\Delta S_s^*$. This is the exact entropy-energy compensation theorem.²² As we shall soon see, $\langle U_N \rangle_s - \langle U_N \rangle_0$

²²To the best of my knowledge, the exact entropy-enthalpy compensation theorem was first published in 1965 (Ben-Naim, 1965b), and repeated in Ben-Naim (1974). Originally, this theorem was stated in terms of a mixture model (*MM*) for water, which at that time was considered an *ad hoc* model for water. However, once the *MM* was established as a legitimate and exact approach to any liquid (Ben-Naim, 1972f), the theorem became exact. Later, it was proved in the most general way to apply to any liquid and to any process in the liquid (Ben-Naim, 1975b, 1978b). The theorem does not depend on the “structure of water,” nor on any specific mixture model for liquid. The theorem was criticized by Marcelja *et al.* (1977) and by Nemethy *et al.* (1981). Much later it was reproved by Yu and Karplus (1988) using different notations.

may be interpreted as structural changes in the solvent induced by s . Now suppose that the structural change is positive, i.e. s induces an increase in the structure (in whatever sense; see below) of the solvent. It is tempting to associate a positive change in the amount or the degree of structure with a negative change in entropy. Although this association is valid in many examples, it is not true in general (see Exercise 3.2 and below). What is important in determining ΔS_s^* is not the *structural* change *per se* but the change in the average interaction energy among the solvent molecules.

Exercise E.3.2. Consider two isomers of a molecule denoted L and H at equilibrium in an ideal gas phase. Let s be a solute that interacts differently with L and H . Calculate the “response function” $(\partial N_L / \partial N_s)_{T,P}$. Let $E_L < E_H$ and assume that L is the more “structured” form. (See Fig. 3.13 for illustration). What is the sign of the “response function”? How is it related to the change in the “structure” in the system? What happens when $E_L > E_H$?

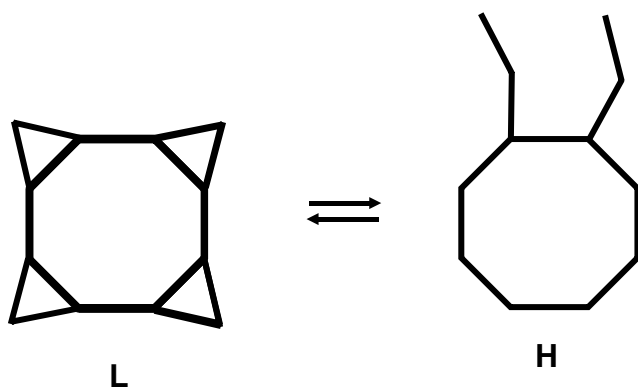


Fig. 3.13 Two isomers of a molecule L and H . L is considered to be the more structured isomer.

We can now re-interpret the quantity $\langle U_N \rangle_s - \langle U_N \rangle_0$ on the right-hand side of (3.4.7) in terms of “structural changes.” A more appropriate term would be redistribution of quasi-components.²³ We shall do it in two steps. First, we use the binding energy distribution function x_{BE} introduced in Sec. 2.3. Second, we shall reformulate this quantity in terms of “structure” as defined in Sec. 2.7.4. Finally, we shall use the same quantity to apply to a two-structure mixture-model approach to water.

Using the binding energy distribution function $x_{BE}(v)$ defined in Sec. 2.3, we can write the total internal energy of the system as

$$E = N\varepsilon^K + \frac{N}{2} \int_{-\infty}^{\infty} vx_{BE}(v)dv \quad (3.4.11)$$

where $x_{BE}(v)dv$ is the mole fraction of molecules with binding energy between v and $v + dv$. The average potential energy of the pure liquid is identified as

$$\langle U_N \rangle_0 = \frac{N}{2} \int_{-\infty}^{\infty} vx_{BE}(v)dv \quad (3.4.12)$$

Similarly, for the conditional average $\langle U_N \rangle_s$, we can derive the analog of (3.4.12) using the conditional distribution function $x_{BE}(v/R_s)$ instead of $x_{BE}(v)$ in (3.4.12):

$$\langle U_N \rangle_s = \frac{N}{2} \int_{-\infty}^{\infty} vx_{BE}(v/R_s)dv \quad (3.4.13)$$

Since we are interested in the limiting case of $N_s \rightarrow 0$, we can rewrite (3.4.7) for a single s as

$$\Delta E_s^* = \langle B_s \rangle_s + \frac{N}{2} \int_{-\infty}^{\infty} v[x_{BE}(v/R_s) - x_{BE}(v)]dv \quad (3.4.14)$$

²³Ben-Naim (1973).

Clearly, the quantity $N[x_{BE}(\nu/R_s) - x_{BE}(\nu)]$ is the change in the average number of ν -components induced by the addition of s . Therefore, the second term on the right-hand side of (3.4.14) may be interpreted as the contribution to ΔE_s^* due to “structural changes” in the solvent. More precisely, this is the effect of s on the distribution of the quasi-components based on the binding energy. Note that ΔE_s^* in (3.4.7) and (3.4.14) are equivalent. In both, the effect of s on the solvent is expressed in terms of the total interaction energy among the solvent molecules. In the second formulation the same quantity is re-interpreted in terms of changes in the distribution of quasi-components based on binding energy. For liquid water, we may further identify this general concept of “structural change” with the particular concept of structural changes as defined in Sec. 2.7.2. We simply use the definition of the pair potential for water as in Sec. 2.7.2 to rewrite

$$\begin{aligned}\Delta E_s^* &= \langle B_s \rangle_s + [\langle U_{LJ} \rangle_s - \langle U_{LJ} \rangle_0] \\ &\quad + \varepsilon_{HB}[\langle N_{HB} \rangle_s - \langle N_{HB} \rangle_0]\end{aligned}\quad (3.4.15)$$

Thus, we see that from the general expression for ΔE^* in (3.4.7) one can extract a quantity that can be described as changes in the *structure* of the system. However, this interpretation is neither necessary nor complete. Even after extracting a term which describes a genuine structural change, there is still a residual term that involves interaction and cannot be interpreted as structural changes.

If the LJ interaction parameter (ε) is very small compared to the HB energy (ε_{HB}), then the first square brackets on the right-hand side of (3.4.15) will be negligibly small (it will be zero for a primitive model in which U_{LJ} is replaced by a hard-sphere potential). In this case, the major contribution to ΔE_s^* comes from “structural changes” induced in the solvent. Here, the

“structural changes” are used in the more conventional sense as will be defined in Sec. 3.7, i.e. changes in the average number of *HBs* in the water induced by the addition of the solute *s*.

Note that in whatever way we define the structure of the solvent, the contribution due to structural changes appearing in (3.4.7) or (3.4.10) also appears in the solvation entropy in either (3.4.5) or (3.4.9). Furthermore, when we form the combination of $\Delta E_s^* - T\Delta S_s^*$, this term cancels out. We can now draw the general conclusion that structural changes in the solvent induced by the solute might affect ΔE_s^* (or ΔH_s^*) and ΔS_s^* but will have no effect on the solvation Helmholtz energy (or ΔG_s^*). We shall see the analog of these quantities applied to a two-structure model in Secs. 3.5 and 3.6.

Until now, we have been dealing with the limit of very dilute solutions of *s* in water. Repeating the same derivation for any mixture of *s* and water, we can rewrite all the expressions above for the solvation thermodynamics of *s* (or the solvent *w*) with a minor re-interpretation of the averages $\langle \cdot \rangle_0$ and $\langle \cdot \rangle_s$. Instead of $\langle \cdot \rangle_0$ in Eqs. (3.4.1), (3.4.5), and (3.4.7), we have an average over all configurations of the system of N_s solute and N_w solvent molecules *before* adding the additional *s* to a fixed position. The conditional average $\langle \cdot \rangle_s$ is similarly re-interpreted as an average over all configurations of N_s and N_w molecules given an *s* molecule at some fixed position $\mathbf{R}_s$.

These results for the entropy and the energy are very important. First, because they are very general and they include all specific results obtained for specific models. Second and perhaps most importantly is the fact that *structural changes* invoked in discussions on entropy changes are nothing but energy changes. In the long history of the concept of entropy, changes in order or of structure were used to explain entropy change. Here, we see that although changes in structure or order are sometimes

useful, they are not necessary and could be potentially misleading (see Exercise 3.2).

A case of interest is the solvation of a water molecule in pure water (see Sec. 1.6). Again, we assume that we have a T, V, N system, and we add one water molecule to a fixed position, say, $\mathbf{R}_w$. The solvation Helmholtz energy in this case is

$$\Delta A_w^* = -k_B T \ln \langle \exp(-\beta B_w) \rangle_0 \quad (3.4.16)$$

where $\langle \cdot \rangle_0$ indicates an average over all the configurations of the N_w water molecules excluding the one at $\mathbf{R}_w$. The corresponding entropy and energy of solvation of a water molecule are obtained by standard relationships. The results are

$$\begin{aligned} \Delta S_w^* &= k_B \ln \langle \exp(-\beta B_w) \rangle_0 \\ &+ \frac{1}{T} (\langle B_w \rangle_w + \langle U_N \rangle_w - \langle U_N \rangle_0) \end{aligned} \quad (3.4.17)$$

and

$$\Delta E_w^* = \langle B_w \rangle_w + \langle U_N \rangle_w - \langle U_N \rangle_0 \quad (3.4.18)$$

In (3.4.17) and (3.4.18), the conditional average is taken with the probability distribution

$$P(\mathbf{X}^N / \mathbf{X}_w) = \frac{\exp[-\beta U_{N+1}(\mathbf{X}^{N+1})]}{\int d\mathbf{X}^N \exp[-\beta U_{n+1}(\mathbf{X}^{N+1})]} \quad (3.4.19)$$

which is the probability density of finding a configuration $\mathbf{X}^N$ given one water molecule at a specific configuration $\mathbf{X}_w$.

Formally, Eqs. (3.4.17) and (3.4.18) are similar to the corresponding Eqs. (3.4.5) and (3.4.7). It follows that one can also give a formal interpretation to the various terms as we have done before. However, in this case we can simplify the expression as follows. First, the average binding energy of a water molecule is the same as the conditional average binding energy of a water

molecule, i.e.

$$\begin{aligned}
 \langle B_w \rangle_w &= \int d\mathbf{X}^N P(\mathbf{X}^N / \mathbf{X}_w) B_w = \frac{\int d\mathbf{X}^N P(\mathbf{X}^N, \mathbf{X}_w) B_w}{P(\mathbf{X}_w)} \\
 &= \frac{\int d\mathbf{X}^N P(\mathbf{X}^N, \mathbf{X}_w) B_w}{8\pi^2/V} = \int d\mathbf{X}_w d\mathbf{X}^N P(\mathbf{X}^N, \mathbf{X}_w) B_w \\
 &= \langle B_w \rangle_0
 \end{aligned} \tag{3.4.20}$$

where $\langle B_w \rangle_0$ is the average binding energy of a water molecule in a system of pure water (of either N or $N + 1$ molecules). Second,

$$\begin{aligned}
 \langle U_N \rangle_w &= \frac{\int d\mathbf{X}^N P(\mathbf{X}^N, \mathbf{X}_w) U_N}{P(\mathbf{X}_w)} = \frac{\int d\mathbf{X}^N P(\mathbf{X}^N, \mathbf{X}_w) U_N}{8\pi^2/V} \\
 &= \int d\mathbf{X}_w d\mathbf{X}^N P(\mathbf{X}^N, \mathbf{X}_w) U_N = \int d\mathbf{X}^N P(\mathbf{X}^N) U_N \\
 &= \langle U_N \rangle_0
 \end{aligned} \tag{3.4.21}$$

which simply means that the average interaction energy among N water molecules is unchanged when we place one water molecule at some configuration $\mathbf{X}_w$.

Hence, we can write

$$\Delta E_w^* = \langle B_w \rangle_0 \tag{3.4.22}$$

Thus, the solvation energy of a water molecule in pure liquid water is simply the average binding energy of a single water molecule.²⁴ This result is of course more general and applies to any liquid.

Finally, we note that the solvation volume (here in the T, P, N ensemble) of a solute s in very dilute solutions may be

²⁴There is an error in Ben-Naim (2006) on page 251 regarding this result.

written as

$$\Delta V_s^* = \langle \phi_s \rangle_s + N_w \int \phi [x_w(\phi/R_s) - x_w(\phi)] d\phi \quad (3.4.23)$$

In (3.4.22), the solvation volume is viewed as consisting of two terms: an average Voronoi polyhedron of the solute and a change in the volume of the solvent due to solute induced changes in the distribution of the volumes of the Voronoi polyhedra of the solvent molecules.

If s is a water molecule, then the solvation volume of w in pure w is simply

$$\Delta V_w^* = \langle \phi_w \rangle_0 \quad (3.4.24)$$

Exercise E.3.3. Derive the expression (3.4.23). How does this expression change if s is a water molecule?

3.5. Application of the Mixture-Model Approach to Water

The idea that a solute changes the “structure” of the solvent is very old. We have mentioned an application of this idea in Sec. 2.3 to explain some puzzling observations (Chadwell, 1927). The addition of solutes such as ether or methyl acetate to water was found to *decrease* the compressibility of the system in spite of the fact that the compressibilities of these pure solutes are about three times larger than the compressibility of pure water. Similar attempts to explain the effect of solute on viscosity, dielectric relaxation, self-diffusion, and many other properties have been suggested in the literature.²⁵

²⁵As we have noted in Chapter 2, the mixture model for water was considered an *ad hoc* model that explained some outstanding properties of water but did not have firm support either from theory or experiment. This situation changed when the mixture-model approach was firmly established in terms of quasi-component distribution functions (Ben-Naim, 1972b, 1974).

There are essentially two fundamental questions that have been the subject of extensive research. The first is concerned with the type of structure that water molecules are assumed to form around the solute molecules. Progress in this field was mainly due to comparison of the thermodynamics of dissolution of gases in water with the thermodynamics of gas-hydrate formation [see, for example, Glew (1962, 1968), and a review by Ben-Naim (1974)]. The second problem is concerned with the mechanism by which a simple solute such as argon enhances the “structure of the solvent.”

Perhaps, one of the most striking pieces of evidence that a simple solute has a significant effect on the structure of water comes from a comparison of the entropy of solution of argon and KCl in water. We have discussed these findings in Sec. 3.1, (Frank and Evans, 1945; Friedman and Krishnan, 1973):

$$\begin{aligned}\Delta S_{KCl}^0 &= -51.9 \text{ cal mol}^{-1}\text{K}^{-1}, \\ 2\Delta S_{Ar}^0 &= -60.4 \text{ cal mol}^{-1}\text{K}^{-1}\end{aligned}\tag{3.5.1}$$

(The standard states are, in the gas, a hypothetical 1 atm; in solution, a hypothetical 1 M concentration. In the present context, the precise meaning of these will be of no concern to us.)²⁶

The fact that the entropy of solution of two moles of argon is more negative than that of KCl is quite surprising (see Sec. 3.1). The molecular explanation for this effect is far from trivial. We shall devote most of the remaining part of this chapter to discussing this effect.

²⁶In this section, we stress the puzzling finding that ΔS of solution of argon is even more negative than the value for two ions. Recently, Ben-Amotz and Underwood (2008) discussed the “mystery” associated with the finding that ΔS of a pair of ions has nearly the same value as that of a pair of argon atoms.

The effect of the solute on the structure of water has been investigated by numerous authors.²⁷ In most studies, one assumes an *ad hoc* mixture model for water, and then examines the shift in chemical equilibrium between the various species involved.

3.5.1. *Application of a two-structure model (TSM)*

In this section, we discuss the application of an *exact* two-structure, mixture-model (MM) approach to aqueous solutions of simple solutes.

Consider a system of N_w water molecules and N_s solute molecules at a given temperature T and pressure P . We shall be interested only in very dilute solutions, $N_s \ll N_w$. We henceforth assume that T and P are constants, and therefore omit them from our notation.

Let N_L and N_H be the average number of L -cules and H -cules obtained by any classification procedure (Sec. 2.3). For the purpose of this section, we need not specify the particular choice of the two species; therefore, our treatment will be very general. For concreteness, one may think of a two-structure model (TSM) constructed from the vector x_{CN} (see Sec. 2.3), i.e.

$$\begin{aligned} N_L &= N \sum_{K=0}^{K^*} x_{CN}(K), \\ N_H &= N \sum_{K=K^*+1}^{\infty} x_{CN}(K), \\ N_w &= N_L + N_H. \end{aligned} \tag{3.5.2}$$

²⁷Examples of such studies are: Frank and Quist (1961), Namiot (1961), Grigorovich and Samoilov (1962), Yashkiraga (1962), Ben-Naim (1965a), Mikhailov (1968), Mikhailov and Ponomareva (1968), and Frank and Franks (1968). We shall start in the next section with the two-structure model and then proceed with the more general MM approach.

Any extensive thermodynamic quantity can be viewed either as a function of the variables (T, P, N_w, N_s) or the variables (T, P, N_L, N_H, N_s) . The equilibrium condition for the conversion between L and H is

$$\mu_L(T, P, N_L, N_H, N_s) = \mu_H(T, P, N_L, N_H, N_s) \quad (3.5.3)$$

In principle, one can solve (3.5.3) in terms of the original set of variables of the system, i.e.

$$N_L = f(T, P, N_w, N_s), \quad N_H = N_w - N_L \quad (3.5.4)$$

An example of such a solution will be discussed in Sec. 3.6. In this section, we adopt the *MM* approach and view the variables N_L and N_H as virtually independent. Of course, at the end of any computation, we must substitute the values of N_L and N_H that fulfill the equilibrium condition (3.5.3).

Consider the volume as an example of an extensive variable. The total differential of the volume (T, P constants) is

$$\begin{aligned} dV = & \left(\frac{\partial V}{\partial N_s} \right)_{N_L, N_H} dN_s + \left(\frac{\partial V}{\partial N_L} \right)_{N_s, N_H} dN_L \\ & + \left(\frac{\partial V}{\partial N_H} \right)_{N_s, N_L} dN_H \end{aligned} \quad (3.5.5)$$

We denote

$$\begin{aligned} V_s^f &= \left(\frac{\partial V}{\partial N_s} \right)_{N_L, N_H}, \\ \bar{V}_L &= \left(\frac{\partial V}{\partial N_L} \right)_{N_s, N_H}, \\ \bar{V}_H &= \left(\frac{\partial V}{\partial N_H} \right)_{N_s, N_L} \end{aligned} \quad (3.5.6)$$

and rewrite the relation (3.5.5) using the condition $dN_L + dN_H = 0$ as

$$dV = V_s^f dN_s + (\bar{V}_L - \bar{V}_H) dN_L \quad (3.5.7)$$

Recognizing that N_L is a function of T, P, N_w , and N_s , and $N_L + N_H = N_w$, we can rewrite (3.5.3) as

$$dV = V_s^f dN_s + (\bar{V}_L - \bar{V}_H) \left(\frac{\partial N_L}{\partial N_s} \right)_{N_w, eq} dN_s \quad (3.5.8)$$

We have appended the subscript *eq* to stress that the derivative in (3.5.8) is taken along the equilibrium line for the “reaction” $L \rightleftharpoons H$.

The splitting of dV in (3.5.8) is characteristic of the application of the *MM* approach to the theory of solutions. It corresponds to splitting the dissolution process into two steps. First, we add dN_s moles (or molecules, or even one *s*) to the system in the “frozen in” state, i.e. keeping the equilibrium values of N_L and N_H fixed. The associated change in volume is the first term on the right-hand side of (3.5.7). (For one molecule this is just V_s^f .) Next, we release the constraint imposed by fixing N_L and N_H , i.e. by adding a hypothetical catalyst to our system. The system, in general, then relaxes to a new equilibrium state, characterized by N'_L, N'_H and the corresponding change in volume is the second term on the right-hand side of (3.5.7); for one molecule this change in volume is $(\bar{V}_L - \bar{V}_H) \left(\frac{\partial N_L}{\partial N_s} \right)_{eq}$. The two contributions to the volume change are schematically shown in Fig. 3.14.²⁸

²⁸In Fig. 3.14, the two changes in volume are positive. These do not have to be positive in general.

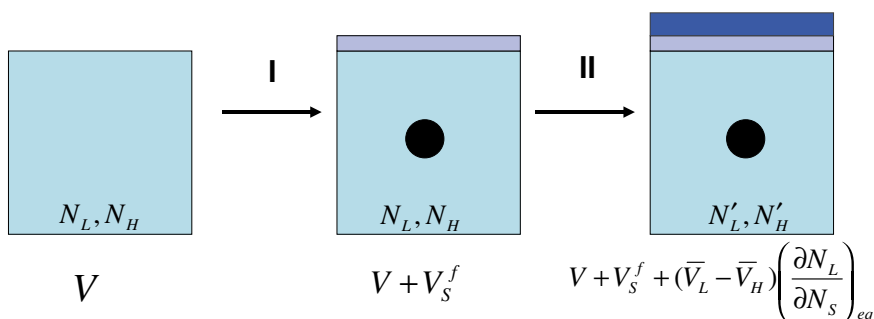


Fig. 3.14 The schematic process of adding one solute to water in two steps. First, add to a frozen-in system; then, allow the system to relax to its final equilibrium state. The corresponding changes in volume are V_s^f and $(\bar{V}_L - \bar{V}_H)(\partial N_L / \partial N_s)_{eq}$, respectively.

The ordinary partial molar volume of the solute s is thus expressed as a sum of two terms

$$\bar{V}_s \equiv \left(\frac{\partial V}{\partial N_s} \right)_{N_w, eq} = V_s^f + (\bar{V}_L - \bar{V}_H) \left(\frac{\partial N_L}{\partial N_s} \right)_{N_w, eq} \quad (3.5.9)$$

In (3.5.9), we have also added the subscript eq in the notation for the partial molar volume to stress the difference between the derivative along an equilibrium line and the derivative when the equilibrium is “frozen in.” In the following, for simplicity of notation, we drop the subscript eq from the derivative along the equilibrium line. The notation “ N_w constant” will henceforth stand for both “ N_w constant” and “equilibrium condition.” We shall also refer to the two terms on the right-hand side of (3.5.9) as the “frozen-in” and “relaxation” parts of the partial molar volume of s . Note that the values of the two terms in (3.5.8) will be dependent on the particular choice of the two components L and H . The partial molar volume $\bar{V}_s$ is, of course, a quantity which is definable in terms of the variables T, P, N_w , and N_s and is independent of the choice of the two components.

A similar splitting can be carried out for any other partial molar quantities. For instance, for the enthalpy, entropy, and the free energy, we have

$$\begin{aligned}\bar{H}_s &= \left(\frac{\partial H}{\partial N_s} \right)_{N_w} = \left(\frac{\partial H}{\partial N_s} \right)_{N_L, N_H} + (\bar{H}_L - \bar{H}_H) \left(\frac{\partial N_L}{\partial N_s} \right)_{N_w} \\ &= H_s^f + \Delta H_s^r\end{aligned}\quad (3.5.10)$$

$$\begin{aligned}\bar{S}_s &= \left(\frac{\partial S}{\partial N_s} \right)_{N_w} = \left(\frac{\partial S}{\partial N_s} \right)_{N_L, N_H} + (\bar{S}_L - \bar{S}_H) \left(\frac{\partial N_L}{\partial N_s} \right)_{N_w} \\ &= S_s^f + \Delta S_s^r\end{aligned}\quad (3.5.11)$$

$$\begin{aligned}\mu_s &= \left(\frac{\partial G}{\partial N_s} \right)_{N_w} = \left(\frac{\partial G}{\partial N_s} \right)_{N_L, N_H} + (\mu_L - \mu_H) \left(\frac{\partial N_L}{\partial N_s} \right)_{N_w} \\ &= \mu_s^f + \Delta \mu_s^r\end{aligned}\quad (3.5.12)$$

In each case, the first term is the “frozen-in” term, and the second is the relaxation term corresponding to the particular partial molar quantity.

An important general result follows from the condition of chemical equilibrium $\mu_L = \mu_H$ as a result of which Eq. (3.5.12) reduces to

$$\mu_s = \mu_s^f \quad (3.5.13)$$

This is a unique feature of the partial molar free energy of the solute s . For any classification into two components we have chosen for the solvent, the chemical potential of the solute will not be affected by the relaxation term. Originally, this result was proved for an *ad hoc* MM approach to liquid water.²⁹ However, once the MM approach was firmly established, this result became an exact result. The result holds true for any

²⁹Ben-Naim (1965b).

multi-component *MM* approach (both discrete and continuous). It is true even if we do not adopt the *MM* approach at all. As we have seen in Sec. 3.4, this result follows from the fact that the chemical potential as well as the pseudo-chemical potential are independent of any changes in the total interaction energy among solvent molecules induced by the solute.

The above result can be rephrased as follows. Suppose that the inter-conversion between *L* and *H* depends on the presence of a catalyst. In the absence of the catalyst, the equilibrium $L \rightleftharpoons H$ is “frozen-in.” The conclusion reached above means that the partial molar quantities of the solute depend, in general, on whether or not the catalyst is present. The chemical potential of the solute is independent of the presence or absence of the catalyst. (This is true provided we measure the chemical potential at the equilibrium concentrations of *L* and *H*. For a specific example, see Sec. 3.6.)

One direct consequence of relation (3.5.12) is that the solubility of *s* does not change if we “freeze in” the equilibrium. This is clear since the solubility of *s* is governed by its chemical potential. Another consequence of considerable importance is the so-called “entropy-enthalpy compensation” law.³⁰ This follows directly from the equilibrium condition (3.5.3), i.e.

$$\bar{H}_L - T\bar{S}_L = \mu_L = \mu_H = \bar{H}_H - T\bar{S}_H \quad (3.5.14)$$

or equivalently

$$\Delta H_s^r = T\Delta S_s^r \quad (3.5.15)$$

The relaxation part of the partial molar enthalpy is equal to the relaxation part of $T\bar{S}_s$. Thus, the fact that the entropy of solution *s* in water is large and negative may be partially due

³⁰Note that here we refer to an exact compensation law. This is different from the approximate “entropy-enthalpy compensation” law discussed extensively by Lumry and Rajender (1970). See also Appendix K.

to the large contribution from the relaxation term in (3.5.15). The latter *cannot*, however, be used to explain the large positive value of the solvation Gibbs energy $\Delta\mu_s^*$ (i.e. the low solubility). Thus, if we write $\Delta\mu_s^* = \Delta H_s^* - T\Delta S_s^*$, only the components of ΔH_s^f and ΔS_s^f contribute to the determination of the value of $\Delta\mu_s^*$; the relaxation parts exactly compensate each other. For further discussion of the effect of “structural changes” on the solubility of s , see Appendix H.

The discussion above is very general and applies to any *MM* for water. However, in order to interpret the large and negative enthalpy and entropy of solution of non-electrolytes in water, we need to identify the *L* form with the hydrogen-bonded molecules and the *H* form with the non-bonded molecules. Hence, it is expected that $\bar{H}_L - \bar{H}_H$ will be negative. If, in addition, one postulates that the solute s stabilizes the *L* form, then we have a negative contribution from the relaxation term to the enthalpy, as well as to the entropy, by virtue of (3.5.15). In Sec. 3.6, we present a simple example showing such a stabilization effect; a more general argument independent of any *ad hoc* model for water is presented in Sec. 3.7.

The assertion that a simple solute such as argon stabilizes the component that is fully hydrogen bonded is somewhat counter-intuitive. The reason is as follows. Suppose we add large quantities of, say, alcohol to water. It is clear that the very fact that water becomes diluted in the water-alcohol mixture will cause a dissociation of hydrogen-bonded water molecules. At a very high dilution of water in any solvent, we expect very little concentration of fully hydrogen-bonded molecules. Therefore, we can conclude that if such a stabilization effect exists, it must occur only in the range of very dilute solutions of a solute in water.

There exists an immense body of experimental results which supports the assertion that non-electrolytes in very dilute

solutions have a stabilizing effect on the “structure of water.” Most of these results were interpreted in terms of structural changes even without having defined the concept of structure. In Secs. 3.6 and 3.7, we shall discuss the molecular reasons for the existence of such an effect. We note here that experimental evidence has come from a wide variety of measurements such as NMR (Glew, 1968; Wen and Hertz, 1972; Zeidler, 1973), dielectric properties (Haggis *et al.*, 1952; Hasted, 1973), the effect of solute on the temperature of maximum density (Wada and Umeda, 1962a,b), the partial molar volume of water (see Sec. 2.3), and many others. (For reviews, see Franks and Ives, 1966; Horne, 1972; and Franks, 1973a.) In fact, the large negative entropy and enthalpy of gases in water were originally used as evidence that solutes stabilize the structure of water.

There are other thermodynamic quantities which, though dependent on the structural changes in the solvent, are not easily explainable in these terms. An important example is the partial molar heat capacity (PMHC) of the solute s , which can be expressed in either one of the following ways:

$$\bar{C}_s = \left(\frac{\partial \bar{H}_s}{\partial T} \right)_{N_w, N_s} = \left(\frac{\partial C}{\partial N_s} \right)_{T, N_w} \quad (3.5.16)$$

where C stands for the heat capacity of the system at constant pressure. (The notation for the pressure is omitted in the following equations.)

Using a TSM for water, one can formally write

$$\bar{C}_s = C_s^f + (\bar{C}_L - \bar{C}_H)(\partial N_L / \partial N_s)_{N_w} \quad (3.5.17)$$

where

$$C_s^f = (\partial C / \partial N_s)_{N_L, N_H} \quad (3.5.18)$$

Exercise E.3.3: Consider the following argument that has appeared many times in the literature:

- (i) The high value of the heat capacity of water is due to the “melting” of the ice-like component in pure water as we heat the mixture (see Sec. 2.3).
- (ii) It is known that a solute s increases the structure of water. Within the MM approach this means that the concentration of the ice-like component *increases* with the addition of the solute s .

If (i) and (ii) are presumed to be true, it follows that the large positive value of the partial molar heat capacity of s in water is explained by the fact that “more of the ice-like component is available for melting.”

Is this argument sound?

The general expression for the $PMHC$ of s is quite involved and is omitted here [see Ben-Naim (1970b)]. Instead, we present here a simple example to demonstrate an important point. Suppose that the mixture of L and H forms a symmetrical ideal solution. Also, for simplicity, we assume that s is very dilute in water. The total heat capacity of the system can be written as (see Sec. 2.3)

$$C = C^f + (\bar{H}_L - \bar{H}_H)^2 x_L x_H N_w / k_B T^2 \quad (3.5.19)$$

Recall that the second term is responsible for the high value of the heat capacity of pure water. The quantity C^f is essentially the contribution of the kinetic degrees of freedom of the two species. We can assume that both C^f and $\Delta H = \bar{H}_L - \bar{H}_H$ will be unchanged by the addition of the solute. Hence, the main contribution to the $PMHC$ of s will come from the derivative of the second term on the right-hand side of

(3.5.19), i.e.

$$\bar{C}_s \cong \frac{(\bar{H}_L - \bar{H}_H)^2}{k_B T^2} (x_H - x_L) \left(\frac{\partial N_L}{\partial N_s} \right)_{N_w} \quad (3.5.20)$$

Clearly, the sign of this term depends on the relative amounts of L and H . Thus, even when we know that s stabilizes the L form, we can still say nothing about the sign of the $PMHC$ of s in water. A detailed and explicit example is worked out in the next section [see also Ben-Naim (1970b)].

A very similar treatment applies to the effect of s on the compressibility of the system. Again, the general expression is quite cumbersome, and we present here only the results for the ideal solution of L and H .

The total volume is

$$V = N_s V_s^f + N_L \bar{V}_L + N_H \bar{V}_H \quad (3.5.21)$$

Instead of dealing with the compressibility, it will be easier to discuss the pressure dependence of the volume, defined by

$$\begin{aligned} D = -V\kappa_T &= \left(\frac{\partial V}{\partial P} \right)_{T, N_w} \\ &= N_s \frac{\partial V_s^f}{\partial P} + N_L \frac{\partial \bar{V}_L}{\partial P} + N_H \frac{\partial \bar{V}_H}{\partial P} \\ &\quad + (\bar{V}_L - \bar{V}_H) \left(\frac{\partial N_L}{\partial P} \right)_{N_w} \end{aligned} \quad (3.5.22)$$

Taking the limit of dilute solution of s in water and using the expression for $(\partial N_L / \partial P)$ for ideal solutions (see Appendix F) and assuming that the first three terms on the right-hand side of (3.5.22) are weakly dependent on N_s , we can arrive at the approximate expression

$$\left(\frac{\partial D}{\partial N_s} \right) \cong \frac{(\bar{V}_L - \bar{V}_H)^2 (x_H - x_L)}{k_B T} \left(\frac{\partial N_L}{\partial N_s} \right)_{N_w} \quad (3.5.23)$$

We can clearly see that even if we know that s stabilizes one of the forms L or H , this information is insufficient to draw conclusions as to the effect of s on the compressibility of the system. Of course, the general expression is more complicated than that given in (3.5.23). However, this example is sufficient to demonstrate the complexity of the expressions for quantities which are second derivatives of the free energy.

3.5.2. *Generalization to any mixture model of water*

In this section, we examine the general aspects of the application of the MM formalism to aqueous solutions. We have already seen that the splitting of partial molar quantities into “frozen-in” and relaxation terms is totally dependent on the choice of the classification procedure. Here, we generalize the discussion of Sec. 3.5.1 and elaborate on the condition under which such a splitting may be useful to the theory of aqueous solutions.

Let $N_w(\alpha)d\alpha$ be the average number (in the T, P, N_w, N_s ensemble) of *water* molecules which are distinguished by some local property having a numerical value between α and $\alpha + d\alpha$. Similarly, $N_s(\beta)d\beta$ is the average number of solute molecules classified according to some other property having a numerical value between β and $\beta + d\beta$. [Here, α and β are continuous parameters; in this section, we will not use the notation $\beta = (k_B T)^{-1}$.] The two normalization conditions are

$$N_w = \int N_w(\alpha)d\alpha, \quad N_s = \int N_s(\beta)d\beta \quad (3.5.24)$$

where the integration in each case extends over all the possible values of α and β , respectively. As in Chapter 2, we use the symbols N_w and N_s to denote the *whole* functions whose components are $N_w(\alpha)$ and $N_s(\beta)$, respectively. Viewing the system as a mixture of quasi-components, we apply the generalized Euler

theorem to express any extensive thermodynamic quantity, say, the energy E , as

$$E(N_w, N_s) = \int \bar{E}_w(N_w, N_s, \alpha) N_w(\alpha) d\alpha + \int \bar{E}_s(N_w, N_s, \beta) N_s(\beta) d\beta \quad (3.5.25)$$

The partial molar quantities in (3.5.25) are obtained by functional differentiation of $E(N_w, N_s)$:

$$\begin{aligned} \bar{E}_w(N_w, N_s, \alpha) &= \frac{\delta E(N_w, N_s)}{\delta N_w(\alpha)}, \\ \bar{E}_s(N_w, N_s, \beta) &= \frac{\delta E(N_w, N_s)}{\delta N_s(\beta)} \end{aligned} \quad (3.5.26)$$

The experimental partial molar energy of the solute s is given by

$$\begin{aligned} \bar{E}_s &= \left(\frac{\partial E}{\partial N_s} \right)_{N_w} = \int \frac{\partial \bar{E}_w(N_w, N_s, \alpha)}{\partial N_s} N_w(\alpha) d\alpha \\ &+ \int \frac{\partial \bar{E}_s(N_w, N_s, \beta)}{\partial N_s} N_s(\beta) d\beta \\ &+ \int \bar{E}_w(N_w, N_s, \alpha) \frac{\partial N_w(\alpha)}{\partial N_s} d\alpha \\ &+ \int \bar{E}_s(N_w, N_s, \beta) \frac{\partial N_s(\beta)}{\partial N_s} d\beta \end{aligned} \quad (3.5.27)$$

This is the most general expression for $\bar{E}_s$ (or any other partial molar quantity) in the MM formalism. We have applied the MM approach here to both the solute and the solvent. The first two terms on the right-hand side of (3.5.27) may be referred to as the “frozen-in” terms whereas the last two are corresponding “relaxation” terms for the solvent and solute, respectively.

From here on we make a specific choice of a quasi-component distribution function (QCDF) based on binding

energy and also treat the case of very dilute solutions of s in w . We also assume pairwise additivity of the total potential. We define the following two $QCDFs$ for w and s molecules:

$$N_w(v) = N_w \int dV \int d\mathbf{X}^N P(\mathbf{X}^N, V) \delta[B_w^{ww}(\mathbf{X}^N) - v] \quad (3.5.28)$$

$$N_s(v) = N_s \int dV \int d\mathbf{X}^N P(\mathbf{X}^N, V) \delta[B_s^{sw}(\mathbf{X}^N) - v] \quad (3.5.29)$$

where $\mathbf{X}^N$ denotes the configuration of the whole system of $N = N_s + N_w$ molecules. $P(\mathbf{X}^N, V)$ is the probability density in the T, P, N_w, N_s ensemble. The binding energies of w and s are defined as:

$$B_w^{ww}(\mathbf{X}^N) = \sum_{j=2}^{N_w} U^{ww}(\mathbf{X}_1, \mathbf{X}_j) \quad (3.5.30)$$

$$B_s^{sw}(\mathbf{X}^N) = \sum_{j=1}^{N_w} U^{sw}(\mathbf{X}_s, \mathbf{X}_j) \quad (3.5.31)$$

where U^{ww} is the solvent-solvent and U^{sw} the solute-solvent pair potential. The symbol $\mathbf{X}_1$ in (3.5.30) stands for the configuration of a solvent molecule, whereas in (3.5.31) $\mathbf{X}_s$ stands for the configuration of a solute molecule. We can neglect solute-solute interactions and assume that we have only one solute s .

The total energy of the system is written as

$$E = N_w \varepsilon_w^K + N_s \varepsilon_s^K + \frac{1}{2} \int v N_w(v) dv + \int v N_s(v) dv \quad (3.5.32)$$

ε_i^K is the average kinetic energy per molecule of species i . Using the normalization conditions (3.5.24), we rewrite

(3.5.32) as

$$E = \int \left[\varepsilon_w^K + \frac{1}{2}v \right] N_w(v) dv + \int [\varepsilon_s^K + v] N_s(v) dv \quad (3.5.33)$$

In this representation, we identify the partial molar energies of the various quasi-components as

$$\bar{E}_w(N_w, N_s, v') = \delta E / \delta N_w(v') = \varepsilon_w^K + \frac{1}{2}v' \quad (3.5.34)$$

$$\bar{E}_s(N_w, N_s, v'') = \delta E / \delta N_s(v'') = \varepsilon_s^K + v'' \quad (3.5.35)$$

Note that for this particular classification, the partial molar quantities given in (3.5.34) and (3.5.35) are independent of the composition (N_w and N_s). Therefore, using the general expression (3.5.27) for this particular choice, we obtain

$$\begin{aligned} \bar{E}_s = & \int \left[\varepsilon_w^K + \frac{1}{2}v \right] [\partial N_w(v) / \partial N_s] dv \\ & + \int [\varepsilon_s^K + v] [\partial N_s(v) / \partial N_s] dv \end{aligned} \quad (3.5.36)$$

In this form, $\bar{E}_s$ involves two structural change terms: one includes a re-distribution among the v -cules of the solvent, and the second, the redistribution in the solutes. In practical applications of the idea of relaxation, we focus our attention on the structural changes in the solvent. To do this, let us rewrite (3.5.36) in a somewhat different form. From the normalization conditions (3.5.24), we get [noting that the derivatives in (3.5.36) are at constant N_w and that $N_s \ll N_w$]

$$\begin{aligned} & \int v [\partial N_s(v) / \partial N_s] dv \\ & = (\partial / \partial N_s) \left[N_s \int v x_s(v) dv \right] \xrightarrow{\rho_s \rightarrow 0} \langle B_s^0 \rangle \end{aligned} \quad (3.5.37)$$

where $\langle B_s^0 \rangle$ is the *average* binding energy of the solute s to the solvent at infinite dilution (it is only in the limit of $\rho_s \rightarrow 0$ that this quantity becomes independent of N_s). Hence, we rewrite (3.5.36) in this limit

$$\bar{E}_s^0 = \varepsilon_s^K + \langle B_s^0 \rangle + \frac{1}{2} \int v[\partial N_w(v)/\partial N_s] dv \quad (3.5.38)$$

Thus, the partial molar energy of s at infinite dilution consists of the average kinetic energy, the average binding energy of the solute to the solvent, and a contribution due to “structural changes” in the solvent brought about by the addition of the solute.

For the solvation energy of s we have

$$\Delta E_s^* = \langle B_s^0 \rangle + \frac{1}{2} \int v[\partial N_w(v)/\partial N_s] dv \quad (3.5.39)$$

A special case of (3.5.39) is for hard-sphere (HS) solutes, for which the average binding energy $\langle B_{HS}^0 \rangle$ must be zero. Hence, the energy of solvation is

$$\Delta E_{HS}^* = \frac{1}{2} \int v[\partial N_w(v)/\partial N_s] dv \quad (3.5.40)$$

Thus, the solvation energy of solution of a hard sphere is viewed here as arising only from structural changes in the solvent. This brings us back to Eley’s speculation that in water one may assume that $\Delta \bar{E}_{HS}^0$ is zero because of the existence of “natural holes” in the water. Clearly, such a conjecture is erroneous if the dissolution of a hard sphere (or creation of a cavity) induces large structural changes in the solvent.

We now examine some special cases of (3.5.39) or (3.5.40):

- (i) The energy of solvation of an *HS* solute in an *HS* solvent $\Delta \bar{E}_{HS}^*$ must be zero:

$$(\partial/\partial N_s) \left[\int v N_w(v) dv \right] = 0 \quad (3.5.41)$$

- (ii) The energy of solvation of *s* in *s* is equal to the average binding energy of *s* to its environment, i.e.

$$\Delta E_s^* = \langle B_s^0 \rangle \quad (3.5.42)$$

This can be shown by direct computation of the energy change for the transfer of an *s* molecule from the gaseous phase to pure liquid *s*.

- (iii) Suppose that $N_w(v)$ is concentrated in two very sharp peaks, a limiting case of which is

$$N_w(v) = N_1 \delta(v - v_1) + N_2 \delta(v - v_2) \quad (3.5.43)$$

where v_1 and v_2 are constant values, and N_1 and N_2 are the average numbers of particles in each “state.” From (3.5.40), we get

$$\begin{aligned} \Delta E_s^* &= \langle B_s^0 \rangle + \frac{1}{2} (\partial/\partial N_s) \int v N_w(v) dv \\ &= \langle B_s^0 \rangle + \frac{1}{2} (v_1 - v_2) (\partial N_1 / \partial N_s)_{N_w} \end{aligned} \quad (3.5.44)$$

Here, the relaxation term is due to “excitation” of solvent molecules from one state to the second caused by the addition of *s*. We recall that the second term on the right-hand side of (3.5.44) is expected to be large if N_1 and N_2 are of comparable magnitude and if the separation between v_1 and v_2 is also large. Although this particular example is very artificial, it serves to demonstrate an important aspect of solution thermodynamics, namely that the two contributions to the energy of solvation in (3.5.44)

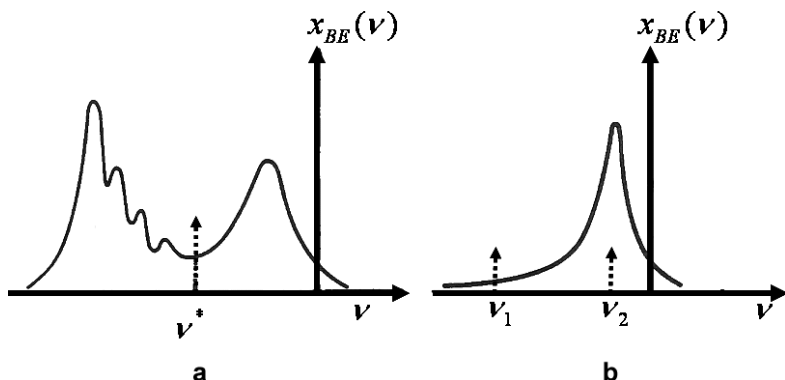


Fig. 3.15 Two possible distributions of $x_{BE}(v)$. In (a) one can find a value of v^* for the construction of a useful two-structure model. In (b) neither v_1 nor v_2 would be a good choice for v^* .

can, in principle, be of different orders of magnitude. For instance, s may interact very weakly with the solvent, so that $\langle B_s^0 \rangle \approx 0$, but it may induce structural changes involving large changes in energy.

- (iv) We now consider a possible distribution function $x_w(v)$ for water. A schematic illustration is given in Fig. 3.15a. Let v^* be any cut-off point for constructing a two-structure model (TSM) as follows:

$$x_1 = \int_{-\infty}^{v^*} x_w(v) dv, \quad x_2 = 1 - x_1 \quad (3.5.45)$$

With this definition, we can rewrite the general expression for ΔE_s^* (3.5.39) as

$$\begin{aligned} \Delta E_s^* &= \langle B_s^0 \rangle + \frac{1}{2}(\partial/\partial N_s) \\ &\quad \times \left[\int_{-\infty}^{v^*} v N_w(v) dv + \int_{v^*}^{\infty} v N_w(v) dv \right] \\ &= \langle B_s^0 \rangle + \frac{1}{2}(\partial/\partial N_s)(\bar{N}_1 \bar{v}_1 + \bar{N}_2 \bar{v}_2) \end{aligned}$$

$$\begin{aligned}
&= \left\{ \langle B_s^0 \rangle + \frac{1}{2}(\bar{N}_1 \partial \bar{v}_1 / \partial N_s) + (\bar{N}_2 \partial \bar{v}_2 / \partial N_s) \right\} \\
&\quad + \frac{1}{2}(\bar{v}_1 - \bar{v}_2)(\partial \bar{N}_1 / \partial N_s) \quad (3.5.46)
\end{aligned}$$

All the derivatives in (3.5.46) are at N_w constant. In the second form on the right-hand side, we have used the average binding energies of the two components $\bar{N}_1$ and $\bar{N}_2$ defined as

$$\bar{v}_1 = \bar{N}_1^{-1} \int_{-\infty}^{v^*} v N_w(v) dv, \quad \bar{v}_2 = \bar{N}_2^{-1} \int_{v^*}^{\infty} v N_w(v) dv \quad (3.5.47)$$

We can now interpret the total structural changes consisting of three contributions. The first two involve the effect of N_s on the “locations” of the two peaks, i.e. shifts of the average values of $\bar{v}_1$ and $\bar{v}_2$. The third term conveys the structural changes between the two components, i.e. the change in the relative area under the two peaks of the distribution function $x_w(v)$.

We can now make a general statement about the conditions required for a useful TSM. If the curve of $x_w(v)$ is such that one can define two values $\bar{v}_1$ and $\bar{v}_2$, which are well separated in such a way that x_1 and x_2 have comparable magnitudes, then it is expected that a major contribution to the energy of solvation will come from structural changes between the two components; this contribution may involve energies of different orders of magnitude compared with the interaction of the solute with the solvent. The shifts in the locations of $\bar{v}_1$ and $\bar{v}_2$ due to the addition of s can be collected in one “frozen-in” term so that (3.5.46) is finally written as

$$\Delta E_s^* = \Delta E_s^f + \frac{1}{2}(\bar{v}_1 - \bar{v}_2)(\partial \bar{N}_1 / \partial N_s)_{N_w} \quad (3.5.48)$$

Note that $\bar{v}_1$ and $\bar{v}_2$ here replace v_1 and v_2 in (3.5.44). Thus, in general, to obtain a large contribution from “structural changes in the solvent” the distribution $x(v)$ does not need to be

bimodal. All we require is that the distribution will be spread over large values of ν , in such a way that we can choose a cut-off value ν^* such that the two components defined in (3.5.45) will be of comparable magnitude and quite different from each other. When the distribution is very sharp such as in Fig. 3.15b, we cannot find such a cut-off ν^* . If we choose $\nu^* = \nu_1$, we get two *different* components, but x_1 will be very small. On the other hand, if we choose $\nu^* = \nu_2$, we get two components that are very *similar* though their concentrations are nearly equal.

We now briefly mention a similar treatment of the partial molar volume of the solute. Consider the quasi-component distribution function based on the volume of the Voronoi polyhedra (VP) (Sec. 2.3). Let $N_w(\phi)$ and $N_s(\phi)$ be the corresponding singlet distribution functions. The total volume of the system is written as

$$V(T, P, N_w, N_s) = \int \phi N_w(\phi) d\phi + \int \phi N_s(\phi) d\phi \quad (3.5.49)$$

Note that in constructing the VP of either s or w , we use the centers of *all* the molecules in the system. The partial molar volume of s is

$$\begin{aligned} \bar{V}_s = (\partial V / \partial N_s)_{N_w} &= \int \phi [\partial N_w(\phi) / \partial N_s] d\phi \\ &+ \int \phi [\partial N_s(\phi) / \partial N_s] d\phi \end{aligned} \quad (3.5.50)$$

which is made up of relaxation terms only. At infinite dilution of s in w , we have

$$\lim_{\rho_s \rightarrow 0} (\partial / \partial N_s) \left[N_s \int \phi x_s(\phi) d\phi \right] \equiv \langle \phi_s^0 \rangle \quad (3.5.51)$$

Hence, for the solvation volume of s we have

$$\Delta V_s^* = \langle \phi_s^0 \rangle + \int \phi [\partial N_w(\phi) / \partial N_s] d\phi \quad (3.5.52)$$

Thus, the solvation volume of s at infinite dilution consists of the average volume of the VP of the solute plus the structural change in the solvent induced by the solute. The latter is the change in the distribution of the volumes of the VP of the solvent molecules.

3.6. Application of an Interstitial Model for Water to Aqueous Solutions

In this section, we extend the application of the interstitial model for water to aqueous solutions of simple solutes. This is the simplest model that contains elements in common with similar models worked out by various authors.³¹ This model can be solved exactly, and therefore, various general results of the mixture-model formalism can be obtained explicitly. In this respect, this model has also pedagogical value.

The description of the model and the basic assumptions have been introduced in Sec. 2.4. To apply this model for aqueous solutions, we further assume that N_s solute molecules occupy the interstitial positions in the framework built up by the L -cules (Fig. 3.16). The new molecular parameter that is introduced in the application of this model to aqueous solutions is the interaction energy between the solute s and its surroundings, which we denote by E_s .

³¹Frank and Quist (1961), Yashkichev and Samoilov (1962), Balsaesa and Samoilov (1963), Ben-Naim (1965a), Malenkov (1966), Mikhailov (1968), Mikhailov and Ponomareva (1968), Frank and Franks (1968), Ben-Naim (1994), Perkyns and Pettitt (1996), Pretti and Buzano (2005), and Buzano and Pretti (2003).

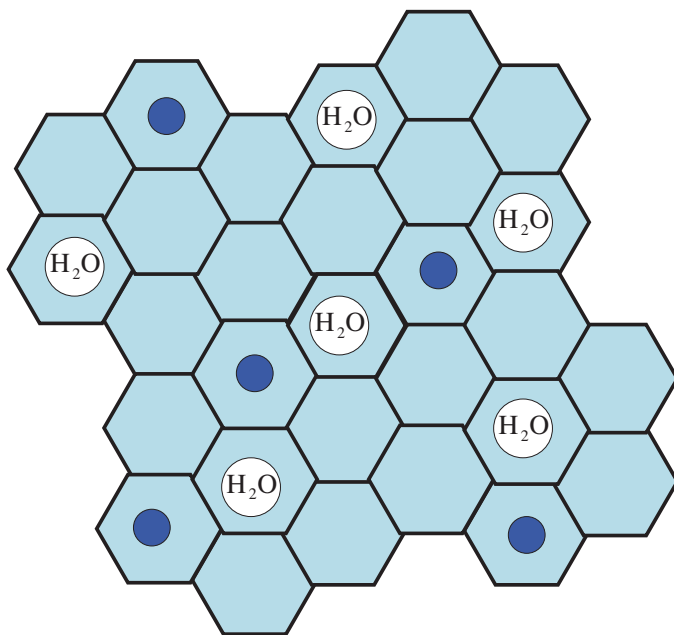


Fig. 3.16 The interstitial model for aqueous solutions.

The total energy of the system is

$$E_T = N_L E_L + N_H E_H + N_s E_s \quad (3.6.1)$$

and the corresponding isothermal-isobaric partition function is

$$\begin{aligned} \Delta(T, P, N_w, N_s) \\ = \sum_{N_L=N_{L\min}}^{N_w} \frac{(N_0 N_L)! \exp[-\beta(N_L E_L + N_H E_H + N_s E_s + P N_L V_L)]}{N_s! N_H! (N_0 N_L - N_H - N_s)!} \end{aligned} \quad (3.6.2)$$

The combinatorial factor in (3.6.2) is the number of ways one can place N_H H -cules and N_s solute molecules into $N_0 N_L$ holes. The summation is carried over all possible volumes of the system, which by virtue of the assumptions of the model is the same as a summation over all N_L . The condition $N_H \leq N_0 N_L$

for pure water is replaced by the condition

$$N_H + N_s \leq N_0 N_L \quad (3.6.3)$$

Hence, the minimum value of N_L is $N_{L_{\min}} = (N_w + N_s)/(N_0 + 1)$.

As in the case of the one-component system, we take the maximal term in the sum (3.6.2), from which we obtain the equilibrium condition:

$$\begin{aligned} \frac{N_H^* (N_0 N_L^*)^{N_0}}{(N_0 N_L^* - N_H^* - N_s^*)^{N_0+1}} &= \exp[\beta(E_L - E_H + P V_L)] \\ &= K(T, P) \end{aligned} \quad (3.6.4)$$

where N_H^* and N_L^* are the equilibrium values of N_L and N_H .

The “mole fractions” of empty holes, holes occupied by H -cules, and holes occupied by s are

$$\begin{aligned} y_0 &= \frac{N_0 N_L - N_H - N_s}{N_0 N_L}, \\ y_1 &= \frac{N_H}{N_0 N_L}, \quad y_s = \frac{N_s}{N_0 N_L} \end{aligned} \quad (3.6.5)$$

With these mole fractions, the equilibrium condition is

$$y_1^*/(y_0^*)^{N_0+1} = K(T, P) \quad (3.6.6)$$

which has the same form as in the one-component case (see Sec. 2.4.2).

Replacing the sum over N_L in (3.6.2) by its maximal term, we write

$$\begin{aligned} \Delta(T, P, N_w, N_s) &= \frac{(N_0 N_L^*) \exp[-\beta(N_L^* E_L + N_H^* E_H + N_s E_s + P N_L^* V_L)]}{N_s! N_H^*! (N_0 N_L^* - N_H^* - N_s)!} \\ &= \Delta(T, P, N_L^*, N_H^*, N_s) \end{aligned} \quad (3.6.7)$$

Note carefully the meaning of the two partition functions on the right-hand side and on the left-hand side of (3.6.7). The quantity $\Delta(T, P, N_w, N_s)$ is the *PF* of a system characterized by the variable T, P, N_w, N_s . There is no mention of any mixture-model approach. On the other hand, the quantity $\Delta(T, P, N_L^*, N_H^*, N_s)$ is the *PF* of a system of *three* components L, H , and s . Here, we explicitly characterize the system as *MM*. Of course, N_L^* and N_H^* are not independent. The equilibrium condition (3.6.4) can, in principle, be solved to obtain both N_L^* and N_H^* as a function of the original variable T, P, N_w, N_s .

The Gibbs free energy of the system with any arbitrary values of N_L, N_H , and N_s is

$$\begin{aligned} G(T, P, N_L, N_H, N_s) = & N_L E_L + N_H E_H + N_s E_s + P N_L V_L \\ & - k_B T [N_0 N_L \ln (N_0 N_L) - N_H \ln N_H \\ & - N_s \ln N_s - (N_0 N_L - N_H - N_s) \\ & \times \ln (N_0 N_L - N_H - N_s)] \end{aligned} \quad (3.6.8)$$

This function has a minimum at a point $N_L = N_L^*$ (and $N_H = N_H^*$) which satisfies the equilibrium condition (3.6.4). The mole fractions of L, H , and s in a dilute solution of s in w may be defined by

$$x_L = \frac{N_L}{N_w}, \quad x_H = \frac{N_H}{N_w}, \quad x_s = \frac{N_s}{N_w} \quad (3.6.9)$$

As we shall see below in this model, the addition of a solute will always lead to an increase in the mole fraction of the L component. This is, of course, unrealistic for high concentrations of the solutes. We shall therefore examine only the limit of very dilute solutions of s in w . In this particular model, the molecular reason for such a stabilization effect is quite obvious. Since we allow s to occupy only interstitial sites, the addition of s to the system causes a decrease in the available number of holes;

hence, interstitial water molecules are forced to transform from the H to the L component.

The total entropy of the system is obtained by differentiating (3.6.8) with respect to temperature:

$$S = -k_B N_0 N_L (y_0 \ln y_0 + y_1 \ln y_1 + y_s \ln y_s) \quad (3.6.10)$$

which, as in the one-component system, has a form similar to the so-called “entropy of mixing” of empty holes, holes with s , and holes with H -cules. Of course, there is no mixing here and the entropy in (3.6.10) is simply related to the total number of configurations in the system. A better interpretation of the quantity $S/(k_B N_0 N_L)$ is the missing information per hole.³²

The total volume, enthalpy, and energy of the system are readily obtainable from (3.6.8) as

$$\begin{aligned} V &= N_L V_L, \\ H &= N_L E_L + N_H E_H + N_s E_s + P N_L V_L, \\ E &= H - PV \end{aligned} \quad (3.6.11)$$

Note that in order to obtain the values of these quantities at equilibrium, one must substitute $N_L = N_L^*$ and $N_H = N_H^*$. The chemical potentials of the three components are

$$\begin{aligned} \mu_L &= (\partial G / \partial N_L)_{N_H, N_s} \\ &= E_L + P V_L - k_B T [N_0 \ln (N_0 N_L) \\ &\quad - N_0 \ln (N_0 N_L - N_H - N_s)] \end{aligned} \quad (3.6.12)$$

$$\begin{aligned} \mu_H &= (\partial G / \partial N_H)_{N_L, N_s} \\ &= E_H - k_B T [\ln (N_0 N_L - N_H - N_s) - \ln N_H] \end{aligned} \quad (3.6.13)$$

$$\begin{aligned} \mu_s &= (\partial G / \partial N_s)_{N_w} = (\partial G / \partial N_s)_{N_L, N_H} \\ &= E_s + k_B T [\ln N_s - \ln (N_0 N_L - N_H - N_s)] \end{aligned} \quad (3.6.14)$$

³²See Ben-Naim (2008a).

All the derivatives in (3.6.12)–(3.6.14) are at constant T, P .

Note that μ_L and μ_H are definable only for a “frozen-in” system (i.e. we must keep N_H and N_L constant in the respective definitions of μ_L and μ_H). On the other hand, the chemical potential of s is definable in both the equilibrated and the “frozen-in” systems. In general, μ_L and μ_H have different values; the equality between the two holds only when we use the equilibrium values: $N_L = N_L^*$ and $N_H = N_H^*$.

Exercise E.3.4: Choose some parameters E_L, E_H , etc., and examine the dependence of μ_L and μ_H on N_L (or $N_H = N_w - N_L$). What happens when we use the values of $N_L = N_L^*$ and $N_H = N_H^*$? Why?

From (3.6.12) and (3.6.13), we can compute the partial molar quantities of the two components. We first evaluate the corresponding quantities for L and H :

$$\begin{aligned}\bar{S}_L &= -(\partial\mu_L/\partial T)_{N_L, N_H} \\ &= k_B N_0 [\ln(N_0 N_L) - \ln(N_0 N_L - N_H - N_s)]\end{aligned}\quad (3.6.15)$$

$$\begin{aligned}\bar{S}_H &= -(\partial\mu_H/\partial T)_{N_L, N_H} \\ &= k_B [\ln(N_0 N_L - N_H - N_s) - \ln N_H]\end{aligned}\quad (3.6.16)$$

$$\bar{H}_L = E_L + PV_L, \quad \bar{H}_H = E_H \quad (3.6.17)$$

$$\bar{V}_L = V_L, \quad \bar{V}_H = 0 \quad (3.6.18)$$

$$\bar{E}_L = E_L, \quad \bar{E}_H = E_H \quad (3.6.19)$$

Note the difference between partial molar (or molecular) quantities on the left-hand side of (3.6.17)–(3.6.19) and the molecular parameters of the model on the right-hand side. Furthermore, we note that all the partial molar quantities of L and H are definable only in the “frozen-in” system.

Next, we turn to the corresponding quantities of the solute definable in either the “frozen-in” or the equilibrated system. Before doing this, we first evaluate the following derivative (see Appendix F):

$$\begin{aligned}
 \left(\frac{\partial N_L}{\partial N_s} \right)_{N_w} &= -(\mu_{LL} - 2\mu_{LH} + \mu_{HH})^{-1} \left[\frac{\partial(\mu_L - \mu_H)}{\partial N_s} \right]_{N_L, N_H} \\
 &= -\frac{x_L x_H (N_0 N_L - N_H - N_s)}{k_B T [N_0 + x_s (N_0 x_H - x_L)]} \frac{-k_B T (N_0 + 1)}{N_0 N_L - N_H - N_s} \\
 &= \frac{x_L x_H (N_0 + 1)}{N_0 + x_s (N_0 x_H - x_L)} \quad (3.6.20)
 \end{aligned}$$

where in the first step we used the thermodynamic identity (F.9) from Appendix F. All the derivatives on the right-hand side can now be evaluated in the “frozen-in” system by direct differentiation of (3.6.12) and (3.6.13). Although we have evaluated this quantity for a “frozen-in” system, at the end of our computation we must substitute $x_L = x_L^*$ and $x_H = x_H^*$, satisfying the equilibrium condition (3.6.4), which, in terms of the mole fractions, is written as

$$\frac{x_H^* (N_0 x_L^*)^{N_0}}{(N_0 x_L^* - x_H^* - x_s)^{N_0+1}} = K(T, P) \quad (3.6.21)$$

Once we have computed $\partial N_L / \partial N_s$, we can write down all the partial molar quantities of the solute (each quantity must be evaluated at the point $N_L = N_L^*$ and $N_H = N_H^*$):

$$\begin{aligned}
 \bar{S}_s &= S_s^f + (\bar{S}_L - \bar{S}_H) \left(\frac{\partial N_L}{\partial N_s} \right)_{N_w} \\
 &= -k_B [\ln N_s - \ln (N_0 N_L - N_H - N_s)] \\
 &\quad + \left(\frac{\partial N_L}{\partial N_s} \right)_{N_w} k_B \ln K \quad (3.6.22)
 \end{aligned}$$

$$\begin{aligned}\bar{H}_s &= H_s^f + (\bar{H}_L - \bar{H}_H) \left(\frac{\partial N_L}{\partial N_s} \right)_{N_w} \\ &= E_s + (E_L - E_H + PV_L) \left(\frac{\partial N_L}{\partial N_s} \right)_{N_w}\end{aligned}\quad (3.6.23)$$

$$\begin{aligned}\bar{V}_s &= V_s^f + (\bar{V}_L - \bar{V}_H) \left(\frac{\partial N_L}{\partial N_s} \right)_{N_w} \\ &= V_L \left(\frac{\partial N_L}{\partial N_s} \right)_{N_w}\end{aligned}\quad (3.6.24)$$

In this particular model, the partial molar volume V_s^f is zero (i.e. inserting a solute in the holes does not contribute to the total volume of the system); hence, all of $\bar{V}_s$ is made up of structural changes in the solvent. Note also that the exact entropy-enthalpy compensation law is fulfilled in this model.

Exercise E.3.5: Calculate the average volume in the system and the partial molar volume of s and w as a function of the mole fraction x_s (within the limits of variation of x_s).

As an illustrative example, consider the case in which $N_0 = 1$ and we take the limit $x_s \rightarrow 0$. The corresponding value of $\bar{H}_s$ in this limit is

$$\bar{H}_s = E_s + (E_L - E_H + PV_L) 2x_L^* x_H^* \quad (3.6.25)$$

For this particular case, we can solve the equilibrium condition (3.6.21) and express x_L and x_H (at equilibrium) in terms of the equilibrium constant K , which, in turn, may be expressed in terms of the molecular parameters of the model [Eq. (3.6.4)]. The result is

$$x_L^* = \frac{1}{2} + \frac{1}{2} \left(\frac{1}{4K + 1} \right)^{1/2} \quad (3.6.26)$$

Hence,

$$x_L^* x_H^* = \left(\frac{K}{4K + 1} \right) \quad (3.6.27)$$

and (3.6.24) is rewritten as

$$\bar{H}_s = E_s + (k_B T \ln K) [2K / (4K + 1)] \quad (3.6.28)$$

The important point to be noted in (3.6.28) is the fact that the relaxation term is independent of any property of the *solute*. Therefore, in principle, the two terms in (3.6.28) may be of a different order of magnitude.

Figure 3.17a shows the variation of the mole fractions x_L and x_H as a function of K . Note that K is always positive. When $E_L - E_H \ll 0$, K is very small and the mole fraction of L is almost unity. For a fixed $E_L - E_H < 0$, when we increase the pressure or the temperature, K becomes very large; in this case, x_L tends to 0.5. Figure 3.17b shows the quantity $[2K / (1 + 4K)] \ln K$ as a function of K . For small values of K ($0 \leq K \leq 1$), this function has a minimum at about $K = 0.18$. For $K > 1$, the

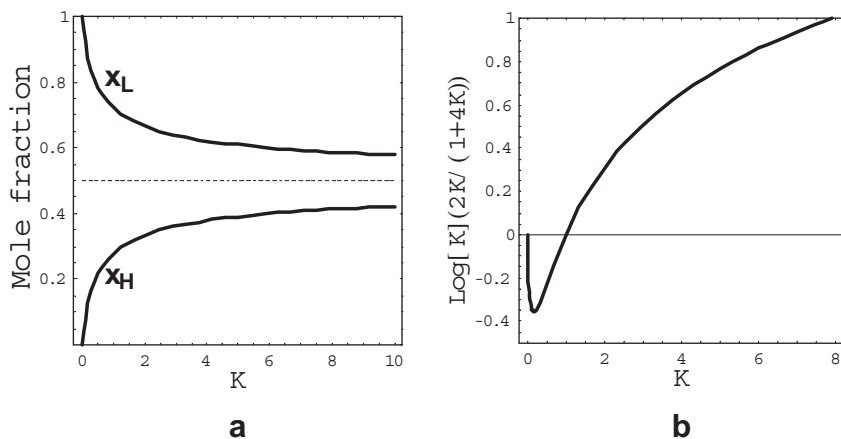


Fig. 3.17 (a) Dependence of x_L and x_H on the equilibrium constant K . (b) The quantity $[2K / (4K + 1)] \ln K$ as a function of K .

function becomes positive. Thus, if we choose molecular parameters (E_L , E_H , and V_L) such that the equilibrium constant is about $K = 0.2$, we shall get the largest negative contribution due to the second term on the right-hand side of (3.6.28).

Exercise E.3.6: Define the solvation process as the process of transferring a simple solute from a fixed position in an ideal gas phase to a specific hole in the interstitial model. Calculate ΔG_s^* , ΔS_s^* , and ΔH_s^* for this process. Examine the effect of changing the molecular parameters on these quantities and on the entropy-enthalpy compensation.

Exercise E.3.7: Choose some numerical values of the molecular parameter and calculate the heat capacity of the system as a function of the mole fraction x_s . Follow also the mole fraction of the structured component L , x_L as a function of x_s . Is there any relationship between the variation of x_L and the value of the heat capacity of the system?

Exercise E.3.8: Examine the isothermal compressibility of the system as a function of T and as a function of x_s for some values of the molecular parameters of the model.

Exercise E.3.9: Examine the following argument frequently made in the literature. The large positive value of ΔG_s^* of, say, argon in water is due to the large degree of structure. As temperature increases, the structure of water breaks down. Hence, we should expect that the value of ΔG_s^* will decrease upon the increase in temperature. Use the ideal mixture model to see why this conclusion is erroneous.

3.7. The Problem of Stabilization of the Structure of Water

This section goes to the heart of the problem of aqueous solutions of inert solutes. Why should a simple solute such as argon, or even a hard sphere, “stabilize” the structure of water? I use the word “stabilize” in the sense of “increasing” or “enhancing” the *structure* of water in whatever sense we choose to define it.

In this section, we shall discuss the theoretical aspects of this problem. Starting with the concept of structural temperature which bypasses the need to define the structure, we formulate the problem within the exact framework of the *MM* approach. This approach naturally leads to the application of the Kirkwood–Buff theory, which provides only the *sign* of the structural changes. Finally, we present a simple measure of the *amount* of structural change in the solvent induced by a simple solute.

3.7.1. The concept of structural temperature

Bernal and Fowler (1933) introduced the idea of “structural temperature,” which is defined as follows. Suppose one measures some physical property ϕ for pure water and for an aqueous solution, both at the same temperature T and pressure P . In this section, P will be fixed and therefore omitted from the notation. We denote the change in the property ϕ due to the addition of N_s solute molecules by

$$\Delta\phi = \phi(T, N_s) - \phi(T, N_s = 0) \quad (3.7.1)$$

where $\phi(T, N_s)$ is the value of the property ϕ at given T, N_s .

Next, consider the change in the same property ϕ for *pure* water caused by a change in temperature:

$$\Delta\phi' = \phi(T', N_s = 0) - \phi(T, N_s = 0) \quad (3.7.2)$$

The “structural temperature” of the solution, with N_s moles of s at temperature T , is defined as the temperature T' for which we have the equality

$$\Delta\phi = \Delta\phi' \quad (3.7.3)$$

Note that the concept of the “structural temperature,” though using the concept of “structure,” does not define the concept of the “structure of water.” The idea underlying this definition is qualitatively clear. It is intuitively clear that, however we choose to define the “structure of water,” this quantity must be a monotonically decreasing function of the temperature. Therefore, the changes in the structure can be detected on a corresponding temperature scale.³³

The concept of “structural temperature,” though a useful operational definition of the “structure of water,” is not entirely satisfactory since it is generally dependent on the property ϕ . Using different properties for the same solution, we can get different structural temperatures. Nevertheless, in the old literature, it was common to classify different solutes in terms of their structural temperature, which in turn classifies solutes according to whether they are “structure makers” or “structure breakers.”

3.7.2. *Formulation of the problem within the mixture-model approach*

As we have seen in Sec. 3.5, the interpretation of the large entropy and enthalpy of solvation of a simple solute in water crucially depends on the relaxation part of the solvation quantities

³³This assertion is both intuitively clear and factually true in most cases. However, it is not always true.

[see Eqs. (3.5.10) and (3.5.11)]. The relaxation term in both (3.5.10) and (3.5.11) consists of two factors: $(\bar{H}_L - \bar{H}_H)$ and $(\partial N_L / \partial N_s)$. The first factor can be made negative by definition. Simply choose the more ice-like, or the more hydrogen-bonded, component as the L molecule, or the component with lower BE . This will make $(\bar{H}_L - \bar{H}_H)$ negative. Once we have made this choice, then also $(\bar{S}_L - \bar{S}_H)$ will be negative by virtue of the equilibrium condition (3.5.3). As we have noted several times in this book, $(\bar{S}_L - \bar{S}_H)$ is made negative not because L is more structured but because L has a lower partial molar enthalpy, or equivalently, has stronger BE relative to H .

The classification of water molecules into two classes according to their binding energies can be rendered exact. The problem is to show that with such a classification of the two components the factor $(\partial N_L / \partial N_s)_{N_w}$ is positive. Recall that Frank and Evans (1945) postulated the building up of icebergs around the inert solute. Whatever the structure of the iceberg is, one needs to show why an inert solute will build such a structure.

In our reformulation of the problem in terms of $(\partial N_L / \partial N_s)_{N_w}$, we *assume* that a structured form called L exists in pure water, and we want to show that the concentration of this *existing* structure increases upon the addition of small amounts of a solute. As we shall see below, the theoretical argument of favoring a large positive value of $(\partial N_L / \partial N_s)_{N_w}$ depends not merely on the pre-existence of the component L but also on its existence in non-negligible concentrations. This clearly could not have been guaranteed for the iceberg structures. It will also be clear that structure *per se* is not the important aspect of the L component. What is important is the relative binding energies of the two components L and H .

We shall first transform the problem of calculating $(\partial N_L / \partial N_s)_{N_w}$ into an equivalent problem which can be treated within the Kirkwood–Buff theory of solutions. Let L and H

be two quasi-components obtained by any classification procedure. The corresponding average numbers of L - and H -cules are N_L and N_H , respectively. We assume that the temperature and the pressure are always constant. The quantity of interest is the derivative $(\partial N_L / \partial N_s)_{T,P,N_w}$. We say that the component L is “stabilized” by the solute s whenever this derivative is positive, i.e. N_L increases upon the addition of the solute.

We now explore the general and exact conditions under which a stabilization of L by s occurs. We can then specialize to a particular choice of the component L and speculate about the possibility of stabilization of the “structure of water” by the solute s .

A convenient starting relation is the thermodynamic identity (see Appendix F):

$$(\partial N_L / \partial N_s)_{N_w} = -(\mu_{LL} - 2\mu_{LH} + \mu_{HH})^{-1}(\mu_{Ls} - \mu_{Hs}) \quad (3.7.4)$$

where $\mu_{ij} = \partial^2 G / \partial N_i \partial N_j$. The advantage of using relation (3.7.4) is that it transforms from a derivative in the equilibrated system [the left-hand side of (3.7.4)] into derivatives in the “frozen-in” system. The latter derivatives are expressible in terms of molecular distribution functions through the Kirkwood–Buff theory of solutions.³⁴

Before using the Kirkwood–Buff theory, we present the qualitative physical idea underlying the application of (3.7.4). Suppose we start with an equilibrated system for which we have the condition

$$\mu_L(N_L, N_H, N_s) = \mu_H(N_L, N_H, N_s) \quad (3.7.5)$$

³⁴In this section, we shall use some results from the Kirkwood–Buff theory of solutions. For details, see Ben-Naim (2006).

As an auxiliary device, we envisage a catalyst which, when absent from the system, causes the reaction $L \rightleftharpoons H$ to become “frozen-in.” Now, at some given equilibrium state, we remove the catalyst and add dN_s moles of the solute s . Generally, at this stage we shall have the inequality

$$\mu_L(N_L, N_H, N_s + dN_s) \neq \mu_H(N_L, N_H, N_s + dN_s) \quad (3.7.6)$$

For concreteness, suppose that at this stage we have the inequality $\mu_L < \mu_H$. Then, if we re-introduce our catalyst, water molecules will “flow” from the state of the high to the state of the low chemical potential. This means that adding dN_s increases the number of L -cules. Figure 3.18 shows schematically the two stages of the process of adding one solute s to water. We start with an equilibrated system with composition N_L and N_H . In the first step a solute is added to the “frozen-in” water, i.e. N_L and N_H are unaltered. Next, we allow the system to relax to the new equilibrium condition, which is now characterized by the composition N'_L, N'_H . In the next subsection, we turn to the mathematical expression for the derivatives on the left-hand side of (3.7.4) in terms of the Kirkwood–Buff integrals.

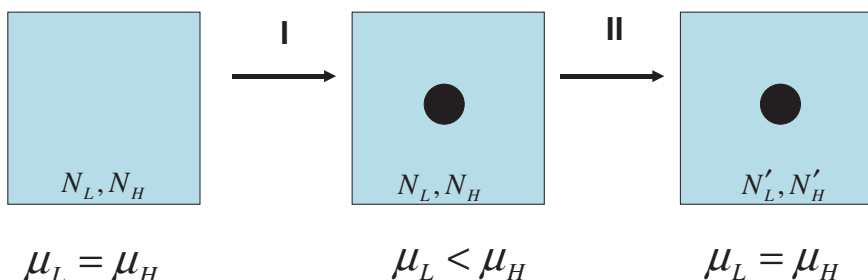


Fig. 3.18 The process of adding a solute to water in two steps. First, we add the solute to a “frozen-in” system; then, the system is relaxed to reach the final equilibrium state in the presence of s .

3.7.3. The application of the Kirkwood–Buff theory

All the derivatives of the chemical potential on the right-hand side of (3.7.4) are the derivatives in the “frozen-in” system, i.e. a system of three independent components L , H , and s .

The Kirkwood–Buff theory provides the following general relation between $\mu_{\alpha\beta}$ and integrals over the molecular distribution functions. The basic relation that we need is

$$\mu_{\alpha\beta} = \frac{k_B T}{V} \frac{B^{\alpha\beta}}{|\mathbf{B}|} - \frac{\bar{V}_\alpha \bar{V}_\beta}{V x_T} \quad (3.7.7)$$

where the determinant $|\mathbf{B}|$ for the three-component system is

$$|\mathbf{B}| = \begin{vmatrix} \rho_s + \rho_s^2 G_{ss} & \rho_s \rho_L G_{sL} & \rho_s \rho_H G_{sH} \\ \rho_L \rho_s G_{Ls} & \rho_L + \rho_L^2 G_{LL} & \rho_L \rho_H G_{LH} \\ \rho_H \rho_s G_{Hs} & \rho_H \rho_L G_{HL} & \rho_H + \rho_H^2 G_{HH} \end{vmatrix} \quad (3.7.8)$$

from which we derive the various co-factors $B^{\alpha\beta}$.

In this section, we only need the limiting case of $\rho_s \rightarrow 0$. In this limit, the partial molar volumes $\bar{V}_L$ and $\bar{V}_H$ and the compressibility of the system tend to their values in pure water, with composition N_L and N_H , i.e.

$$\bar{V}_L = [1 + \rho_H(G_{HH} - G_{LH})]/\eta \quad (3.7.9)$$

$$\bar{V}_H = [1 + \rho_L(G_{LL} - G_{LH})]/\eta \quad (3.7.10)$$

$$\kappa_T^f = \zeta/k_B T \eta \quad (3.7.11)$$

where ζ and η are defined by

$$\eta = \rho_L + \rho_H + \rho_L \rho_H (G_{LL} + G_{HH} - 2G_{LH}) \quad (3.7.12)$$

$$\begin{aligned} \zeta = & 1 + \rho_L G_{LL} + \rho_H G_{HH} \\ & + \rho_L \rho_H (G_{LL} G_{HH} - G_{LH}^2) \end{aligned} \quad (3.7.13)$$

Note that κ_T^f in (3.7.11) is the isothermal compressibility of the mixture of L and H , in the “frozen-in” system, where N_L and N_H are assumed to behave as independent variables. Note also that $\bar{V}_L$ and $\bar{V}_H$ are definable only in the “frozen-in” system, and therefore there is no need to add a superscript to these symbols.

The quantities $G_{\alpha\beta}$ that feature in Eqs (3.7.8)–(3.7.13) are referred to as the Kirkwood–Buff integrals (KBI). We have encountered these integrals in Sec. 1.5 for pure liquid water. The significance of these integrals in mixtures is discussed in great detail in Ben-Naim (2006). Here, we briefly note the following meaning of these integrals.

It is known from both experiments and theoretical work that the range of the pair correlation functions $g_{\alpha\beta}(R)$ is only a few molecular diameters. This means that there exists a correlation radius R_{CORR} , such that for $R \geq R_{CORR}$, $g_{\alpha\beta}(R)$ is nearly unity. Alternatively, there is no correlation at distances beyond the correlation radius.

Let us choose a specific molecule of type α and draw a sphere of radius R_{CORR} around the center of this molecule. The average number of β molecules in this sphere is³⁵

$$\rho_\beta \int_0^{R_{CORR}} g_{\alpha\beta}(R) 4\pi R^2 dR \quad (3.7.14)$$

Clearly, the average number of β molecules in a volume $\frac{4\pi R_{CORR}^3}{3}$ taken in an arbitrary place in the mixture is simply

$$\rho_\beta \frac{4\pi R_{CORR}^3}{3} = \rho_\beta \int_0^{R_{CORR}} 4\pi R^2 dR \quad (3.7.15)$$

Taking the difference between (3.7.14) and (3.7.15) we get

$$\rho_\beta \int_0^{R_{CORR}} [g_{\alpha\beta}(R) - 1] 4\pi R^2 dR \quad (3.7.16)$$

³⁵Note that in this section β is not $(k_B T)^{-1}$.

Since $g_{\alpha\beta}(R)$ is practically unity for $R \geq R_{CORR}$, we can extend the upper limit of the integral³⁶ (3.7.16) to obtain the *KBI*, i.e.

$$\begin{aligned} G_{\alpha\beta} &\equiv \int_V [g_{\alpha\beta}(R) - 1] d\mathbf{R} \\ &= \int_0^\infty [g_{\alpha\beta}(R) - 1] 4\pi R^2 dR \end{aligned} \quad (3.7.17)$$

The first integral on the right-hand side of (3.7.17) is the original definition of the *KBI*. Thus, the meaning of $\rho_\beta G_{\alpha\beta}$ is simply the change in the average number of β molecules in the sphere of radius R_{CORR} caused by placing an α molecule at the center of this sphere. Since for $R > R_{CORR}$, $g(R)$ is nearly unity, one can extend the upper limit of the integral to infinity. Note, however, that the lower limit of the integral is simply a result of the integration over the entire volume of the system. It has nothing to do with the radius of either α or β molecules.³⁷

Next, we derive the limiting value of the partial molar volume of the solute s in the frozen-in mixture. The general expression for the partial molar volume of the species α in a mixture of c -components is

$$\bar{V}_\alpha = \left(\sum_{\beta=1}^c \rho_\beta B^{\alpha\beta} \right) / \left(\sum_{\alpha=1}^c \sum_{\beta=1}^c \rho_\alpha \rho_\beta B^{\alpha\beta} \right) \quad (3.7.18)$$

³⁶There is a subtle point here that should be carefully noted. The *KBI* are defined in an open system. In a closed system the pair correlation function is not unity even at $R \geq R_{CORR}$, and the upper limit of the integral (3.7.16) cannot be extended to infinity. See Ben-Naim (2006).

³⁷This comment sounds trivial. Unfortunately, this “interpretation” of the lower limit of the integral appears in the literature. See Ben-Naim (2008b) and Shulgin and Ruckenstein (2008).

For the three-component system of L , H , and s , (3.7.18) reduces to³⁸

$$V_s^f = \frac{\rho_s B^{ss} + \rho_L B^{Ls} + \rho_H B^{Hs}}{\rho_s^2 B^{ss} + \rho_L^2 B^{LL} + \rho_H^2 B^{HH} + 2\rho_s \rho_L B^{Ls} + 2\rho_s \rho_H B^{Hs} + 2\rho_L \rho_H B^{LH}} \quad (3.7.19)$$

Taking the appropriate co-factors from (3.7.8) and retaining only linear terms in ρ_s , we get the final result³⁹

$$\begin{aligned} \lim_{\rho_s \rightarrow 0} V_s^f &= [\zeta - \rho_L G_{Ls}(1 + \rho_H G_{HH} - \rho_H G_{LH}) \\ &\quad - \rho_H G_{Hs}(1 + \rho_L G_{LL} - \rho_L G_{HL})]/\eta \\ &= k_B T \kappa_T^f - \rho_L G_{Ls} \bar{V}_L - \rho_H G_{Hs} \bar{V}_H \end{aligned} \quad (3.7.20)$$

This is the limiting value of the partial molar volume of a solute s in any three-component system L , H , and s expressed in terms of the KBI .

Next, we express the derivatives of the chemical potential in terms of $G_{\alpha\beta}$. From (3.7.7), we have

$$\mu_{Ls} - \mu_{Hs} = \frac{k_B T}{V} \left[\frac{B^{Ls} - B^{Hs}}{|\mathbf{B}|} - \frac{V_s^f (\bar{V}_L - \bar{V}_H)}{k_B T \kappa_T^f} \right] \quad (3.7.21)$$

Using the notation

$$\Delta_{LH}^s = G_{Ls} - G_{Hs} \quad (3.7.22)$$

and the identity

$$\bar{V}_L \bar{V}_H = (\zeta - \eta G_{LH})/\eta^2 \quad (3.7.23)$$

³⁸Note that $\bar{V}_\alpha$ in (3.7.18) is the partial molar volume of α in any mixture. V_s^f in (3.7.19) is the partial molar volume of the solutes in the “frozen-in” mixture of L and H .

³⁹For more details, see Ben-Naim (1992).

we get the limiting form of (3.7.21), i.e.

$$\begin{aligned} \lim_{\rho_s \rightarrow 0} (\mu_{Ls} - \mu_{Hs}) \\ = -(k_B T/V)(\bar{V}_L - \bar{V}_H + \rho_w \Delta_{LH}^s/\eta) \end{aligned} \quad (3.7.24)$$

where $\rho_w = \rho_L + \rho_H$. Note that the limiting behavior of the determinant $|\mathbf{B}|$ is

$$|\mathbf{B}| \xrightarrow{\rho_s \rightarrow 0} \rho_s \rho_L \rho_H \zeta \quad (3.7.25)$$

Using relations (3.7.24) and (3.7.4), we get

$$\begin{aligned} \lim_{\rho_s \rightarrow 0} (\partial N_L / \partial N_s)_{N_w} \\ = x_L x_H [\eta(\bar{V}_L - \bar{V}_H) + \rho_w \Delta_{LH}^s] \end{aligned} \quad (3.7.26)$$

Applying relations (3.7.9) and (3.7.10) and an identity from Appendix F,⁴⁰ we can rewrite (3.7.26) as

$$\begin{aligned} \lim_{\rho_s \rightarrow 0} (\partial N_L / \partial N_s)_{N_w} \\ = \rho_w x_L x_H [(G_{wH} - G_{wL}) + (G_{Ls} - G_{Hs})] \end{aligned} \quad (3.7.27)$$

Relation (3.7.27) is very general. First, it applies to any two-component system at chemical equilibrium,⁴¹ as well as to any classification procedure we have chosen for the two quasi-components. Second, because of the application of the Kirkwood–Buff theory of solutions, we do not have to restrict ourselves to any assumption of additivity on the total potential energy of the system. Furthermore, the quantities $G_{\alpha\beta}$ appearing

⁴⁰Note that G_{wH} is the KBI connecting *any* water molecule w and an H -molecule. A similar meaning applies to G_{wL} . See Appendix F for details.

⁴¹Here, we refer to a system of two real components in chemical equilibrium, such as two isomeric forms of a molecule. Relation (3.7.27) was derived for a system of two quasi-components, but the derivative on the left-hand side refers to a system at equilibrium.

here depend only on the *spatial* pair correlation functions $g_{\alpha\beta}(R)$, even though we may be dealing with non-spherical particles.

Let us consider some general implications of (3.7.27) with regard to the conditions for the stabilization of L by s . Suppose we start with a distribution $x_{BE}(\nu)$ as in Fig. 3.15 and construct two components x_L and x_H .

- (i) If either x_L or x_H is very small, then the whole right-hand side of (3.7.27) is small and we cannot get a large stabilization effect (this occurs if we choose a cut-off ν_1 in Fig. 3.15b). If we choose, for instance, L to be strictly ice molecules, then it is likely that x_L will be small; hence, a small stabilization effect will be expected. This conclusion is important regarding the conjecture of iceberg formation discussed in Sec. 3.1. Recall also that this condition had featured in the interpretation of the anomalous properties of pure water as discussed in Chapter 2.
- (ii) If we choose two components L and H which are *similar* in the sense that

$$G_{Ls} \approx G_{Hs} \quad \text{and} \quad G_{wH} \approx G_{wL} \quad (3.7.28)$$

then we again end up with a small stabilization effect. A possible cut-off for this case is ν_2 as in Fig. 3.15b. In order to get a large relaxation term in Eqs. (3.5.10) and (3.5.11), we must choose two components that are very different.

As we have seen in Chapter 2, a large difference in the two components was also a requirement in the interpretation of the outstanding properties of pure water. Here, we should also bear in mind the relevance of this requirement to the assumption of ideality, often made in applying the MM to aqueous solutions. If the system is presumed to be a symmetrical ideal solution, then, in general, the species cannot be too different. On the other hand, if the assumption

is made that the mixture L and H is dilute-ideal, then either x_L and x_H must be small, and hence, no large relaxation effect could be obtained.

- (iii) Suppose that $x_L x_H$ is not too small and that L and H differ appreciably. The right-hand side of (3.7.27) will tend to zero as $\rho_w \rightarrow 0$. Note that all the $G_{\alpha\beta}$ tend to a constant value in the limit of zero total density.

All the considerations made thus far apply to any fluid. We have seen that a large stabilization effect is attainable only under very restricted conditions. Water, as one of its unique features, may conform to all the necessary conditions leading to a relatively large stabilization effect.

Before applying what we have learned so far for the interpretation of the solvation entropy and enthalpy, we note that on the right-hand side of (3.7.27) there are two terms in the squared brackets. One, $G_{wH} - G_{wL}$, depends only on the solvent and on the choice we have made regarding the two components. The second, $G_{Ls} - G_{Hs}$, depends on the relative affinity of the solute s to the two components.

Let us now make a specific choice of two components for water, which seems to be the most useful one for interpreting the thermodynamic behavior of aqueous solutions. We use the singlet distribution function $x_{CN}(K)$ based on coordination number (CN), and define the two mole fractions by

$$x_L = \sum_{K=0}^4 x_{CN}(K), \quad x_H = \sum_{K=5}^{\infty} x_{CN}(K) \quad (3.7.29)$$

Clearly, we may refer to L and H as the components of relatively low (L) and high (H) local densities. Another useful choice could be based on the singlet distribution function for molecules with a different number of hydrogen bonds. With

this particular choice, we have

$$\bar{V}_L - \bar{V}_H > 0 \text{ or equivalently } G_{wH} - G_{wL} > 0 \quad (3.7.30)$$

We recall that $\rho_w(G_{wH} - G_{wL})$ measures the excess of *water* molecules around *H* as compared to the excess of water molecules around *L*. This means that if we can define two components which are very different and for which $x_L x_H$ is close to its maximum value, then we have already guaranteed one positive term for the stabilization effect (3.7.27) which is independent of the solute. In fact, one may think of an ideal solute which does not interact with the solvent at all. In such a case, we get $G_{Ls} - G_{Hs} = 0$, and the whole stabilization effect becomes a property of the solvent *only*. It will be positive for any classification for which (3.7.30) is fulfilled.

The next question concerns the sign of $G_{Ls} - G_{Hs}$ for simple solutes. From the definition of the *KBI*, we have

$$\begin{aligned} \rho_s \Delta_{LH}^s &= \rho_s \int_0^\infty [g_{Ls}(R) - 1] 4\pi R^2 dR \\ &\quad - \rho_s \int_0^\infty [g_{Hs}(R) - 1] 4\pi R^2 dR \\ &= \rho_s \int_0^\infty [g_{Ls}(R) - g_{Hs}(R)] 4\pi R^2 dR \end{aligned} \quad (3.7.31)$$

Clearly, $\rho_s \Delta_{LH}^s$ measures the overall average excess of *s* molecules in the neighborhood of *L* relative to *H*. From the definition of the two components as in (3.7.29), we expect that an *L* molecule characterized by a low local density will allow more solute molecules to enter its surroundings.⁴² This is schematically shown in Fig. 3.19. Therefore, Δ_{LH}^s is likely to be positive.

⁴²Note that in defining the components *L* and *H* we count only water molecules in the neighborhood of the quasi-components.

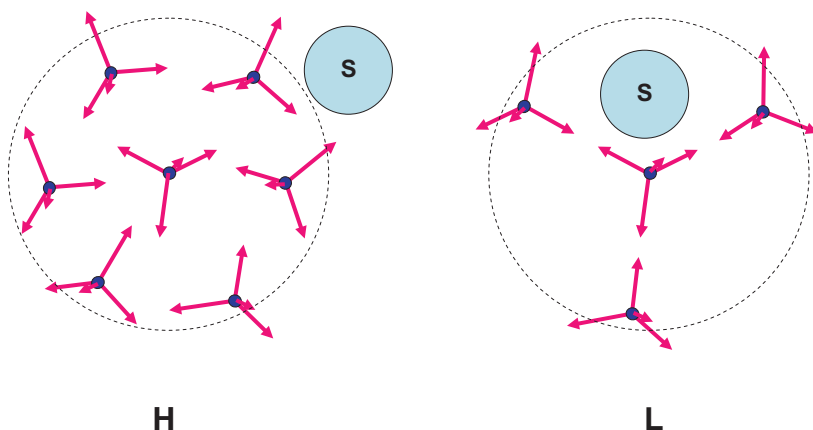


Fig. 3.19 The surroundings of H and L molecules. The L has more room in its immediate surroundings to accommodate a solute s .

Thus far, we have shown that if we choose two components in such a way that one has a relatively low local density (L), then it is likely that this component will be stabilized by the addition of the solute s . This argument applies for any fluid. It is expected, though, to be particularly large for water, which has this outstanding mode of packing of water molecules. More important, however, is the peculiar and unique correlation between low local density and strong binding energy. The latter is essential in an interpretation of the large negative enthalpy and entropy of solution discussed in Sec. 3.5. Consider, for example, the relaxation term of $\bar{H}_s$ in (3.5.10) [because of the compensation relation (3.5.14), the same argument applies to the relaxation part of $\bar{S}_s$]:

$$\Delta H_s^r = (\bar{H}_L - \bar{H}_H)(\partial N_L / \partial N_s)_{N_w} \quad (3.7.32)$$

Thus, by definition of the two components, we have secured a positive value of $(\partial N_L / \partial N_s)$. Using the *principle*, we can claim that the difference $\bar{H}_L - \bar{H}_H$ must be negative, i.e. the component

with low local density is also the one with relatively large binding energy, and hence lower partial molar energy or entropy.

Although we have not explicitly introduced either the concept of hydrogen bonds or of the structure of water in the present discussion, it is clear that the L component may be identified with, say, fully hydrogen-bonded molecules or the more structured component. In such a case, the addition of solute s is likely to enhance the formation of hydrogen bonds in the system. Other solvents, such as ammonia or hydrogen fluoride also have strong hydrogen bonds. However, a fully hydrogen-bonded molecule is not expected to exist in a low local density; hence, a stabilization of hydrogen-bonded molecules by simple solutes is unlikely to occur in these fluids.

Finally, we reiterate that the explanation of the origin of the large negative enthalpy of solvation was based on the local density and the binding energy of the quasi-components L and H . The stabilization of the L component occurs because of its low local density. This shift towards more of the L component carries with it a *decrease* in energy or enthalpy ($\bar{H}_L - \bar{H}_H < 0$). Because of the compensation effect, the same explanation applies to the entropy of solvation; one does not need to invoke the concept of “structure” to explain the negative entropy of solvation.

3.7.4. *An exact argument for a hard-point solute*

In Appendix G we derive the solvation Gibbs energy of a point hard sphere. This is the same as the work required to create a cavity of radius $r \leq \sigma/2$ in a liquid consisting of hard spheres with diameter σ and density ρ . A cavity of radius $\sigma/2$ can be formed by a hard solute of diameter zero (Fig. 3.20). We shall refer to such a particle as a hard point. The solvation Gibbs

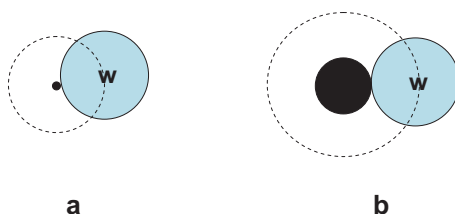


Fig. 3.20 (a) A hard sphere of zero diameter creates a cavity of a radius $\sigma/2$, where σ is the hard-core diameter of the solvent molecules (w). (b) A cavity formed by a hard sphere of diameter σ_s has a radius of $(\sigma_w + \sigma_s)/2$.

energy of such a hard point is thus

$$\Delta G_{\bullet}^* = -k_B T \ln (1 - \rho V_{\bullet}^{EX}) \quad (3.7.33)$$

where $V_{\bullet}^{EX}$ is the excluded volume of the hard point (the dashed circle in Fig. 3.20a). Since $\rho V_{\bullet}^{EX}$ is the probability of finding $V_{\bullet}^{EX}$ occupied, $1 - \rho V_{\bullet}^{EX}$ is the probability of finding $V_{\bullet}^{EX}$ empty, it follows that $\Delta G_{\bullet}^*$ is always positive. Clearly, this result can be applied to any liquid. The volume $V_{\bullet}^{EX}$ is roughly the volume of the region impenetrable by the hard sphere. It will be proportional to the actual volume of the solvent molecules. Note that the work required to create a cavity of size zero at some fixed position is always zero; here, a hard point always creates a cavity of finite size provided that the solvent molecules can be assigned a finite hard-core diameter.

Relationship (3.7.33) suggests that we use the hard-point particle as our test solute to compare the solvation thermodynamics of this solute in different solvents. We immediately see from (3.7.33) that our test solute will be more soluble in a liquid for which the quantity $\rho V_{\bullet}^{EX}$ is smaller. In other words, decreasing either the density or the size of the solvent particles causes a decrease in $\Delta G_{\bullet}^*$ or an increase in solubility. Here, we refer to solubility from an ideal gas phase. For real solutes, the attractive

part of the solute-solvent interaction contributes significantly to ΔG_s^* . We shall discuss this further in Secs. 3.8 and 3.9.

The corresponding solvation entropy and enthalpy of the hard point are

$$\begin{aligned}\Delta S_\bullet^* &= - \left(\frac{\partial \Delta G_\bullet^*}{\partial T} \right)_P \\ &= k_B \ln(1 - \rho V_\bullet^{EX}) - \frac{k_B T V_\bullet^{EX}}{1 - \rho V_\bullet^{EX}} \left(\frac{\partial \rho}{\partial T} \right)_P\end{aligned}\quad (3.7.34)$$

$$\Delta H_\bullet^* = \Delta G_\bullet^* + T \Delta S_\bullet^* = \frac{-k_B T^2 V_\bullet^{EX}}{1 - \rho V_\bullet^{EX}} \left(\frac{\partial \rho}{\partial T} \right)_P \quad (3.7.35)$$

Note that since the hard point has no “soft” interaction, the average binding energy $\langle B_s \rangle_s$ is zero (as for any hard particle of any size). Therefore, all of $\Delta H_\bullet^*$ must be due to “structural changes” induced in the solvent. This can be interpreted in terms of a relaxation term using any method for classifying the solvent molecules into quasi-components. The following important conclusion can be derived from (3.7.34) and (3.7.35): for normal liquids, the density always decreases with temperature, i.e. $\partial \rho / \partial T < 0$, and hence $\Delta H_\bullet^*$ is positive. In water, we know that there exists a region between 0 and 4°C for which $\partial \rho / \partial T > 0$. Therefore, $\Delta H_\bullet^*$ is negative. Since this must be due to structural changes in water, we conclude that the unique temperature dependence of the density is intimately related to the negative relaxation part of the $\Delta H_\bullet^*$. Because of the exact compensation effect, the same conclusion applies to the relaxation part of $\Delta S_\bullet^*$.

This exact relation has been derived here for a hypothetical hard-point particle. For a real solute, essentially the same conclusion was also inferred from the discussion based on the Kirkwood–Buff theory. Note also that the relaxation term in

$\Delta H_{\bullet}^*$ appears also in $T\Delta S_{\bullet}^*$. Therefore, in the formation of the combination $\Delta H_{\bullet}^* - T\Delta S_{\bullet}^*$, this part cancels out.

3.7.5. *An approximate measure of the structural change induced by the solute*

We present here an approximate measure similar to that used in Sec. 2.7 to estimate the amount of structural change induced by the solute. This estimate is based on the assumption that light and heavy water have nearly the same pair potential, differing only in the HB parameter ε_{HB} , which we denote by ε_D and ε_H for D_2O and H_2O , respectively.

We start with the expression for the solvation Gibbs energy of a solute s :

$$\Delta G_s^* = -k_B T \ln \langle \exp(-\beta B_s) \rangle_0 \quad (3.7.36)$$

Differentiating with respect to the parameter ε_{HB} , we obtain⁴³

$$\left(\frac{\partial \Delta G_s^*}{\partial \varepsilon_{HB}} \right)_{T,P,N} = \langle N_{HB} \rangle_s - \langle N_{HB} \rangle_0 \quad (3.7.37)$$

where on the right-hand side of (3.7.37) we have the change in the average number of hydrogen bonds caused by placing s at a fixed position in the solvent.

Assuming that $\varepsilon_D - \varepsilon_H$ is small enough, we can expand ΔG_s^* to first order in $(\varepsilon_D - \varepsilon_H)$ to obtain

$$\begin{aligned} \Delta G_s^*(D_2O) - \Delta G_s^*(H_2O) \\ = (\langle N_{HB} \rangle_s - \langle N_{HB} \rangle_0)(\varepsilon_D - \varepsilon_H) \end{aligned} \quad (3.7.38)$$

The estimate of the average change in the structure of water depends on the experimental values of the solvation Gibbs

⁴³For details, see Sec. 2.7 and Ben-Naim (2006).

energies and an estimate of the difference $\varepsilon_D - \varepsilon_H$. Alternatively, we can use the experimental or the theoretical evidence that simple solutes do increase the structure of water to conclude that

$$\left(\frac{\partial \Delta G_s^*}{\partial(-\varepsilon_{HB})} \right)_{T,P,N} < 0 \quad (3.7.39)$$

This means that increasing the *HB* energy ($-\varepsilon_{HB} > 0$) will decrease ΔG_s^* (or increase the solubility of *s*). This finding helps to resolve the apparent puzzling fact that the solubility of small inert solute in D_2O is *larger* than in H_2O .⁴⁴ Traditionally, the low solubility of simple solutes in water is attributed to the high degree of *structure* in water. If that is true, then one would expect that the solubility in D_2O , which is a more *structured* liquid, will be even lower than in H_2O . The inequality (3.7.39) shows that the contrary conclusion is correct, i.e. the solubility will increase with the degree of structure. We have already seen in Sec. 2.7 that increasing $-\varepsilon_{HB}$ will cause an increase in the structure of the water. Therefore, from (3.7.39) we can also conclude that

$$\left(\frac{\partial \Delta G_s^*}{\partial \langle N_{HB} \rangle_0} \right)_{P,T,N} < 0 \quad (3.7.40)$$

for solute *s* that is known to increase the structure of water.

As an example of the application of (3.7.38), we use the solvation Gibbs energy of argon in H_2O and D_2O , for which we have, at $25^\circ C$,

$$\Delta G_s^*(D_2O) - \Delta G_s^*(H_2O) = 59.7 \text{ cal mol}^{-1} \quad (3.7.41)$$

For an estimate of $\varepsilon_D - \varepsilon_H \approx 0.23 \text{ kcal mol}^{-1}$,⁴⁵ we find

$$\langle N_{HB} \rangle_s - \langle N_{HB} \rangle_0 = 0.27 \quad (3.7.42)$$

⁴⁴This is not true for all inert solutes (see Table 3.4).

⁴⁵Estimated by Nemethy and Scheraga (1964).

As in Sec. 2.7 this value seems to be quite low. The main reason is that the first-order expansion (3.7.38) is probably unjustified. We note that if we take larger solutes such as krypton and xenon, we obtain a negative value for $\langle N_{HB} \rangle_s - \langle N_{HB} \rangle_0$, i.e. those solutes destabilize the structure of water.

We use the experimental results of the solvation Gibbs energies of argon, methane, and ethane to estimate the structural change in the solvent induced by placing such solutes at a fixed position in the liquid. Table 3.7 presents such numerical results. The values shown in this table are all positive. This is consistent with similar conclusions reached by many other authors, i.e. these solutes increase the structure of the solvent and therefore may justifiably be referred to as “structure markers” or “structure promoters.”

We conclude this section by noting that, given the assumptions of this section, the parameter ε_{HB} may serve as an indicator as to the degree of structure of water. To show this, we differentiate $\langle N_{HB} \rangle_0$ as defined in Sec. 2.7:

$$\langle N_{HB} \rangle_0 = \frac{\int dV \int d\mathbf{X}^N \exp[-\beta U(\mathbf{X}^N) - \beta PV] \sum_{i < j} G(\mathbf{X}_i, \mathbf{X}_j)}{\int dV \int d\mathbf{X}^N \exp[-\beta U(\mathbf{X}^N) - \beta PV]} \quad (3.7.43)$$

to obtain the result

$$\left[\frac{\partial \langle N_{HB} \rangle_0}{\partial (-\varepsilon_{HB})} \right]_{T,P,N} = \beta [\langle (\langle N_{HB} \rangle_0 - N_{HB})^2 \rangle_0] \geq 0 \quad (3.7.44)$$

Table 3.7. Values of $\langle N_{HB} \rangle_s - \langle N_{HB} \rangle_0$ for Argon, Methane, and Ethane in Water at Different Temperatures^a

t (°C)	5	10	15	20	25
Argon	0.28	0.25	0.23	0.22	0.20
Methane	0.21	0.19	0.17	0.15	0.13
Ethane	0.19	0.14	0.12	0.12	0.14

^aFrom Ben-Naim (1975).

which means that the average structure of the system, as measured by the quantity $\langle N_{HB} \rangle_0$, is a monotonic increasing function of the positive parameter $(-\varepsilon_{HB})$. Applying this result to H_2O and D_2O , we may conclude from (3.7.44) that D_2O is more structured than H_2O . This conclusion has been reached by many authors, using other more qualitative arguments.

So far, we have discussed the isotope effect on the Gibbs energy of transfer of s from H_2O to D_2O . Regarding the entropy and the enthalpy of transfer, we can write the following three equations [Ben-Naim (1965a)]⁴⁶:

$$\Delta S_{tr}^* = \Delta S_{tr}^f + \Delta S_{tr}^r \quad (3.7.45)$$

$$\Delta H_{tr}^* = \Delta H_{tr}^f + \Delta H_{tr}^r \quad (3.7.46)$$

$$\Delta H_{tr}^r = T \Delta S_{tr}^r \quad (3.7.47)$$

Since ΔS_{tr}^* and ΔH_{tr}^* are known, we have here three equations and four unknown quantities. If we assume that the interaction between argon and H_2O is nearly the same as between argon and D_2O , i.e. we put $\Delta H_{tr}^f \approx 0$, then we can solve the three equations to obtain ΔS_{tr}^f , ΔS_{tr}^r , and ΔH_{tr}^r . Thus, for argon in H_2O and D_2O at 283 K, we obtain

$$\Delta S_{tr}^f \cong 0.23 \text{ cal mol}^{-1} \text{K}^{-1} \quad (3.7.48)$$

$$\Delta S_{tr}^r \cong -1.49 \text{ cal mol}^{-1} \text{K}^{-1} \quad (3.7.49)$$

$$\Delta H_{tr}^r \cong 421 \text{ cal mol}^{-1} \quad (3.7.50)$$

Clearly, in this case we see that the difference in the solvation entropy of argon between H_2O and D_2O is dominated by the structural changes induced in the solvents.

⁴⁶The superscripts “ f ” and “ r ” stand for “frozen-in” and “relaxation.”

Exercise E.3.10 (Solvation in binding system):

This is a simple system where one can obtain an explicit expression for the solvation thermodynamic quantities. It is also a warm-up example for the two more complex problems that bear resemblance to the problem of the effect of a solute on the structure of water. The reader is urged to do this exercise before turning to exercises E.3.11 and 3.12.

Assumptions:

(1) The system consists of M binding sites. (2) Each site can absorb only one solute (ligand) s . (3) All sites are identical but distinguishable (i.e. different arrangements of s molecules on the M sites are different states of the system). (4) The sites are independent (i.e. the occupancy on one site does not affect the probability of any other site being empty or occupied). (5) Each solute s is characterized by an internal partition function q_s which does not change upon binding. (6) The interaction between the solute and the site is U_s , and no other degrees of freedom are ascribed to the solute in the site.

With these assumptions in mind, write the canonical PF of the system of N_s solutes absorbed on M sites at a given temperature. From the PF calculate the general form of the chemical potential of the solute. The solvation process is defined as the process of transferring a solute from a *fixed* position in an ideal gas phase to a *fixed* site (say, the i th site). Calculate the solvation Helmholtz energy, the entropy, and the energy of solvation of s in the limit of $N_s/M \rightarrow 0$.

Exercise E.3.11 (Solvation in two kinds of binding sites):

This is a generalization of Exercise E.3.10 in one respect. Instead of one type of site, we have two types of sites, L and H . All other assumptions listed in Exercise E.3.10 are the same.

It is important to study this example before moving on to Exercise E.3.12 which has some features relevant to aqueous solutions.

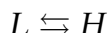
Let M_L and M_H be the number of sites of type L and H , respectively. Let U_{sL} and U_{sH} be the binding energies of s to the sites L and H , respectively. We denote by q_s the internal PF of s , and

$$q_L = \exp[-\beta U_{sL}], \quad q_H = \exp[-\beta U_{sH}]$$

For simplicity, we assume that the sites L and H are localized and that the adsorption of s on a site does not change the internal degrees of freedom of the site. Calculate the Helmholtz energy of solvation, the entropy and enthalpy of solvation of s in this system. Compare the results with Exercise E.3.10.

Exercise E.3.12 (Solvation with “structural changes” in the “solvent”):

This is a generalization of exercises E.3.10 and E.3.11. Instead of a fixed number of sites of types L and H , the sites themselves are in chemical equilibrium:



Therefore, the mole fractions of L and H are not fixed and they may be changed by changing T , P or by the addition of the solute.

In this exercise, we use the same assumptions as in Exercise E.3.11, but now the number of sites of each kind, M_L and M_H , are not fixed but are determined by the equilibrium condition

$$\mu_L = \mu_H$$

Calculate the solvation quantities of s in this model and compare with the results of Exercise E.3.11.

3.7.6. *An empirical estimate of the structural changes induced by the solute on the solvation entropy*

We have seen that the solvation Gibbs energy of an inert solute depends only on the ΔH_s^f and ΔS_s^f , and not on the relaxation terms. Hence, we write

$$\Delta\mu_s^* = \Delta H_s^f - T\Delta S_s^f \quad (3.7.51)$$

It is known that the solubility of argon in ethylene glycol is as low as in water (see Fig. 3.6). For instance, at $t = 20^\circ\text{C}$, the solvation Gibbs energy of argon in water (w) and in ethylene glycol (EG) are nearly the same, i.e.

$$\Delta\mu_s^*(\text{in } w) = \Delta\mu_s^*(\text{in } EG) \quad (3.7.52)$$

We now write the solvation entropy in the two solvents

$$\Delta S_s^*(\text{in } w) = \Delta S_s^f(\text{in } w) + \Delta S_s^r(\text{in } w) \quad (3.7.53)$$

$$\Delta S_s^*(\text{in } EG) = \Delta S_s^f(\text{in } EG) + \Delta S_s^r(\text{in } EG) \quad (3.7.54)$$

and similarly for the enthalpy of solvation

$$\Delta H_s^*(\text{in } w) = \Delta H_s^f(\text{in } w) + \Delta H_s^r(\text{in } w) \quad (3.7.55)$$

$$\Delta H_s^*(\text{in } EG) = \Delta H_s^f(\text{in } EG) + \Delta H_s^r(\text{in } EG) \quad (3.7.56)$$

We now assume that $\Delta H_s^r(EG) \approx 0$. There are two reasons for this assumption. First, we believe that the structural change of the type that occurs in water is peculiar to water and probably arises from the existence of the open structure of water. Second, if there were any appreciable structural changes of this kind in ethylene glycol, these should have shown up in the total enthalpy and the entropy of solvation. The experimental data shows that $\Delta H_s^*(EG)$ has a “normal” value, i.e. of

the same order of magnitude as in other organic solvents. We therefore put $\Delta H_s^r(EG) \approx 0$ and instead of (3.7.54) and (3.7.56) write

$$\Delta H_s^*(in EG) \cong \Delta H_s^f(in EG) \quad (3.7.57)$$

$$\Delta S_s^*(in EG) \cong \Delta S_s^f(in EG) \quad (3.7.58)$$

Since ΔH_s^f arises mainly from the total interaction energy of argon with the solvent, we can assume that both $\Delta H_s^f(in w)$ and $\Delta H_s^f(in EG)$ are of the same order of magnitude; about -400 cal/mol. The experimental value for $\Delta H_s^*(in w)$ is much more negative than this, so we can put

$$\Delta H_s^*(in w) \approx \Delta H_s^r(in w) \quad (3.7.59)$$

From the above assumptions we arrive at the following estimation (valid for the particular temperature chosen above):

$$\Delta S_s^f(in w) \approx \Delta S_s^*(in EG) \approx -7 \text{ cal mol}^{-1} \text{ K}^{-1} \quad (3.7.60)$$

$$\begin{aligned} \Delta S_s^r(in w) &\approx \Delta S_s^*(in w) - \Delta S_s^f(in w) \\ &\approx -10 \text{ cal mol}^{-1} \text{ K}^{-1} \end{aligned} \quad (3.7.61)$$

This is an interesting result since we now have an idea of the order of magnitude of the two terms that contribute to the entropy of solvation. The conclusion is that about half of the anomalous large and negative entropy of solvation comes from the “frozen-in” part, the other half being from structural changes induced in the solvent. Since the only part that affects the solubility comes from the “frozen-in” terms and since ΔH_s^f is assumed to be relatively small, we conclude that about $-7 \text{ cal mol}^{-1} \text{ K}^{-1}$ from the total entropy of solvation is responsible for the low solubility of gases in water.

3.8. Application of the Scaled Particle Theory

The scaled particle theory (*SPT*) was developed mainly for the study of hard-sphere liquids.⁴⁷ It is not an adequate theory for the study of aqueous solutions. Nevertheless, it has been extensively applied for aqueous solutions of simple solutes. The scaled particle theory (*SPT*) provides a prescription for calculating the work of creating a cavity in liquids. We will not describe the *SPT* in detail; only the essential result relevant to our problem will be quoted. Let σ_w and σ_s be the effective diameters of the solvent and the solute molecules, respectively. A suitable cavity for accommodating such a solute must have a radius of $\sigma_{ws} = \frac{1}{2}(\sigma_w + \sigma_s)$ (Fig. 3.20b). The work required to create a cavity of radius σ_{ws} at a fixed position in the liquid is the same as the pseudo-chemical potential of a hard sphere of radius σ_s . The *SPT* provides the following approximation for the pseudo-chemical potential:

$$\mu_{HS}^* = K_0 + K_1\sigma_{ws} + K_2\sigma_{ws}^2 + K_3\sigma_{ws}^3 \quad (3.8.1)$$

where the coefficients K_i are functions of the temperature, pressure, and the solvent density ρ_w :

$$K_0 = k_B T [-\ln(1 - y) + 4.5z^2] - \frac{1}{6}\pi P \sigma_w^3 \quad (3.8.2)$$

$$K_1 = -(k_B T / \sigma_w)(6z + 18z^2) + \pi P \sigma_w^2 \quad (3.8.3)$$

$$K_2 = (k_B T / \sigma_w^2)(12z + 18z^2) - 2\pi P \sigma_w \quad (3.8.4)$$

$$K_3 = 4\pi P / 3 \quad (3.8.5)$$

where we have used

$$y = \pi \rho_w \sigma_w^3 / 6, \quad z = y / (1 - y) \quad (3.8.6)$$

⁴⁷ See Reiss *et al.* (1959, 1960), Helfand *et al.* (1960), and Reiss (1966), and for more recent developments, Tully-Smith and Reiss (1970), Reiss and Tully-Smith (1971), and Stillinger (1973).

It should be noted that the *SPT* is not a pure molecular theory in the following sense. A molecular theory is supposed to provide, say, the Gibbs free energy as a function of T, P, N as well as of the molecular parameters of the system. Once this function is available, the density of the system can be computed from the relation $\rho^{-1} = (\partial\mu/\partial P)_T$ (with $\mu = G/N$). The *SPT* utilizes the effective diameter of the solvent molecules as the only molecular parameter (which is the case for a hard-sphere fluid) and, in addition to the specification of T and P , the solvent density ρ_w is also used as input in the theory. The latter being a measurable quantity carries with it implicitly any other molecular properties of the system. The first application of the *SPT* to calculate the thermodynamics of solvation in liquids was carried out by Pierotti (1963, 1965).

Table 3.8 shows some values for the solvation Gibbs energy, enthalpy and entropy of cavity formation computed by Pierotti (1963, 1965) for water and benzene at 25°C and at 1 atm. The effective diameters of argon and water for these calculations are $\sigma_s = 3.4 \text{ \AA}$ and $\sigma_w = 2.75 \text{ \AA}$, respectively. (The subscript *HS* corresponds to the hard part of the solvation of argon.)

From these results, Pierotti concluded that: "It is the entropy of cavity formation that gives rise to the large negative entropies associated with aqueous solutions."

Table 3.8. Computed Values of $\Delta\mu_{HS}^*$, ΔH_{HS}^* , and ΔS_{HS}^* for Argon in Water and Benzene at 25°C and 1 atm^a

Solvent	$\Delta\mu_{HS}^*$ (cal mol ⁻¹)	ΔH_{HS}^* (cal mol ⁻¹)	ΔS_{HS}^* (cal mol ⁻¹ K ⁻¹)
Water	4430	690	-12.5
Benzene	3610	3520	-0.3

^aFrom Pierotti (1965).

Perhaps, the most striking figure in Table 3.8 is the relatively large and negative entropy of cavity formation in water compared to that of benzene. This means that the anomalous properties of water are already revealed for the simplest possible solute, a hard sphere. The hard part of the enthalpy of solution is positive here, though much smaller than the corresponding value for benzene. This indicates that the “switching on” of the soft part of the interaction energy contributes significantly to the enthalpy of solvation.⁴⁸ The application of the *SPT* to aqueous solutions has been extended by many authors. See, for example, Stillinger (1973), Floris *et al.* (1997), Wilhelm (1973), Wilhelm and Battino (1971), Lee (1991), Graziano (2002, 2006, 2007, 2008ab), Ashbaugh and Pratt (2006), and many others.

Some general comments regarding the application of the *SPT* to water are now in order. First, the *SPT* was originally devised for treating a fluid of hard spheres or simple non-polar fluids. The extension of the theory to complex fluids such as water is questionable. Second, the *SPT* employs an effective diameter of the solvent as the only molecular parameter. It is very likely that this diameter is temperature dependent. It is not clear, however, which kind of temperature dependence should be assumed for σ_w . [This topic was discussed by Ben-Naim and Friedman (1967) and Pierotti (1967).] Finally, we stress again that the *SPT* is not a pure molecular theory. Even if it can predict the properties of aqueous solutions of gases, it is still incapable of providing an “explanation” of these properties. This is an inherent drawback of the theory since it cannot tell us *why* aqueous solutions behave in such a peculiar way as compared with other fluids.

⁴⁸Very recently, Graziano (2008b) has calculated the solvation entropies of a series of molecules in their own liquid (referred to as condensation entropy). He found that for all non-polar liquids the calculated values were in good agreement with the experimental values. On the other hand, for hydrogen-bonded liquids significant discrepancies between the calculated and experimental values were observed.

3.9. Application of a One-Dimensional Model

3.9.1. *Introduction*

In Sec. 2.5, we introduced two 1-D models for water. The two models are almost equivalent in their capacity to unveil the molecular reasons for the outstanding properties of liquid water. Extending the application of these two models for aqueous solutions shows that while the primitive model fails to show large negative anomalous entropy and enthalpy of solvation of inert solutes, the primitive cluster succeeds. The reason is that the entropy and enthalpy of solvation of a solute in water are due to the capability of the solute to induce “structural changes” in the solute. In the 1-D primitive model, one could not achieve that effect, not because of any deficiency of the model but because of the assumption of nearest-neighbor interactions only.

In order to produce large negative entropy and enthalpy of solvation, one needs to find a “mechanism” by means of which a solute can “stabilize” or enhance the formation of hydrogen bonds. This could have been achieved in the primitive model by introducing second nearest-neighbor interactions for triplets of water-solute-water in such a way that when the two water molecules are hydrogen bonded, the in-between solute molecule will stabilize the triplet, and hence enhance the formation of hydrogen bonds “across” the solute. This is shown schematically in Fig. 3.21.

In Fig. 3.21a, we show the primitive model for water. If we place a solute (dark circle) between two hydrogen-bonded molecules, then the hydrogen bond energy between these two molecules will not be counted in the partition function. This is a result of using only pairwise interactions between pairs of consecutive water molecules. In real liquid water, we assume that a solute can penetrate a hole within the hydrogen-bonded network of water molecules without breaking the hydrogen bonds.

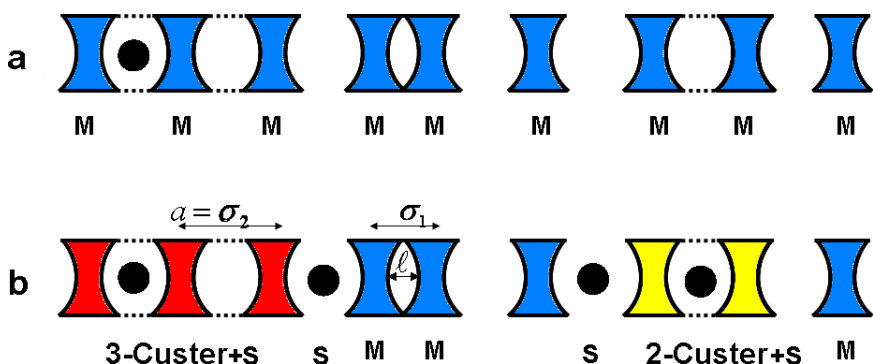


Fig. 3.21 Adding solutes (dark circles) in (a) the primitive model and (b) the primitive cluster model.

Thus, in order to achieve a stabilization of clusters in the primitive model, we have to introduce three-body potentials.⁴⁹ The addition of three-body potentials in the primitive model would have rendered the solution of the 1-D partition function impossible.⁵⁰ Instead, the primitive cluster model takes into account all the hydrogen bondings as part of the internal function of the cluster. The very design of the primitive cluster model (Fig. 3.21b) is such that when a solute penetrates in between the hydrogen-bonded molecule it leaves the hydrogen bond intact. Therefore, a solute penetrating a hole within a cluster is expected to “stabilize” the cluster, i.e. it will shift the equilibrium towards formation of more hydrogen bonds.

In the next section, we show some results for the solvation of hard rods (HRs) in the primitive model. This is important since the primitive model can show the low solubility of HRs

⁴⁹Strictly, it is not the three-body potentials that we need, but interactions between two molecules “across” an intervening solute. In the partition function of the primitive model only *nearest neighbors* interactions are taken into account.

⁵⁰Recently, Lyubartsev and Ben-Naim (unpublished) have carried out Monte Carlo simulations on the primitive model, where next nearest neighbor interactions are included. In this model, the entropy of solvation is indeed much lower than in the cluster model reported in this section.

but not the large entropy and enthalpy of solvation. The latter quantities depend on the capability of the solute to enhance hydrogen bonding. This effect can be demonstrated within the primitive cluster model. In Sec. 3.9.3, we shall present more results on the solvation in the primitive cluster model.

3.9.2. *Solvation of hard rods in the primitive model for water*

The water-like particles' pair potential is the same as in Sec. 2.5. (see Fig. 2.10d):

$$U_{WW}(R) = \begin{cases} \infty & 0 \leq R < \sigma_1 \\ 0 & \sigma_1 \leq R < \sigma_2 \\ \varepsilon_{HB} & \sigma_2 < R < \sigma_2 + \delta_2 \\ 0 & R \geq \sigma_2 + \delta_2 \end{cases} \quad (3.9.1)$$

The solute-solvent interaction as well as the solute-solute interactions are assumed to be either square well or *HR* interactions (Figs. 2.10a and 2.10b). We shall use the square well potential (Fig. 2.10b) defined by

$$U_{SS}(R) = \begin{cases} \infty & 0 \leq R < \sigma_1 \\ \varepsilon & \sigma_1 \leq R < \sigma_1 + \delta_1 \\ 0 & R \geq \sigma_1 + \delta_1 \end{cases} \quad (3.9.2)$$

We shall also compare the results for the solvation of the solute *s* in the primitive model (which we shall refer to as the *HBed* solvent) with results in a reference solvent which has the same pair potential as in (2.9.2) and will be referred to as the square-well *SW* solvent.⁵¹ Thus, the *SW* will be the reference “simple” solvent for the solvation of *HRs*.

⁵¹Note the *SW* stands for both *square well* and for *solute* and water.

We denote the Laplace transform of the function $\exp[-\beta U_{WW}(R)]$ by

$$\psi_{WW}(T, P) = \int_0^\infty \exp[-\beta PR - \beta U_{WW}(R)] dR \quad (3.9.3)$$

This is the same as the function used in Sec. 2.5. In addition, we have the solute-solvent Laplace transform defined by

$$\psi_{SW}(T, P) = \int_0^\infty \exp[-\beta PR - \beta U_{SW}(R)] dR \quad (3.9.4)$$

where $U_{SW}(R)$ is the solute-solvent pair potential, which is also an SW potential but with parameters defined by

$$\sigma_{sw} = \frac{(\sigma_{ss} + \sigma_{ww})}{2}, \quad \varepsilon_{sw} = \sqrt{\varepsilon_{ss} \varepsilon_{ww}} \quad (3.9.5)$$

Note that σ_{ij} refers to the hard-core diameters of the pair of species i and j . We shall use $\sigma_1 = \sigma_{ww}$ for the water diameter and σ_2 for the HB distance.

In this section, we shall present only the solvation quantities of the solute s in the limit of very dilute solutions in the solvent. For this case, the solvation Gibbs energy has already been derived⁵²:

$$\Delta\mu_s^* = -T \ln \left[\frac{-\psi_{WW}(T, P)^2}{T \psi'_{SW}(T, P)} \right] \quad (3.9.6)$$

where

$$\psi'_{SW}(T, P) = \frac{\partial \psi_{SW}(T, P)}{\partial P} \quad (3.9.7)$$

It is easy to check that in the limit of an ideal gas, we have

$$\lim_{P \rightarrow 0} \Delta\mu_s^* = 0 \quad (3.9.8)$$

⁵²For details, see Ben-Naim (1992, 2008c).

The entropy, enthalpy, volume, and energy of solvation are calculated by taking the derivatives of $\Delta\mu_s^*$ in (3.9.6), i.e.

$$\begin{aligned}\Delta S_s^* &= \frac{-\partial\Delta\mu_s^*}{\partial T} \\ \Delta H_s^* &= \Delta\mu_s^* + T\Delta S_s^* \\ \Delta V_s^* &= \frac{\partial\Delta\mu_s^*}{\partial P} \\ \Delta E_s^* &= \Delta H_s^* - P\Delta V_s^*\end{aligned}\tag{3.9.9}$$

Figure 3.22 shows the solvation Gibbs energy of the *HR* solute in two solvents, the *SW* and *HB* solvents. In these two solvents, the range of variation of ε (the depth of the *SW* potential; Fig. 2.10b) and ε_{HB} (the strength of the *HB* energy; Fig. 2.10d) is the same. Clearly, the values of $\Delta\mu_s^*$ are nearly the same in the two solvents. We can conclude that what determines the solubility of the *HR* is only the strength of the interactions (in the 1-D model, the diameter has no effect on the solubility). Whether the solvent particles form *HBs* or not is immaterial; what matters is the strength of the solvent-solvent interactions and not the interactions at distances larger than the hard-core diameter σ_1 .

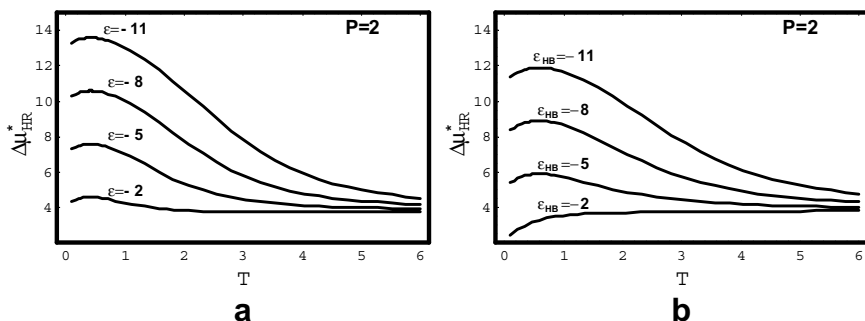


Fig. 3.22 The solvation Gibbs energy of an *HR* in (a) the reference solvent (*SW*) and (b) the primitive (*HB*) solvent, for different values of the energy parameters. The parameters in this illustration are: $\sigma_1 = 1, \sigma_2 = 2, \delta = 0.3, k = 1000$, and ε and ε_{HB} as indicated.

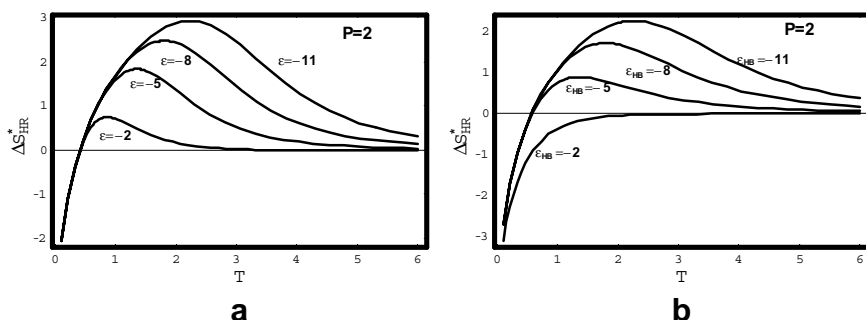


Fig. 3.23 The dependence of the solvation entropy on the energy parameters in the *SW* and the *HB* models (parameters as in Fig. 3.22).

Next, we turn to the entropy of solvation in the two solvents. Fig. 3.23 shows the values of ΔS_s^* in the two solvents. In both solvents, the solvation entropy starts with negative values at very low temperatures, then becomes positive at intermediate temperature, and finally tends to zero at very high temperature. We see the values of ΔS_s^* are nearly the same in the two solvents (the *SW* and the *HB*) — provided the strengths of the interaction energy are the same — but independent of the location of the potential well.

Figure 3.24 shows the enthalpy of solvation in the two solvents. Again, we observe similar trends in the two solvents. As

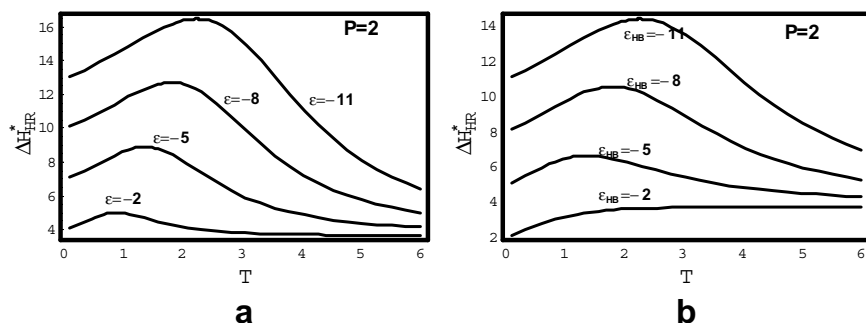


Fig. 3.24 The solvation enthalpy of an *HR* in the reference solvent (*SW*) and in the primitive (*HB*) solvent (parameters as in Fig. 3.22).

the solvent-solvent interactions become stronger, it is more difficult to insert a solute in the solvent. All the values obtained for ΔH_s^* are positive here. The main reason for this is that the insertion of an *HR* between two strongly interacting particles eliminates the interactions between these two particles (recall that in the 1-D model, only nearest-neighbor interactions are taken into account). This effect is clearer when we examine the energy of solvation in Fig. 3.25. We see that in *both* solvents, as the temperature increases, ΔE_s^* tends to zero. In this case, inserting an *HR* between two solvent molecules eliminates the solvent-solvent interaction. As can be seen from Fig. 3.25, the energy required to insert an inert solute is exactly equal to minus the interaction energy between the two solvent particles and is independent of either the location or the range of the interactions (either in the *SW* or the *HB* potential).

Finally, we show in Fig. 3.26 the solvation heat capacity of an *HR* in the two solvents. The general trends are similar in the two solvents. Note, however, that the values of $\Delta C_{P,HR}^*$ are systematically larger in the *SW* solvent than in the *HB* solvent. For instance, with $\varepsilon = \varepsilon_{HB} = -11$, the maximum $\Delta C_{P,HR}^*$ is about 20 for the *SW* solvent and about 14 in the *HB* solvent. The interpretation of these findings is not easy. The solvation heat capacity is related to the temperature dependence of the

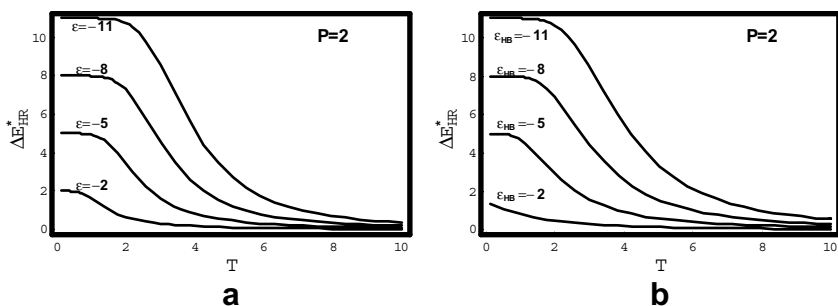


Fig. 3.25 The dependence of the solvation energy on the energy parameters in the *SW* and the *HB* models (parameters as in Fig. 3.22).

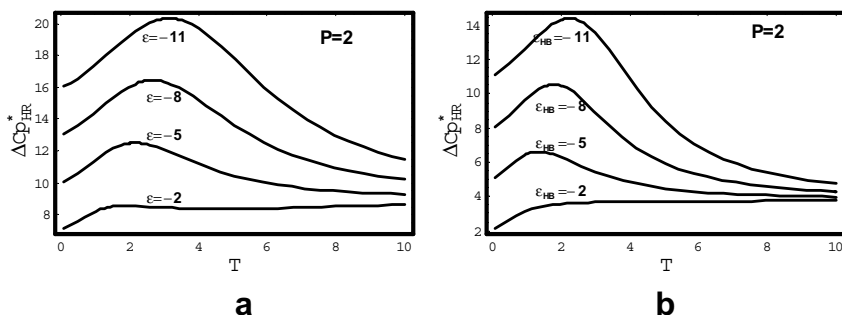


Fig. 3.26 The solvation partial molar heat capacity of an *HR* in the primitive (*HB*) solvent and in the reference solvent (*SW*) (parameters as in Fig. 3.22).

extent of structural changes in the solvent. This relationship is rather complicated even in the simplest two-structure model for water. In the next sections, we shall use the primitive cluster model for the solvent, where we shall find a dramatic difference in the solvation heat capacity.

3.9.3. *Application of the primitive cluster model for dilute solutions of inert solutes*

In this section, we extend the application of the primitive cluster model discussed in Sec. 2.5.4 to examine the solvation thermodynamics of simple solutes in the water-like solvent. The model is schematically described in Fig. 3.21b. The only new feature that is added here compared with the model discussed in Sec. 2.5.4 is that clusters of water-like particles contain “holes” in which solute molecules can be accommodated. This feature is the analog of the cavities formed by the network of hydrogen-bonded molecules in real water.

This model was first studied by Lovett and Ben-Naim (1969). The entropy and the enthalpy of solvation were found to be large and negative, as are the corresponding values for the solvation of, say, argon in water. A major failure of the model discussed earlier is that the solvation Gibbs energy was found to be smaller

in the *HB* solvent than in the reference solvent. This is, of course, in contrast to the experimental results on the solvation of, say, argon in water and in some “normal” solvents.

In this section, we show that one can mimic both the large solvation Gibbs energy (i.e. the low solubility) and the large negative entropy and enthalpy of solvation in the same model by choosing a larger distance for the *HB* energy. The rationale for doing so is that in real liquid water there is a limited number of cavities to accommodate an inert solute. Hence, there is a limit on the solubility of the solutes within the clusters of water molecules determined by the maximum number of holes and the volume of the cluster.

In the primitive cluster model used in Sec. 2.5, we chose $(n-1)$ holes (or cavities) in an n -cluster and a hydrogen-bonding distance of $\sigma_2 = 2$ (where $\sigma_1 = 1$ was the hard-core diameter). Clearly, one can cause a *decrease* in the solubility of the solute either by decreasing the number of holes or by increasing the *HB* distance (i.e. making the size of a cluster of *HBed* particles larger). In this section, we examine the effect of increasing σ_2 . The interesting finding is that with a choice of a larger value σ_2 , we get not only larger values of the solvation Gibbs energies (corresponding to low solubility) but also the characteristic temperature dependence of $\Delta\mu_s^*$, namely first an increase in $\Delta\mu_s^*$ with T , and then a decrease with T . This is similar to the well-known solubilities of inert solutes in water. At low temperatures, the solubility decreases with temperature, then passes through a minimum, and then increases at higher temperatures.

The partition function for the system of two-component, water-like and inert solute particles is fairly complicated. Details are provided in Lovett and Ben-Naim (1969). Here, we present the final form of the partition function and the computational procedure to obtain the cluster-size distribution and the solvation quantities in a very dilute solution of *HRs* in a solvent.

Extending the same procedure as described in Sec. 2.5, we can write the Laplace transform of the grand partition function as

$$\begin{aligned}\psi(\Xi(T, L, \lambda)) &= \int \exp[-\beta PL] \Xi(T, L, \lambda) dL \\ &= \sum_{N=0}^{\infty} \text{Tr}(\mathbf{M}^N)\end{aligned}\quad (3.9.10)$$

where $\mathbf{M}$ is a matrix with the following elements:

$$M_{0,0} = \frac{\lambda_0}{\Lambda_0} \psi_{SS}, \quad M_{0,1} = M_{1,0} = \left(\frac{\lambda_0 \lambda_1}{\Lambda_0 \Lambda_1} \right)^{1/2} \psi_{SW}$$

$$M_{0,ni} = M_{ni,0}$$

$$= \left[\frac{\lambda_{ni} \lambda_0}{\Lambda_1^n \Lambda_0^{i+1}} \psi_{HB}^{(n-1)} \exp[-\beta \varepsilon_{ni}] l^i \binom{n-1}{i} \right]^{1/2} \psi_{SW}$$

$$M_{1,1} = \frac{\lambda_1}{\Lambda_1} \psi_{WW},$$

$$M_{1,ni} = M_{ni,1}$$

$$= \left[\frac{\lambda_{ni} \lambda_1}{\Lambda_1^{n+1} \Lambda_0^i} \psi_{HB}^{(n-1)} \exp[-\beta \varepsilon_{ni}] l^i \binom{n-1}{i} \right]^{1/2} \psi_{WW}$$

$$M_{ni,mj} = M_{mj,ni}$$

$$\begin{aligned}&= \left[\frac{\lambda_{ni} \lambda_{mj}}{\Lambda_1^{m+n} \Lambda_0^{i+j}} \psi_{HB}^{m+n-2} \exp[-\beta(\varepsilon_{ni} + \varepsilon_{mj})] l^{(i+j)} \right. \\ &\quad \left. \times \binom{n-1}{i} \binom{m-1}{j} \right]^{1/2} \psi_{WW}\end{aligned}\quad (3.9.11)$$

where n_i denotes a cluster of size n containing i solute molecules, and

$$\varepsilon_{ni} = (n-1)\varepsilon_{HB} + i\varepsilon_0 \quad (3.9.12)$$

ε_0 is the interaction energy of the solute with the hole in the cluster, ε_{HB} is the HB energy, and l is the “free volume,” which is essentially the size of the holes in the cluster. ψ_{HB} is defined by

$$\psi_{HB} = \int_0^\infty dR \exp \left[-\beta P R - \beta \frac{1}{2} k (R - a)^2 \right] \quad (3.9.13)$$

where k is a force constant for the harmonic potential function between two particles engaged in an HB , and a is the HB distance.

It is convenient to transform the elements of the matrix $\mathbf{M}$ by defining the quantities

$$t_0^2 = \frac{\lambda_0}{\Lambda_0} \left[\frac{\psi_{SW}}{\psi_{WW}} \right]^2, \quad t_1^2 = \frac{\lambda_1}{\Lambda_1} = \lambda_1 q_1 \quad (3.9.14)$$

$$t_{ni}^2 = \frac{\lambda_{ni}}{\Lambda_1^n \Lambda_0^i} \psi_{HB}^{(n-1)} \exp[-\beta \varepsilon_{ni}] l^i \binom{n-1}{i} = \lambda_{ni} q_{ni}$$

With these transformations one can transform the matrix $\mathbf{M}$ into a new matrix $\mathbf{M}'$ having the same eigenvalues⁵³ but a simpler form:

$$\mathbf{M}' = \psi_{WW} \begin{pmatrix} \alpha t_0^2 & t t_0 & 0 & 0 & 0 & \cdots \\ t t_0 & t^2 & 0 & 0 & 0 & \cdots \\ 0 & 0 & 0 & 0 & 0 & \\ \vdots & \vdots & & & & \end{pmatrix} \quad (3.9.15)$$

where $\alpha = \psi_{WW} \psi_{SS} / \psi_{SW}^2$ and

$$t^2 = t_1^2 + \sum_{n=2}^{\infty} \sum_{i=0}^{n-1} t_{ni}^2 \quad (3.9.16)$$

⁵³For details, see Lovett and Ben-Naim (1969).

Now, it is easy to find the eigenvalues of the matrix $\mathbf{M}'$, which are the same as the eigenvalues of $\mathbf{M}$.⁵⁴ The two eigenvalues are

$$\gamma_{\pm} = \frac{\psi_{WW}}{2} \{ \alpha t_0^2 + t^2 \pm [(\alpha t_0^2 - t^2)^2 + 4t^2 t_0^2]^{1/2} \} \quad (3.9.17)$$

The correct solution is the one with the plus sign (for $t_0^2 = 0$, we recover the equation for pure water; see Sec. 2.5). Using the eigenvalue γ_+ in the Laplace transform of the grand partition function and requiring that this “generalized” partition function diverges, one gets the equation of state of this system in the form

$$F(T, P, \lambda) = \frac{\psi_{WW}}{2} \{ \alpha t_0^2 + t^2 + [(\alpha t_0^2 - t^2)^2 + 4t^2 t_0^2]^{1/2} \} = 1 \quad (3.9.18)$$

We use the equation of state $F(T, P, \lambda) = 1$ for all of the following computations. Note that in this equation all the λ_{ni} are independent variables, i.e. the system is viewed as a mixture of clusters characterized by n monomers and i solute particles.

In all the calculations carried out for this system, we first treat the absolute activities λ_{ni} as independent variables. In the final expression, we must evaluate the result at equilibrium, i.e. we must introduce the condition $\mu_{ni} = n\mu_i + i\mu_0$ or equivalently

$$\lambda_{ni} = \lambda_1^n \lambda_0^i \quad (3.9.19)$$

From (3.9.18), we can express t^2 in terms of t_0^2 :

$$t^2 = \frac{\alpha t_0^2 \psi_{WW} - 1}{\psi_{WW} [\alpha t_0^2 \psi_{WW} - \psi_{WW} t_0^2 - 1]} \quad (3.9.20)$$

Note that for $t_0^2 = 0$, we recover the equation of state for pure water (see Sec. 2.5):

$$t^2 \psi_{WW} = 1$$

⁵⁴For details, see Lovett and Ben-Naim (1969).

The number densities of the various species are calculated from

$$\rho_{ni} = \frac{N_{ni}}{L} = -\frac{\partial F / \partial \mu_{ni}}{\partial F / \partial P} = -\frac{(\partial F / \partial \lambda_{ni}) \beta \lambda_{ni}}{\partial F / \partial P} \quad (3.9.21)$$

and

$$\rho_i = \frac{-(\partial F / \partial \lambda_i) \beta \lambda_i}{\partial F / \partial P} \quad (3.9.22)$$

$$\rho_0 = \frac{-(\partial F / \partial \lambda_0) \beta \lambda_0}{\partial F / \partial P} \quad (3.9.23)$$

All the derivatives in (3.9.21) to (3.9.23) can be obtained from the equation of state (3.9.18). We shall be interested only in ratios of the densities. These are

$$\frac{\rho_{ni}}{\rho_1} = \frac{\lambda_{ni}(\partial F / \partial \lambda_{ni})}{\lambda_i(\partial F / \partial \lambda_i)} = \frac{t_{ni}^2}{t_1^2} \quad (3.9.24)$$

$$\frac{\rho_0}{\rho_1} = \frac{\lambda_0(\partial F / \partial \lambda_0)}{\lambda_i(\partial F / \partial \lambda_i)} = \frac{t_0^2 \left[\alpha + \frac{4t^2 + 2\alpha(\alpha t_0^2 - t^2)}{\Gamma} \right]}{t_1^2 \left[1 + \frac{t^2 + 2t_0^2 - \alpha t_0^2}{\Gamma} \right]} \quad (3.9.25)$$

where

$$\Gamma = [4t^2 t_0^2 + (t^2 - \alpha t_0^2)^2]^{1/2} \quad (3.9.26)$$

The total number density of water molecules is

$$\begin{aligned} \rho_w &= \rho_1 + \sum_{n,i} n \rho_{ni} = \rho_1 \left[1 + \sum_{n,i} n \frac{\rho_{ni}}{\rho_1} \right] \\ &= \rho_1 \left[1 + \sum_{n,i} n \frac{t_{ni}^2}{t_1^2} \right] \end{aligned} \quad (3.9.27)$$

and the total number density of solute molecules is

$$\begin{aligned}\rho_s &= \rho_0 + \sum_{n,i} i \rho_{ni} \\ &= \rho_1 \left[\frac{\rho_0}{\rho_1} + \sum_{n,i} i \frac{\rho_{ni}}{\rho_1} \right] = \rho_1 \left[\frac{\rho_0}{\rho_1} + \sum_{n,i} i \frac{t_{ni}^2}{t_1^2} \right] \quad (3.9.28)\end{aligned}$$

Next, we define the mole fraction of clusters of the size n :

$$X_n = \frac{\sum_{i=0}^{n-1} \rho_{ni}}{\rho_w} \quad (3.9.29)$$

and the average number of HBs per water molecule:

$$\langle X_{HB} \rangle = \sum_{n=2}^{\infty} (n-1) X_n \quad (3.9.30)$$

The mole fraction of the solute s in the system is

$$y_s = \frac{\rho_s}{\rho_s + \rho_w} = \frac{1}{1 + \left(\frac{\rho_w}{\rho_s} \right)} \quad (3.9.31)$$

For the numerical calculations of X_n and X_{HB} , we proceed as follows. First, we can evaluate the sum

$$\begin{aligned}t^2 &= t_1^2 + \sum_{n=2}^{\infty} \sum_{i=0}^{n-1} t_{ni}^2 \\ &= \lambda_1 q_1 + \sum_{n=2}^{\infty} \sum_{i=0}^{n-1} \lambda_{ni} q_{ni} = \frac{t_1^2}{1 - \eta t_1^2 (1 + \xi t_0^2)} \quad (3.9.32)\end{aligned}$$

where q_{ni} are defined in (3.9.14), $\eta = \psi_{HB} \exp[-\beta \varepsilon_{HB}]$ and $\xi = [\psi_{WW}/\psi_{SW}]^2 l \exp[-\beta \varepsilon_0]$.

The last relation, Eq. (3.9.32), can be inverted to obtain

$$t_1^2 = \frac{t^2}{1 + \eta t^2(1 + \xi t_0^2)} \quad (3.9.33)$$

Since t^2 is already given as a function of T, P, λ_s in (3.9.20), we also have t_1^2 as a function of T, P, λ_s (note that λ_s is the same as λ_0 at equilibrium).

The average number of HBs per molecule is given by

$$\begin{aligned} \langle X_{HB} \rangle &= \sum_{n=2}^{\infty} (n-1)X_n \\ &= \sum_{n=2}^{\infty} nX_n - \sum_{n=2}^{\infty} X_n = 1 - \sum_{n=2}^{\infty} X_n \\ &= \eta t_1^2(1 + \xi t_0^2) \end{aligned} \quad (3.9.34)$$

And the mole fraction of the n -cluster is

$$X_n = \frac{\rho_n}{\rho_w} = \frac{\sum_{i=0}^{n-1} \rho_{ni}}{\rho_w} = \frac{\sum_{n=0}^{n-1} t_{ni}^2/t_1^2}{1 + \sum_{i=0}^{n-1} n t_{ni}^2/t_1^2} \quad (3.9.35)$$

This is all we need to calculate the distribution of species and the average number of HBs. The latter is sometimes referred to as the *structure* of the system. In real water, a larger number of HBs in the system is indeed associated with a higher degree of structure. In the 1-D model, we shall continue to use the term *structure* although there is clearly no such structure as it exists in liquid water.

Next, we turn to the calculation of the solvation quantities. Since we are interested only in the limit of the infinite dilution system, we expand the equation of state to first order in t_0^2 to obtain

$$\psi_{WW}(t^2 - t_0^2) = 1 \quad (3.9.36)$$

Since t_0^2 is proportional to λ_0 and t^2 is expressed in terms of t_0^2 , we can extract λ_0 , or equivalently the chemical potential of the solute, to obtain the explicit expression

$$\begin{aligned}\mu_s &= (T, P, \rho_s) \\ &= T \ln \rho_s \Lambda_0 \\ &\quad + T \ln \left[\frac{\exp[\beta \varepsilon_0](\psi_{HB} + \exp[\beta \varepsilon_{HB}] \psi_{WW})}{\rho_w [l \psi_{HB} + \exp[\beta(\varepsilon_0 + \varepsilon_{HB})] \psi_{SW}^2]} \right]. \quad (3.9.37)\end{aligned}$$

From (3.9.37), we get the solvation Gibbs energy at infinite dilution

$$\begin{aligned}\Delta \mu_s^* &= \mu_s(T, P, \rho_s) - T \ln \rho_s \Lambda_0 \\ &= T \ln \left[\frac{\exp[\beta \varepsilon_0](\psi_{HB} + \exp[\beta \varepsilon_{HB}] \psi_{WW})}{\rho_w [l \psi_{HB} + \exp[\beta(\varepsilon_0 + \varepsilon_{HB})] \psi_{SW}^2]} \right]. \quad (3.9.38)\end{aligned}$$

From $\Delta \mu_s^*$ we can get all the thermodynamic quantities of solvation of the solute.

3.9.4. Results for HR solute in dilute solutions of the primitive cluster model

We begin with some results on the effect of the solute on the distribution of cluster size. In all of the following discussions, the *HB* solvent refers to the primitive cluster model for water.

Figure 3.27 shows the dependence of X_1 (the mole fraction of the monomeric “water” particles) as a function of the mole fraction of the solute y_s . The behavior of X_1 as a function of y_s is unique in the sense that initially at low values of y_s , X_1 decreases. This means that monomers are used to build up clusters. As we shall see below, this behavior is typical for aqueous solutions and is part of the explanation for the unusually large negative entropy and enthalpy of solvation of the solute. At higher concentrations of the solute s , the concentration of all

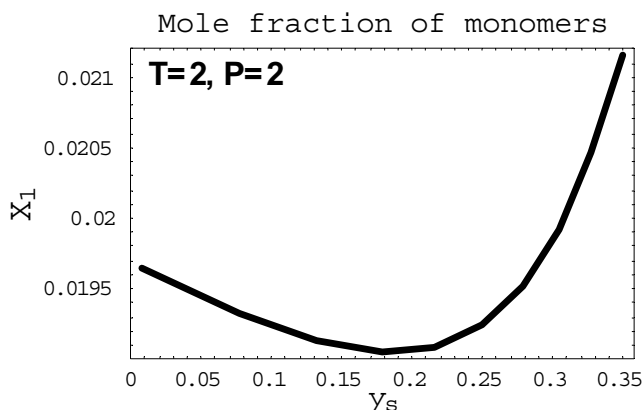


Fig. 3.27 The mole fraction X_1 as a function of the mole fraction of the solute s (parameters as in Fig. 3.22).

clusters must decrease, and eventually water monomers become diluted in s .

For some intermediate $n \geq 2$ (Fig. 3.28), there is an initial decrease in X_n as we add s , then X_n increases but eventually decreases to zero as y_s approaches unity. For larger clusters, say, $n \geq 20$, the mole fraction X_i initially increases but eventually decreases as the concentration of the solute increases. The details of which cluster size is stabilized or destabilized by the solute depends on the temperature and pressure, but the typical behavior of X_n for small n and X_n for large n is the same for the entire range of temperatures and pressures we are interested in.

To understand the unusually large and negative entropy and enthalpy of solvation, it is not necessary to examine the detailed variation of each of the X_n . Instead, we examine the average number of HBs per water molecule, which we denote by $\langle X_{HB} \rangle$. This is a measure of the overall “structure” of the system. Variation of this quantity with y_s determines the value of the entropy and the enthalpy of solvation of the solute s .

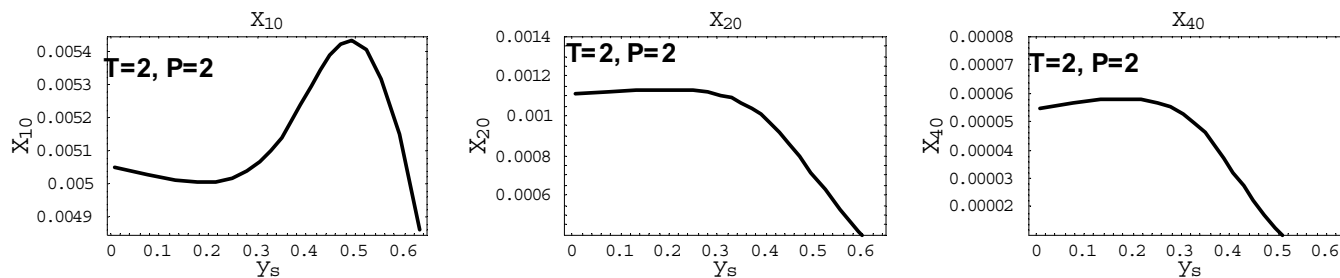


Fig. 3.28 The mole fractions X_{10} , X_{20} , and X_{40} as functions of the mole fraction of the solute s .

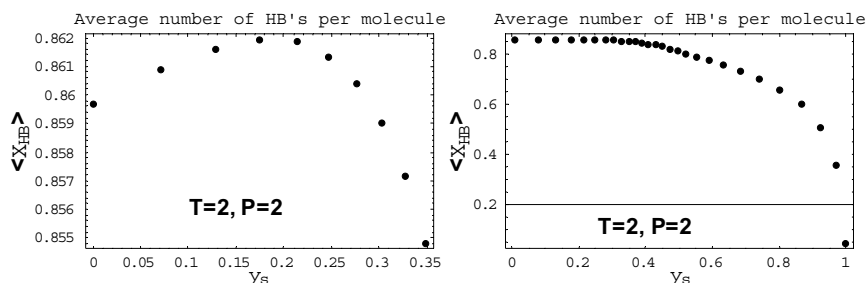


Fig. 3.29 Dependence of $\langle X_{HB} \rangle$ on the mole fraction of solute concentration y_s at low and high concentrations of s .

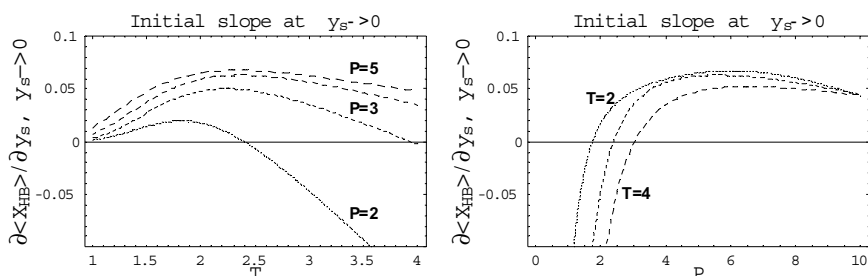


Fig. 3.30 Dependence of the limiting slope of $\langle X_{HB} \rangle$ at $y_s \rightarrow 0$ on the temperature and the pressure.

Figure 3.29 shows the dependence of $\langle X_{HB} \rangle$ on y_s . It is seen that initially $\langle X_{HB} \rangle$ increases with y_s . Beyond a certain value of y_s , it starts to decrease towards zero, when water becomes diluted in s .

Since we are concerned here only with the solvation properties in the limit of $y_s \rightarrow 0$, only the slope of $\langle X_{HB} \rangle$ at $y_s \rightarrow 0$ is of interest. Figure 3.30 shows the limiting slope

$$\lim_{y_s \rightarrow 0} \frac{\partial \langle X_{HB} \rangle}{\partial y_s}$$

as a function of T and P . The larger the limiting slope, the larger the “stabilization of the structure” or the larger the enhancement

of the formation of *HB*s in the system. This enhancement also carries with it large and negative enthalpy and energy of solvation. The same argument holds for the large negative entropy of solvation. After some experimentation with the range of T and P at which we observe large stabilization as $y_s \rightarrow 0$, we have chosen this range to calculate the thermodynamics of solvation at infinite dilutions of the solute s .

As was noted by Lovett and Ben-Naim (1969), the solvation Gibbs energy may be increased by either decreasing the number of holes in the clusters or increasing the distance at which an *HB* is formed. In this work, we chose to change the length $a = \sigma_2$ at which an *HB* is formed. Figure 3.31 shows the Gibbs energy of solvation of an *HR* solute in the cluster model with different values of parameter a . As expected, $\Delta\mu_s^*$ increases with increasing a . This corresponds to a decrease in the solubility. We chose the parameter $a = \sigma_2 = 6$ for the rest of the calculation. As shown in Fig. 3.31, the values of $\Delta\mu_s^*$ are very sensitive to

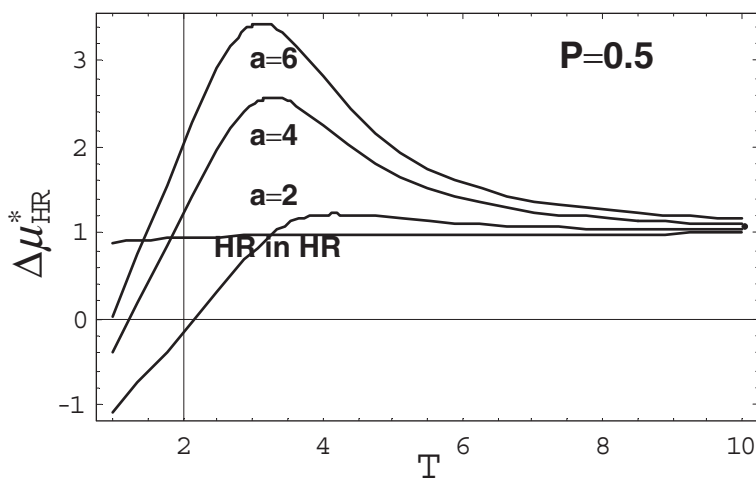


Fig. 3.31 Solvation Gibbs energy of *HR* in *HR* and in *HB* solvents for various values of the parameter a (parameters as in Fig. 3.22).

the choice of σ_2 . The values of ΔS_s^* and ΔH_s^* are relatively less sensitive, as can be seen from the slopes of the curves in Fig. 3.31.

The *HB* energy was initially chosen to be about 10 times larger than the depth of the *SW* solvent, which was chosen to be about 1. This is in accordance with the actual ratio of the *HB* energy and the van der Waals interaction energy between two water molecules and two neon atoms, which is about 10:1. However, it should be noted that this ratio is per bond. In the 1-D model, each water molecule can form at most two *HBs* (one on each side), but in real water each molecule can form up to four hydrogen bonds. Since the solvation entropy and enthalpy depends on the *binding* energies of the two species, one should also consider larger *HB* energies in the 1-D model.

Figure 3.32 shows the solvation Gibbs energies of an *HR* in the “water” (*HB*) and in the *HR* for different values of ϵ_{HB} . All the values of $\Delta\mu_s^*$ are large and positive, corresponding to low

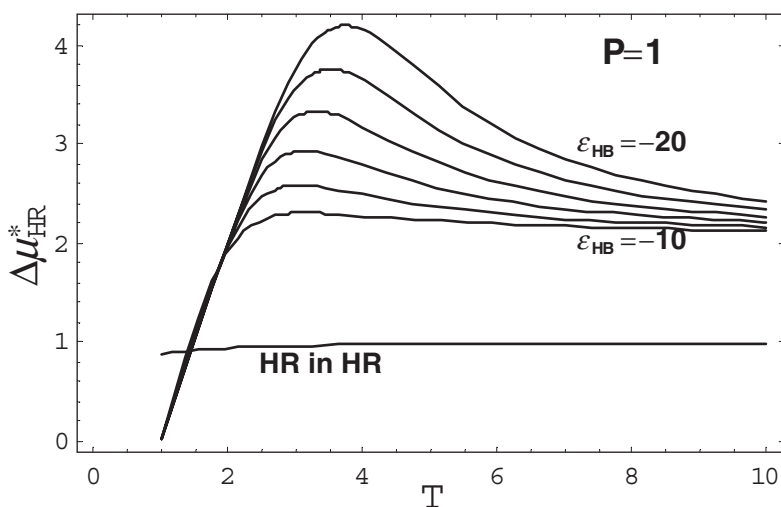


Fig. 3.32 Solvation Gibbs energy of *HR* in *HR* and in *HB* solvents for various values of the *HB* energy ϵ_{HB} (parameters as in Fig. 3.22).

solubility compared with the solubility in the *HR*. The maximum of $\Delta\mu_s^*$ as a function of T is in accordance with the experimental data on solvation of inert gases in water. Note that as $|\varepsilon_{HB}|$ increases, we get larger and larger $\Delta\mu_s^*$. Note also that the slope of $\Delta\mu_s^*$ versus T is large and positive, but not very sensitive to variation of ε_{HB} in the range of temperatures between 1 and 3. This corresponds to the entropy of solvation discussed below.

As we have done in Sec. 2.5, we examine in Fig. 3.33 the “isotope” effect on the solvation Gibbs energy $\Delta\mu_s^*$ by changing ε_{HB} by about 20% (in real water, the difference in the *HB* energy of H_2O and D_2O is about 10%; we chose a 20% change for better clarity in this demonstration). Note that the curves in Fig. 3.33 cross at about $T = 2.4$. In the range of lower temperatures ($1 \leq T \leq 2.2$), $\Delta\mu_s^*$ of the “ D_2O ” is smaller than the value for “ H_2O .” This is in accordance with the values of $\Delta\mu_s^*$ of neon and argon in real H_2O and D_2O .⁵⁵ It should be noted

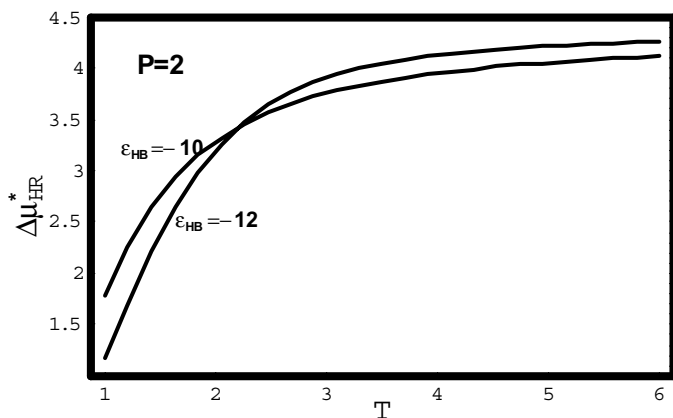


Fig. 3.33 “Isotope” effect on the solvation Gibbs energy ($\sigma_2 = 6$ and other parameters as in Fig. 3.22).

⁵⁵See Table 3.4 and Ben-Naim (1987).

that this trend is reversed for krypton and xenon. In the 1-D model, we use an *HR* solute which is “closer” — in the sense of the strength of the interaction parameter — to neon and argon than to krypton and xenon.

For the following illustrations, we first examined the region of T, P for which there is maximal “structural changes” in the solvent. Then, we selected T, P that produce large negative values of ΔS_s^* and ΔH_s^* .

Figure 3.34 shows the values of ΔS_s^* for an *HR* in the cluster model with two values of $\epsilon_{HB} = -10, -12$. We also show ΔS_s^* in the *HR*. The difference is quite striking. The solvation entropy is about 10 times larger in the cluster model than in the *HR* (this is also true for the *SW* model, not shown here). In this model, ΔS_s^* values also cross at about $T = 1.5$. (It crosses again at $T \approx 3$, but this is not the range of temperatures of interest in this study.) Below $T = 1.5$, the values of ΔS_s^* are more negative for the “H₂O” than for the “D₂O.” This is in accordance with the isotope effect on the entropy of solvation of neon, krypton, and xenon in real H₂O and D₂O, but not for argon for which ΔS_s^* is more negative in D₂O.⁵⁶

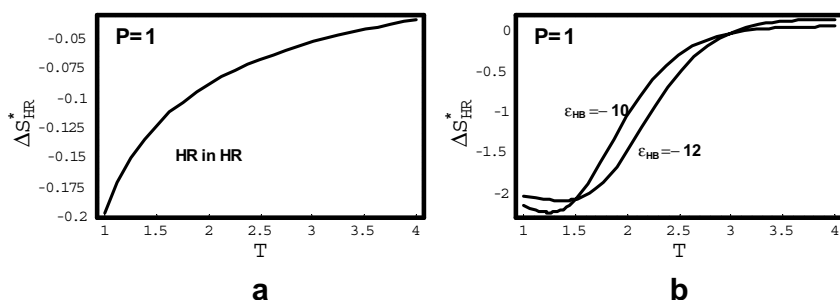


Fig. 3.34 The solvation entropy of *HR* in *HR* and in the cluster model (*HB*).

⁵⁶See Table 3.4 and Ben-Naim (1987).

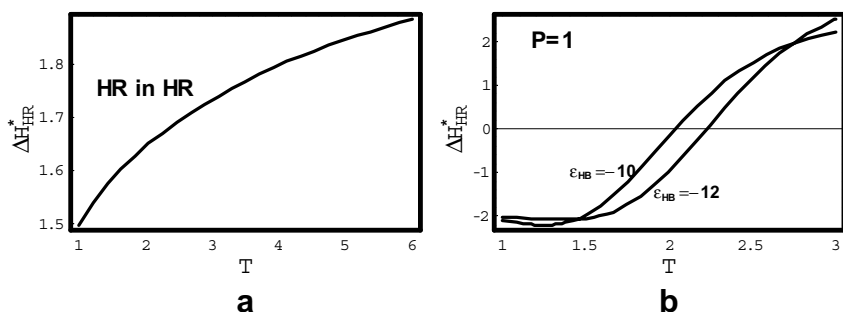


Fig. 3.35 The solvation enthalpy of *HR* in *HR* and in the cluster model (*HB*) ($\sigma_2 = 6$ and other parameters as in Fig. 3.22).

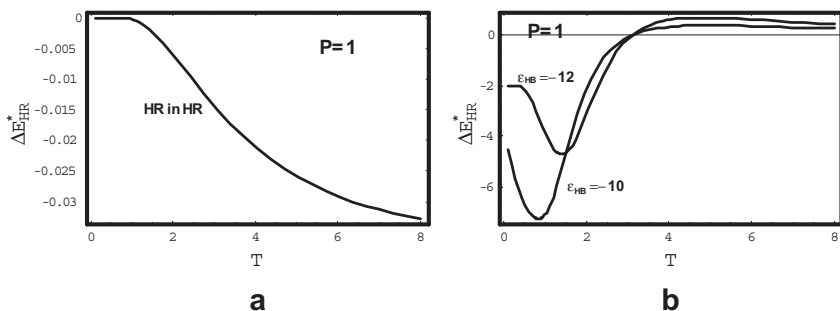


Fig. 3.36 The solvation energy of *HR* in *HR* and in the cluster model (*HB*).

Figure 3.35 shows the values of the solvation enthalpies in the cluster model and in the *HR* solvent. Again, we find that ΔH_s^* in the *HR* solvent are *positive*, but they are large and negative in the cluster model. The isotope effect is relatively small.

Figure 3.36 shows the solvation energies in the two systems. Again, we see that there is a range of temperatures for which ΔE_s^* is far more negative than the corresponding values in the *HR* solvent.

Finally, we show in Fig. 3.37 the values of $\Delta C_{P,s}^*$ defined by

$$\Delta C_{P,s}^* = \frac{\partial \Delta H_s^*}{\partial T} \quad (3.9.39)$$

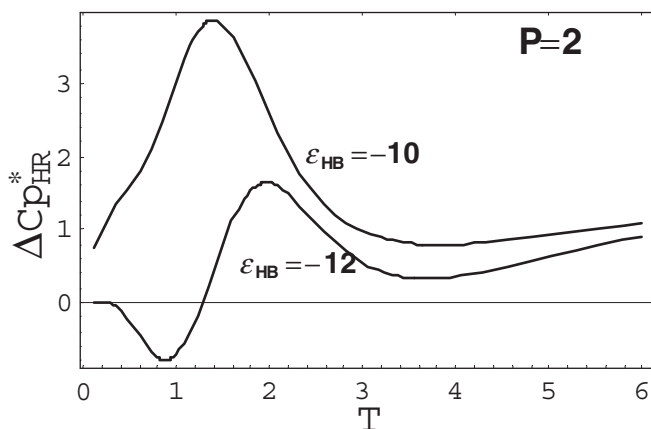


Fig. 3.37 The solvation heat capacity of *HB* in the cluster model and in the *HR* solvent (the straight line at zero is for the *HR* solvent).

for an *HR* solute in *HB* solvent. (Note that $\Delta C_{P,s}^*$ is zero for the *HR* solvent.)

Inert gas solutes show large values of heat capacity of solvation in water compared with normal solvents. This quantity reflects the sharp slope of ΔH_s^* as a function of temperature. Clearly, this trend is a result of the breakdown of the *HBs* (or the “structure”) in real water as well as in the 1-D model.

It is remarkable that a simple 1-D model can exhibit some of the most outstanding properties of water, a liquid which is considered to be one of the most complicated. The success of the primitive model in mimicking the properties of pure water confirms the conjecture that the most important aspect of the molecular interactions in water is the *principle*, i.e. the specific correlation between low local density and large binding energy. At first sight, one may think that the success of the same model in mimicking some outstanding properties of aqueous solutions is even more surprising. However, as was pointed out in Sec. 3.7, there is a deep connection between the sources of the anomalous behavior of pure liquid water and the outstanding values of the

entropy and enthalpy of solvation of inert solutes in water. Both phenomena are intimately connected, and both originate from the same principle.

As we have seen in Sec. 3.7, the large negative entropy and the enthalpy of solvation of an inert solute (even a hard-sphere solute) is a result of the “stabilization” of the “structure” of water. This stabilization, when translated into the language of the 1-D model, means that the inert solute enhances the formation of *HB*ed clusters. This enhancement requires energy of the order of the *HB* energy — hence the large negative enthalpy (and energy) of solvation. The entropy of solvation is usually interpreted by invoking the concept of *structure* or *order* in the solvent. However, from the exact entropy-enthalpy compensation principle, one can conclude that whatever the contribution to ΔH_s^* due to structural changes in the solvent, the same is true for the contribution to the entropy of solvation. Therefore, it is not necessary to invoke the concept of structure (or order) to explain the unusual entropy of solvation.

3.10. Applications of Two-Dimensional Models

The two-dimensional water-like model referred to as the BN2D model described in Sec. 2.6 has also been applied to aqueous solutions of simple *LJ* solute particles.

Two preliminary results obtained by solving the Percus–Yevick equations for a mixture of water-like solvent and Lennard–Jones solute are⁵⁷:

- (i) The preferential orientation of a water molecule near a solute molecule is such that the water molecule does not orient any of its “arms” towards the solute. In other words,

⁵⁷Ben-Naim (1971, 1972abc).

the water-like molecules do not lose their capability of hydrogen-bond formation along the three arms even when they are adjacent to a solute molecule.

- (ii) With some experimentation with the model's parameters of the model, it was found that the height of the first peak of the solute-solute pair correlation function increases as the *HB* energy of the water-like particles increases. This aspect will be further discussed in Chapter 4.

The application of the BN2D model to aqueous solutions was extended by Andaloro and Sperandeo-Mineo (1990). They carried out a Monte Carlo simulation on a system of water-like particles and *LJ* solutes with diameter $\sigma = 0.7$ and energy parameter $\varepsilon/k_B T = -0.5$ (with $\varepsilon_{HB}/k_B T = -5.0$). The radial distribution function for the water-like particles was very similar to that obtained earlier (see Fig. 2.42): a first relatively weak peak at the distance of $R \approx 0.7-0.8$; a second strong peak at $R = R_{HB} = 1.0$ (which was chosen as the unit of length in this work, and corresponds to the *HB* distance); a third peak at $R \approx 1.7-1.8$, as expected, corresponding to triplets of molecules engaged successively in hydrogen bonding. These findings support the idea that the correlation between particles in water-like systems propagate through hydrogen bondings rather than by "filling of space" between the molecules. The solute-solute pair correlation function showed a first peak at about $R = 0.7-0.8$ corresponding to the diameter of the *LJ* particles. Because of the small number of solute particles, they could not obtain clear-cut second or third peaks.

An important result that corroborates an earlier finding⁵⁸ is the distribution of binding energy x_{BE} discussed in Sec. 2.3. This distribution shows a clear-cut resolution into four peaks corresponding to particles engaged in zero, one, two, and three *HB*s. Adding a solute to the water-like solvent enhances the

⁵⁸Ben-Naim (1974).

peaks in the distribution x_{BE} corresponding to fully hydrogen-bonded particles. This corroborates again the earlier contention that a simple solute would enhance those quasi-components having low local density, which in this case are the hydrogen-bonded molecules.

An extensive study of the BN2D model was carried out by Dill and co-workers. These works were recently reviewed by Dill *et al.* (2005). We shall mention only a few of their results.

Silverstein *et al.* (1998, 1999) performed a Monte Carlo simulation of a system of pure water as well as for aqueous solutions of LJ particles. They examined the angular distribution of a water-like particle near the solute. As expected, the water molecules “straddle” the solute to avoid the loss of hydrogen bonds. A very detailed study of the solvation of simple solutes in the 2-D model was undertaken by Silverstein *et al.* (1999). A more recent investigation of this model was carried out by Southall and Dill (2000, 2002), Southall *et al.* (2002), and more recently by Urbic *et al.* (2002, 2003, 2004, 2007). The application of a 2-D model of water was extended to solvation of polymers.⁵⁹

As in the one-dimensional model, a great deal of insight into the molecular reasons for the outstanding properties of water has been achieved by this relatively simple model. In my opinion, the overwhelming success of this BN2D model is mainly due to the fact that the *principle* was a built-in feature of the model. The interested reader is referred to an extensive review by Dill *et al.* (2005).

3.11. Applications of Three-Dimensional Models

In this section, I shall present only a few results obtained by simulation methods, which in my opinion are important to

⁵⁹Bruscolini and Casetti (2001).

understanding the thermodynamics of aqueous solutions of simple solutes.

- (i) Geiger *et al.* (1979) carried out a molecular dynamic simulation of water-like particles and Lennard–Jones solutes. They found that the orientation of the water molecules surrounding the solute is such that no “arm” of the water molecule is directed towards the inert solute. This result is as expected. Water molecules orient themselves in such a way that their capability of hydrogen bonds with other water molecules is not lost.
- (ii) The distribution of binding energy for water-like molecules is almost uni-modal. Adding the solute causes a shift of the curve leftwards, i.e. towards lower binding energy. This is clear-cut evidence that inert solutes cause an increase in the average interaction energy among water molecules. This may also be interpreted as a structural enhancement induced by the solute. Monte Carlo calculations by Alagona and Tani (1980) confirmed that argon promotes the structure of water.
- (iii) An interesting case of solvation of a molecule with internal rotational degrees of freedom is the case of *n*-butane. Several calculations⁶⁰ have shown that while the trans-conformation is more stable in the gaseous phase, the gauche conformation is the more likely conformation in water. This may be interpreted as an intra-molecular hydrophobic interaction (see also Chapter 4).
- (iv) Recently, Peter and van der Vegt (2007) calculated the solvation enthalpies of inert solutes. They focused on the contribution of the “modification of solvent-solvent

⁶⁰Rosenberg *et al.* (1982ab), Jorgensen (1982ab), Jorgensen and Buckner (1987), Tobias and Brooks (1990), Zichi and Rossky (1986), Imai and Hirata (2003), and Travis and Searles (2006).

interactions (solvent reorganization)” to the solvation enthalpy. They found a linear relationship between the latter quantity and the solvation volumes of various solvents.

- (v) An extensive investigation of the hydration of non-polar solutes in water was undertaken by Guillot and Guissani (1993) and Guillot *et al.* (1991). The “structure” of these solutions as measured in terms of pair distribution functions as well as the solvation quantities were calculated from molecular dynamics. These authors also investigated the whole range of temperatures from the triple point to the critical point of water.
- (vi) Finally, it is worthwhile mentioning that Arthur and Haymet (1999) used the information theory approximation along with simulation to calculate the solvation properties of simple solutes both in 2-D and 3-D models for water. In the case of the 2-D model, they found that the two methods give very similar results for the solvation Gibbs energy. The agreement between the two methods was less satisfactory for the entropy of solvation and very poor for the solvation heat capacity.

To summarize this section and the whole chapter, we can pause to reflect on the merits of the various models suggested for water in 1-D, 2-D, and 3-D. In my opinion, the molecular reasons underlying the anomalous thermodynamics of solvation of inert solutes in water are now well understood. This situation has been arrived at mainly by studying simple molecular models of water. Further refinements of the models will certainly add more detail but no new insights into the molecular origins of the outstanding properties of aqueous solutions of inert solutes.

CHAPTER 4

Water with Two Solute Molecules; Hydrophobic Hydrophilic Phenomena

Personal Introduction

In 1969, I was asked by Ralph Horne to contribute a chapter to a book he was editing on aqueous solutions of inert gases. At that time, this was my “expertise,” as I have described in Chapter 3. I was also asked to include a section on hydrophobic ($H\phi O$) interactions. Very little was known on $H\phi O$ interactions at that time. There was, of course, the classic review article by Kauzmann (1959), and a few other papers.

Preparing to write those sections, I asked myself two questions: What are $H\phi O$ interactions, and what evidence exists to support the claim that these interactions are important in biochemical processes such as protein folding and protein-protein association?

Regarding the first question, there was the vague and qualitative description of $H\phi O$ interaction as a “tendency of non-polar solutes to adhere to each other.” This was later translated in terms of standard free energy of dimerization of some compounds such as carboxylic acids in water. That descriptive definition was not satisfactory and I felt a new and more precise definition was needed. The standard free energies of dimerization were known for molecules that dimerize. They dimerize because they form hydrogen bonds. Therefore, it was not clear which part of the standard free energy was due to the hydrogen

bonding and which was due to the $H\phi O$ interactions. There were no data on the “standard free energy of dimerization” of pure $H\phi O$ molecules. Therefore, I had reformulated the concept of $H\phi O$ interaction in terms of the potential of mean force (PMF) between two non-polar solutes in water. This function is related to the concept of standard free energy of dimerization. However, in contrast to the standard free energy of dimerization which could be measured experimentally only for solutes that form real dimers in water but are determined by both $H\phi O$ and $H\phi I$ groups (say, the methyl and the carboxylic groups of acetic acid), the PMF could be defined for any two non-polar solutes (say, methane molecules) in water but could not be measured. Methane, or other similar $H\phi O$ molecules, is sparingly soluble in water, and does not form dimers. Thus, although the definition of $H\phi O$ interactions in terms of the PMF turned out to be a useful one in later simulations and theoretical calculations, it was useless at that time for the actual determination of the strength of $H\phi O$ interactions.

In the early 1970s, while I was analyzing the statistical mechanical expression for the PMF between two simple solutes in water, I felt as if the theory indicated a way of measuring the strength of pure $H\phi O$ interaction. This was an awesome experience. Normally, one would tinker with the mathematical formulas of statistical mechanics to find a way of calculating some quantity which would eventually be compared with the corresponding experimental quantities. In this case, there were no experimental quantities that measure the strength of the $H\phi O$ interaction. Nevertheless, the theory itself was helpful in this case, not in calculating a quantity but rather in suggesting how to measure a quantity. This procedure is described in Sec. 4.4. Basically, it exploits the fact that one can separate the PMF into two parts: the direct and the indirect. The direct part depends only on the direct interactions between the two solutes.

This part was irrelevant to the problem of $H\phi O$ interaction. On the other hand, the indirect part, which was very relevant to the problem of $H\phi O$ interaction, is independent of the solute-solute interactions. Therefore, this part could be determined even at small separations that are inaccessible to real particles. From this realization, it was easy to relate the indirect part of the PMF to experimentally measurable quantities. The main idea was to “fool the solvent” by replacing two methane molecules at very short distance by a single ethane molecule.

Once we had a measure of “pure” $H\phi O$ interaction, we collected a large amount of information on these interactions: between two or more particles; the effect of temperature, pressure, the addition of solutes, low and high concentrations; and even in the entire range of compositions from pure water to pure ethanol or dioxane. An intense study of the PMF between two solutes in water ensued, both via simulation and using theoretical methods. It was generally believed that understanding $H\phi O$ interactions would lead to the understanding of protein folding as well as other biochemical processes.

In the late 1980s, however, while analyzing the solvent induced contributions to the free energy of protein folding and protein-protein association, my views shifted and were taken in two new directions. First, I realized that the quantity one should study was not the PMF between two solutes in water but the conditional PMF between two solutes attached to some backbone. (Similarly, the solvation Gibbs energy should be replaced by the conditional solvation Gibbs energy.) Thus, although the PMF between two solutes such as methane in water was interesting in the context of studying the properties of aqueous solutions, it was not so relevant to the $H\phi O$ contribution of, say, methyl groups to protein folding in real proteins. The newly defined concepts were the conditional solvation Gibbs energy (and the corresponding entropy, enthalpy, etc.) and the conditional PMF.

Both of these concepts were defined exactly as the solvation process and the PMF, but instead of pure water as the solvent, one must take into account that the water is perturbed by the presence of the backbone (BB). It was found that different BBs could have a significant effect on the size of the solvation free energy of the solute as well as the strength of the $H\phi O$ interaction.

Unfortunately, this realization was “on paper” only. There were no experimental data on either the conditional solvation quantities or on the conditional PMF. Once again, it was the theory which indicated how to measure these conditional quantities. The theory provided the guidance for extracting information on conditional $H\phi O$ interactions from the relevant experimental data.

While studying the conditional solvation and the conditional PMF by means of model compounds, I had made a quite astonishing discovery. This was the second time I was compelled to change my views about the $H\phi O$ interaction.

My overarching problem was to analyze the contribution of each amino acid side-chain to the free energy of the protein folding process (sometimes referred to as the thermodynamic driving force for protein folding). That was virtually impossible to do for all of the 20 amino acid side-chains. Therefore, I limited myself to the study of a few representatives of the side-chains: a methyl or ethyl group for a $H\phi O$ side-chain, and a hydroxyl or carbonyl group for a $H\phi I$ side-chain.

To my surprise, I found that contrary to the prevailing belief, the hydrophilic ($H\phi I$) rather than the $H\phi O$ interactions are probably the more important interactions in biochemical processes. In fact, both hydrophilic solvation and hydrophilic interactions were found to be stronger than the corresponding $H\phi O$ solvation and interactions. These findings were supported

by experimental data, theoretical calculations, and simulations. They suggested that perhaps the $H\phi O$ effects were not the most important contributions to the thermodynamic driving forces for biochemical processes. If this against-the-mainstream view is true, then we are thrown back to the pre- $H\phi O$ era when protein chemists believed that hydrogen bonding was crucial to the thermodynamic driving forces for biochemical processes, specifically in the formation of direct intramolecular hydrogen bonds in proteins. At that time, the contribution of HBin between groups of proteins in aqueous solutions was believed to be negligible. This belief led to the dismissal of the contribution from direct hydrogen bonding. It also ignored a whole array of possible contributions due to $H\phi I$ groups.

In my view, the “vacuum” created by the abandonment of the $H\phi I$ effects was filled by the $H\phi O$ effects. The study of the $H\phi O$ effects prevailed for over 40 years. It was only in the 1980s that the inventory argument which led to the dismissal of the $H\phi I$ effects was found to be fallacious. This paved the way (and perhaps opened researchers’ minds) for a rethink of the $H\phi I$ interactions and their contributions to biochemical processes. I shall discuss a few aspects of $H\phi I$ interactions in Secs. 4.8 and 4.12. The relevance of these interactions to biochemical processes will be deferred to a future book.

4.1. Introduction

In the previous chapter, we examined the properties of extremely dilute solutions. In this limit, we can ignore solute-solute interactions. From the formal theoretical point of view, it is sufficient to examine the case of one solute in a pure solvent (the solvent can be pure water or any mixture of solvents, but we exclude any other solutes in the solvent).

In this chapter, we go one step further and examine slightly more concentrated solutions such that pairwise solute-solute interactions are taken into account but not interactions among three or more solute molecules. From the formal theoretical viewpoint, it is sufficient to examine the properties of only two solute particles in the solvent (the solvent can be either pure water or a mixture of solvents).

The *formal theoretical* framework for studying deviations from dilute ideal solutions is embodied in the so-called virial expansion of the osmotic pressure (π), through the McMillan–Mayer (1945) theory of solutions:

$$\beta\pi = \rho_s + B_2^* \rho_s^2 + B_3^* \rho_s^3 + \cdots \quad (4.1.1)$$

This expansion is completely analogous to the virial expansion of the pressure,¹ where ρ_s is the number density of the solute and B_k^* is the k th virial coefficient of the osmotic pressure. There is a complete analogy between virial expansion of the pressure in the density in the gaseous phase and the expansion of the osmotic pressure in the solute density in solution (McMillan and Mayer, 1945). The statistical mechanical expression for B_2^* as obtained from the McMillan–Mayer theory is

$$\begin{aligned} B_2^* &= \lim_{\rho_s \rightarrow 0} \left\{ -\frac{1}{2} \int_0^\infty [g_{ss}(R) - 1] 4\pi R^2 dR \right\} \\ &= -\frac{1}{2} \int_0^\infty [g_{ss}^0(R) - 1] 4\pi R^2 dR \end{aligned} \quad (4.1.2)$$

where $g_{ss}(R)$ is the solute-solute pair correlation function in the solvent. The limit is taken at constant temperature and chemical potential of the solvent.

¹See, for example, Hill (1960) and Ben-Naim (2006).

The corresponding expression for the second virial coefficient in the gaseous phase of pure s is

$$\begin{aligned} B_2 &= \lim_{\rho_s \rightarrow 0} \left\{ -\frac{1}{2} \int_0^\infty [g_{ss}(R) - 1] 4\pi R^2 dR \right\} \\ &= -\frac{1}{2} \int_0^\infty \{\exp[-\beta U(R) - 1]\} 4\pi R^2 dR \end{aligned} \quad (4.1.3)$$

where $U(R)$ is the pair potential between two solutes.

In this chapter, we shall discuss the function $g_{ss}^0(R)$, the so-called solute-solute pair correlation function at infinite dilution. This function is related to the potential of mean force (PMF) by

$$W_{ss}(R) = -k_B T \ln g_{ss}(R) \quad (4.1.4)$$

In Sec. 4.3, we shall discuss the relation between $W_{ss}(R)$ and the problem of the hydrophobic interaction [or the hydrophobic bond as originally coined by Kauzmann (1959)].² In fact, the problem of the hydrophobic interaction was the main motivation for the study of the function $W_{ss}(R)$ in water. In this chapter, however, the emphasis will be not so much on the relevance of the $H\phi O$ (or $H\phi I$) interactions to biological systems, but as an aspect of the outstanding properties of water; here, water is perturbed by inserting two solute particles. In the remaining part of this section, we shall present a brief description of the motivation for studying hydrophobic interactions.³

It is well-known that a particular conformation of a biopolymer maintains its stability only in aqueous solutions. The addition of, say, 30% alcohol causes a conformational change that eventually leads to the process of denaturation, a very complex process involving the combination of many factors such

²As we noted in Chapter 3, the terms “hydrophobic” and “hydrophilic” solutes are not strictly antonyms; the same is true of $H\phi O$ and $H\phi I$ interactions, which are used in this context as antonyms.

³For more details, see Ben-Naim (1974).

as hydrogen bonding, ionic interactions, and van der Waals interactions between the various residues of the polymer. It has been conjectured that the tendency of the non-polar groups (such as methyl or ethyl groups attached to the amino acids) to avoid the aqueous environment is one of the major reasons for the stabilization of the native conformation of the biopolymer. This is shown schematically in the process depicted in Fig. 4.1. There are two effects that were studied under what is now referred to as the $H\phi O$ effect. One is when side-chains are *completely* removed from the aqueous medium and transferred to the interior of the polymer, where they are exposed to an environment similar to that of a typical non-polar solvent (see, for example, group R_5 in Fig. 4.1). The second is the correlation between the two $H\phi O$ groups. For instance, groups R_1 and R_2 are initially independently solvated; in the folded form these two groups become correlated.

The transfer of side-chains from being exposed to the solvent into the interior of the protein may be viewed as a reversal of the transfer of a non-polar solute from an organic liquid to water. However, in this chapter, we are not interested in the *solvation* of a non-polar solute in a solvent but rather in the pair interactions between two side-chains of a protein that are initially

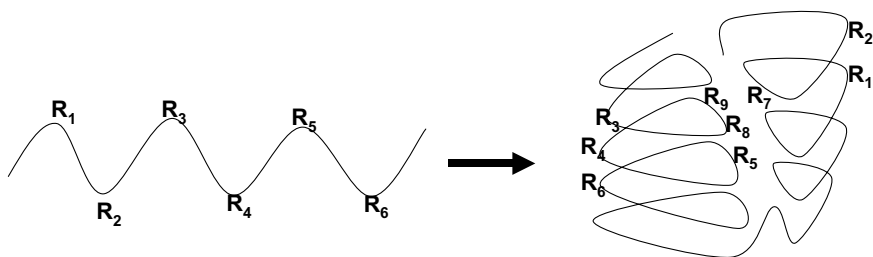


Fig. 4.1 Schematic process of protein folding. Side-chains of amino acids (R_i) are initially exposed to the solvent. In the folded form some groups (e.g. R_5 and R_8) are buried in the interior of the protein; others might be pair-correlated (e.g., R_1 and R_2), or triply-correlated (e.g. R_3 , R_4 and R_6).

far apart and in the final configuration become close to each other (see, for example, groups R_1 and R_2 in Fig. 4.1). The contribution of this pair of groups to the driving force for protein folding was originally reduced to the problem of studying the interaction between two solutes in water.⁴ Much of the ensuing research focused on the study of a system of two solutes in a solvent, which for $H\phi O$ solutes will be referred to as $H\phi O$ interactions (strictly, $H\phi O$ pair interactions). As we have pointed out in Sec. 3.3, the study of the solvation of a non-polar solute in water might not be relevant to the study of the contribution of $H\phi O$ groups that are transferred to the interior of the protein. The more relevant quantities are the *conditional* solvation quantities. Likewise, the study of two simple solutes in pure water might not be relevant to the study of the overall “driving force” for protein folding. Instead, one should study the *conditional PMF*, i.e. the *PMF* between two groups that are attached to the protein.

In the following sections of this chapter, we shall first review the experimental facts, then proceed to discuss some of the theoretical calculations of both $H\phi O$ and $H\phi I$ interactions.

4.2. The Experimental Evidence

Early in the 1960s, virtually nothing was known about the strength of the $H\phi O$ interactions. What was known was based on two kinds of experimental data that support the idea that $H\phi O$ interactions exist.

The first experimental quantity is the dimerization constant and the corresponding standard free energy of dimerization of carboxylic acids in various solvents (Schrier *et al.*, 1964; Schneider *et al.*, 1965; Moon *et al.*, 1965; Kunimitsu *et al.*, 1968). Consider the dimerization constants for association of

⁴Ben-Naim (1971, 1972b, 1974).

carboxylic acids:



for which we can write the equilibrium constant

$$K_D = [(\text{R-COOH})_2] / [\text{R-COOH}]^2 \quad (4.2.2)$$

where the square brackets stand for the molar concentration. (It is assumed that the system is dilute ideal with respect to both the monomer and the dimer.) One can envisage two possible configurations of these dimers: one involving a single hydrogen bond between the two monomers and the other, the cyclic dimer, involving two hydrogen bonds (Fig. 4.2).

The experimental findings are that the dimerization constants for a homologous series of carboxylic acids in water are much larger than the corresponding values in non-polar solutes. For example, K_D for acetic acid in water is about $160 \text{ cm}^3 \text{ mol}^{-1}$, whereas in CCl_4 , the value is $0.42 \text{ cm}^3 \text{ mol}^{-1}$ (Katchalsky *et al.*, 1951; Wenograd and Spurr, 1957). Furthermore, it is found that K_D in water increases with the chain length of the hydrocarbon residue (Mukerjee, 1965), whereas in non-polar solvents it is far less sensitive to variations of the hydrocarbon residue. These facts suggest that the dimers in water are of the form depicted

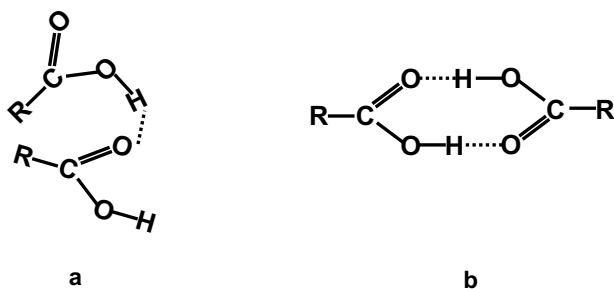


Fig. 4.2 Two possible configurations of dimers of carboxylic acid: (a) when the two alkyl groups (R) are near each other, and (b) when they are far apart.

in Fig. 4.2a, i.e. the two non-polar groups, R , are close to each other; and hence, they contribute to the dimerization constant. In a non-polar solvent, the dimers involve two HB s (Fig. 4.2b); the two alkyl groups are relatively far apart and therefore do not contribute to the dimerization constant.

Schrier *et al.* (1964) suggested the following method of extracting information on $H\phi O$ interactions from these data.⁵ Suppose that the standard free energy of dimerization ($\Delta\mu_D^0 = -RT \ln K_D$) could be split into two contributions:

$$\Delta\mu_D^0 = \Delta\mu_{H\phi O}^0 + \Delta\mu_{HB}^0 \quad (4.2.3)$$

where the first term on the right-hand side of (4.2.3) is the contribution due to the hydrophobic interaction ($H\phi O$), and the second term is due to the hydrogen bond (HB) formation. Furthermore, one assumes that the standard free energy of dimerization of formic acid is due only to the hydrogen bond formation, i.e.

$$\Delta\mu_D^0(\text{H-COOH}) = \Delta\mu_{HB}^0(\text{H-COOH}) \quad (4.2.4)$$

The third assumption made is that variations in the values of $\Delta\mu_D^0$ are attributed only to variations in $\Delta\mu_{H\phi O}^0$, i.e. the contribution of the quantity $\Delta\mu_{HB}^0$ in (4.2.3) is independent of the chain length of the hydrocarbon. Hence, the following equality is assumed to hold for any R :

$$\Delta\mu_{HB}^0(R\text{-COOH}) = \Delta\mu_{HB}^0(\text{H-COOH}) \quad (4.2.5)$$

From (4.2.3) to (4.2.5), one concludes that

$$\begin{aligned} \Delta\mu_{H\phi O}^0(R\text{-COOH}) \\ = \Delta\mu_D^0(R\text{-COOH}) - \Delta\mu_D^0(\text{H-COOH}) \end{aligned} \quad (4.2.6)$$

Schrier *et al.* calculated the values of $\Delta\mu_{H\phi O}^0$ for a series of carboxylic acids. The results are shown in Table 4.1. From the

⁵This work was recently extended by Chen *et al.* (2007).

Table 4.1. Values of $\Delta\mu_{H\phi O}^0$ (R-COOH) defined in (4.2.6) in kcal mol⁻¹ at 25°C^a

CH ₃ -COOH	-0.8
CH ₃ CH ₂ -COOH	-1.1
CH ₃ CH ₂ CH ₂ -COOH	-1.4
C ₆ H ₅ CH ₂ -COOH	-1.6

^a From Schrier *et al.* (1964).

values in this table, we can conclude that the $H\phi O$ interaction increases with the chain length of the hydrocarbon residue.

One should be careful when adopting these values as measures of $H\phi O$ interactions. The main source of uncertainty of the meaning of these quantities is the assumption made in (4.2.3). Note that our main interest at this stage is the $H\phi O$ interaction between two simple non-polar solutes in water. Since the carboxyl groups are polar, they might alter the properties of water around the non-polar groups, i.e. the two non-polar groups “see” each other through a medium which is already perturbed by the presence of the polar groups. Therefore, the extent of attraction between the two alkyl groups could be different from that in pure water. One may argue that the environment around side-chain non-polar groups attached to the biopolymer is also not immersed in pure water.⁶ This is certainly true, and we shall return to this problem in Sec. 4.5. However, here we are concerned with isolating the “pure” $H\phi O$ interaction, i.e. with the problem of the interaction between two $H\phi O$ solutes in a solvent.

From the data in Table 4.1, it is not clear which is the medium of the interaction between the two alkyl groups; is it pure water or water, the properties of which were altered by the presence of

⁶Wetlaufer *et al.* (1964), Tanford (1962), Nozaki and Tanford (1963), and Nemethy (1967).

the polar group? It is also not clear what the distance is between the two alkyl groups.

The second experimental quantity relevant to the problem of $H\phi O$ is the second virial coefficient B_2^* in the density expansion of the osmotic pressure.⁷ Consider the statistical mechanical expression for B_2^* given in (4.1.2), which for simplicity of notation is written as

$$B_2^* = -\frac{1}{2} \int_0^\infty [g_{ss}^0(R) - 1] 4\pi R^2 dR \quad (4.2.7)$$

where g_{ss}^0 denotes the limit of the solute-solute pair correlation function at infinite dilution. For spherical particles, one can extract some information on $H\phi O$ from (4.2.7) as follows. Suppose that σ is the effective diameter of the solute particles. Then, for $R \leq \sigma$, the pair correlation function is practically zero and we can rewrite (4.2.7) as

$$\begin{aligned} B_2^* &= -\frac{1}{2} \int_0^\sigma (-4\pi R^2) dR - \frac{1}{2} \int_\sigma^\infty [g_{ss}^0(R) - 1] 4\pi R^2 dR \\ &= \frac{1}{2} (4\pi\sigma^3/3) - A_2^* \end{aligned} \quad (4.2.8)$$

In this manner, we have split B_2^* into two contributions. The first results from the strongly repulsive region $R \leq \sigma$ and is proportional to the volume of the solute. The second results from both the attractive and the repulsive regions. The precise regions of attraction and repulsion can be identified through the form of the potential of average force between the two solute particles. A schematic description of this function is given in Fig. 4.3. A positive slope of $W_{ss}(R)$ corresponds to attraction; a negative slope corresponds to repulsion. Thus, although it is clear that the first term in (4.2.8) results from a repulsive region, the second term includes alternating regions of attraction and

⁷Kozak *et al.* (1968). This work was extended by Matteoli and Lepori (1981).

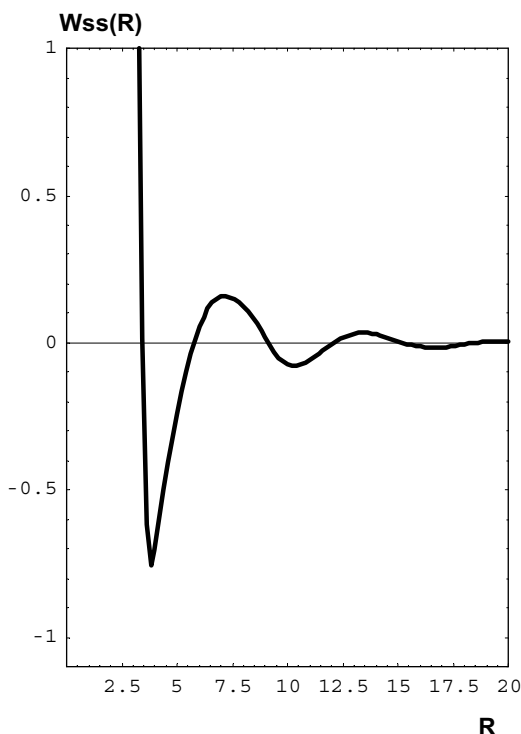


Fig. 4.3 Schematic illustration of the potential of mean force (PMF) between two solute molecules in a solvent.

repulsion. The first term depends only on the size of the solute; the second depends on the properties of both solute and the solvent molecules.

Since the major contribution to A_2^* comes from the area under the first peak of $g_{ss}^0(R)$, it is expected that this quantity is positive. In a qualitative manner, it can serve as a measure of the overall correlation, or “affinity,” between two solute particles in the region $\sigma < R < \infty$. This is the basis of the work of Kozak *et al.* (1968). In practice, one cannot obtain values of B_2^* for simple solutes such as argon or methane since their solubilities are very low. Therefore, one must apply this method for more complex solutes such as alcohols, amines, amino acids, etc.

The generalization of the splitting of B_2^* as in (4.2.8) for such molecules is not simple however. First, there is no clear-cut distinction between a purely repulsive region which produces a term proportional to the volume of the solute molecules and an attractive region. Kozak *et al.* assumed that instead of the first term on the right-hand side of (4.2.8), one may take a quantity which is proportional to the partial molar volume of the solute at infinite dilution.

The second difficulty involves the interpretation of the second term in (4.2.8) as a measure of the extent of $H\phi O$. This term will now include many regions of attraction and repulsion, some of which are due to the interaction between the polar groups such as OH, COOH, or NH_2 . The identification of the contribution of the $H\phi O$ groups to A_2^* is difficult, if not impossible. In spite of these difficulties, computed values of A_2^* for a homologous series of, say, alcohols show that it is positive and the values increase with the chain length of the solute. This trend is similar to that for the results obtained from the study of dimerization constants as discussed above.

Thus far we have mentioned only two experimental facts having the most direct bearing on the problem of the $H\phi O$ interaction. There are other experimental data from which it is more difficult to extract quantitative information on $H\phi O$ interactions. Examples are the comparison of the behavior of various synthetic polymers, such as polymethacrylic acid with polyacrylic acid (Eliassaf and Silberberg, 1959; Priel and Silberberg, 1970), or the study of alternating co-polymers with various side-chain non-polar groups (Dubin and Strauss, 1970). These and other experimental evidence were summarized by Ben-Naim (1980).

In the next section, we shall define the concept of the $H\phi O$ interaction in statistical mechanical terms. This will lead us naturally to a measure of the "pure" $H\phi O$ interaction.

4.3. Redefinition of the $H\phi O$ Interaction

In this section, we formulate the problem of the $H\phi O$ interaction in statistical mechanical terms. We shall be working in the T, V, N ensemble. The corresponding treatment in the T, P, N ensemble is similar but slightly more complicated.

Consider a system of N solvent molecules (we use the subscript w for water or any other solvent molecule) and two simple spherical solute molecules at fixed positions $\mathbf{R}_1$ and $\mathbf{R}_2$, the system being in a volume V and at a temperature T . For simplicity of notation, we reserve the first two indices $i = 1, 2$ for the solutes and the remaining indices $i = 3, 4, \dots, N + 2$ for the solvent molecules. The Helmholtz energy of such a system is given by

$$\begin{aligned} & \exp[-\beta A_{N+2}^I(\mathbf{R}_1, \mathbf{R}_2)] \\ &= \left(q_w^N q_s^2 / N! \right) \int \cdots \int d\mathbf{X}^N \exp[-\beta U_N(\mathbf{X}^N) \\ & \quad - \beta U(\mathbf{R}_1, \mathbf{R}_2) - \beta U(\mathbf{X}^N | \mathbf{R}_1, \mathbf{R}_2)] \end{aligned} \quad (4.3.1)$$

where q_w^N and q_s^2 are the internal partition functions for a single solvent and the solute molecules, respectively. We have also included in q_w the momentum partition function and a normalization constant $8\pi^2$. Note that since the two solute particles are assumed to have a fixed position, q_s does not include a momentum partition function. The total potential function of the whole system is

$$\begin{aligned} & U_{N+2}(\mathbf{X}^N, \mathbf{R}_1, \mathbf{R}_2) \\ &= U_N(\mathbf{X}^N) + U(\mathbf{R}_1, \mathbf{R}_2) + U(\mathbf{X}^N | \mathbf{R}_1, \mathbf{R}_2) \end{aligned} \quad (4.3.2)$$

where $U_N(\mathbf{X}^N)$ denotes the potential energy of interaction among the N solvent molecules for the specific configuration $\mathbf{X}^N$. The direct pair potential between the two solute particles is denoted by $U(\mathbf{R}_1, \mathbf{R}_2)$, and the total interaction

between the solvent molecules at $\mathbf{X}^N$ and the two solute particles at $\mathbf{R}_1, \mathbf{R}_2$ is denoted by $U(\mathbf{X}^N | \mathbf{R}_1, \mathbf{R}_2)$. The integration (4.3.1) extends over all the configurations of the solvent molecules $\mathbf{X}^N = \mathbf{X}_3, \mathbf{X}_4, \dots, \mathbf{X}_{N+2}$. Equation (4.3.1) does not involve the assumption of pairwise additivity for the solvent molecules. However, later we will require that the last term on the right-hand side of (4.3.2) be represented by a sum of the form

$$U(\mathbf{X}^N | \mathbf{R}_1, \mathbf{R}_2) = \sum_{k=1}^2 \sum_{i=3}^{N+2} U(\mathbf{X}_i, \mathbf{R}_k) \quad (4.3.3)$$

where $U(\mathbf{X}_i, \mathbf{R}_k)$ is the solute-solvent pair potential.⁸

The Helmholtz energy of the two solute particles at fixed positions $\mathbf{R}_1$ and $\mathbf{R}_2$ in vacuum is

$$\exp[-\beta A_2^g(\mathbf{R}_1, \mathbf{R}_2)] = q_s^2 \exp[-\beta U(\mathbf{R}_1, \mathbf{R}_2)] \quad (4.3.4)$$

and the Helmholtz energy of the pure solvent is

$$\exp(-\beta A_N^l) = (q_w^N / N!) \int \cdots \int d\mathbf{X}^N \exp[-\beta U_N(\mathbf{X}^N)] \quad (4.3.5)$$

Consider the work associated with transferring the two solute particles from fixed positions in vacuum to fixed positions in the liquid⁹ (Fig. 4.4):

$$\Delta A^*(\mathbf{R}_1, \mathbf{R}_2) = A_{N+2}^l(\mathbf{R}_1, \mathbf{R}_2) - A_N^l - A_2^g(\mathbf{R}_1, \mathbf{R}_2) \quad (4.3.6)$$

⁸Note that we use the same letter, U , for different pair potentials. We refrain from using additional subscripts to indicate the species involved whenever this is clear from the argument. Here, $\mathbf{X}_i$ is always the configuration of a *solvent* molecule, whereas $\mathbf{R}_k$ refers to a solute molecule.

⁹We use here $\mathbf{R}_1$ and $\mathbf{R}_2$ for the positions of the solute particles in the two phases. The important requirement is, of course, that the distance $R = |\mathbf{R}_2 - \mathbf{R}_1|$ be the same in the two phases. The quantity $\Delta A^*(\mathbf{R}_1, \mathbf{R}_2)$ is essentially the solvation Gibbs energy for the pair of solutes at a specific distance R .

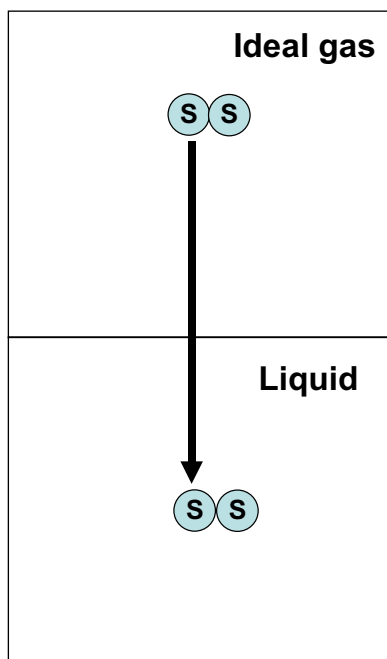


Fig. 4.4 The process of solvation of a pair of solutes.

The corresponding statistical mechanical expression is

$$\begin{aligned}
 & \exp[-\beta \Delta A^*(\mathbf{R}_1, \mathbf{R}_2)] \\
 &= \frac{\int \cdots \int d\mathbf{X}^N \exp[-\beta U_N(\mathbf{X}^N) - \beta U(\mathbf{X}^N | \mathbf{R}_1, \mathbf{R}_2)]}{\int \cdots \int d\mathbf{X}^N \exp[-\beta U_N(\mathbf{X}^N)]} \\
 &= \left\langle \exp[-\beta U(\mathbf{X}^N | \mathbf{R}_1, \mathbf{R}_2)] \right\rangle \quad (4.3.7)
 \end{aligned}$$

On the right-hand side of (4.3.7) we have an average over all the configurations of the solvent molecules. It is important to realize that the internal properties and the pair potential of the solutes do not appear in (4.3.7). The effect of the solutes on the solvent enters only through the “field of force” that the solute produces, i.e. $U(\mathbf{X}^N | \mathbf{R}_1, \mathbf{R}_2)$. This property will later be

exploited to obtain a relation between the $H\phi O$ interaction and experimental quantities.

Next, consider the work required to bring the two solute particles from fixed positions at infinite separation from each other to the final configuration $\mathbf{R}_1, \mathbf{R}_2$, the process being carried out within the liquid keeping T and V constant. From (4.3.1), we have

$$\begin{aligned} & \exp \{ -\beta [A_{N+2}^I(\mathbf{R}_1, \mathbf{R}_2) - A_{N+2}^I(R = \infty)] \} \\ &= \frac{\int \cdots \int d\mathbf{X}^N \exp [-\beta U_N(\mathbf{X}^N) - \beta U(\mathbf{R}_1, \mathbf{R}_2) - \beta U(\mathbf{X}^N | \mathbf{R}_1, \mathbf{R}_2)] }{\int \cdots \int d\mathbf{X}^N \exp [-\beta U_N(\mathbf{X}^N) - \beta U(\mathbf{X}^N | R = \infty)] } \end{aligned} \quad (4.3.8)$$

where $R = \infty$ indicates a configuration $(\mathbf{R}_1, \mathbf{R}_2)$ for which $R = |\mathbf{R}_2 - \mathbf{R}_1| = \infty$.

For any configuration of the two solutes $\mathbf{R}_1$ and $\mathbf{R}_2$, we define the quantity $\delta A(\mathbf{R}_1, \mathbf{R}_2)$ by

$$\begin{aligned} & \exp [-\beta \delta A(\mathbf{R}_1, \mathbf{R}_2)] \\ &= \frac{\int \cdots \int d\mathbf{X}^N \exp [-\beta U_N(\mathbf{X}^N) - \beta U_N(\mathbf{X}^N | \mathbf{R}_1, \mathbf{R}_2)] }{\int \cdots \int d\mathbf{X}^N \exp [-\beta U_N(\mathbf{X}^N) - \beta U(\mathbf{X}^N | \infty)] } \end{aligned} \quad (4.3.9)$$

Hence, from (4.3.8) and (4.3.9), we have

$$\begin{aligned} \Delta A^I(R) &= A_{N+2}^I(\mathbf{R}_1, \mathbf{R}_2) - A_{N+2}^I(R = \infty) \\ &= U(\mathbf{R}_1, \mathbf{R}_2) + \delta A(\mathbf{R}_1, \mathbf{R}_2) \end{aligned} \quad (4.3.10)$$

Thus, the total work $\Delta A^I(R)$ required to bring the two solutes from fixed positions at infinite separation to a distance R is split in (4.3.10) into two parts. The first is the direct work against the solute-solute pair potential, and the second is the indirect work resulting from the presence of the solvent.

We can now formulate the problem of the $H\phi O$ interaction in terms of the function $\Delta A^I(R)$. Suppose we compare this

function for a given pair of solutes in two different solvents, water and non-aqueous solvent. The question is whether this function has a notably lower minimum at some separation $R \approx \sigma$ (σ being the diameter of the solute) in water as compared to other solvents.

A glance at (4.3.9) shows that the direct pair potential $U(\mathbf{R}_1, \mathbf{R}_2)$ is totally irrelevant to our problem. The *direct* interactions contribute to the total work $\Delta A^I(R)$, but this part is the same in all the solvents; therefore, we need to focus only on $\delta A(R)$. If there exists any anomaly in water, it must show up in the *indirect* part of the work $\delta A(R)$. It was Kirkwood¹⁰ who first stressed the point that more attention should be paid to the role of the solvent, i.e. water, than to the direct van der Waals attraction in establishing any excessive tendency for the two solutes to adhere to each other in aqueous media. It is for this reason that we shall focus our study on the quantity $\delta A(\mathbf{R}_1, \mathbf{R}_2)$ in connection with the problem of $H\phi O$.¹¹

We now turn to a different, though equivalent formulation of the problem. To do this, we use the following two identities¹²:

$$\begin{aligned} & \exp\{-\beta[A_{N+2}^I(R) - A_{N+2}^I(R = \infty)]\} \\ & = g_{ss}(R)/g_{ss}(R = \infty) \end{aligned} \quad (4.3.11)$$

$$g_{ss}(R) = y_{ss}(R) \exp[-\beta U(R)] \quad (4.3.12)$$

where $g_{ss}(R)$ is the solute-solute pair correlation function.

In the first relation, we may take $g_{ss}(R = \infty) = 1$, assuming that we have already taken the infinite-system-size limit of $g_{ss}(R)$. Relation (4.3.11) tells us that in order to study the work

¹⁰Kirkwood (1954).

¹¹In this chapter, we use quantity δA mainly for the "hydrophobic interaction." Clearly, this quantity can also apply to any other solvent for which the term "solvophobic interaction" may be more appropriate. Also, this term applies to any type of solutes. We shall also use it for hydrophilic interactions in Sec. 4.8.

¹²See Ben-Naim (1974, 2006).

required to bring the two solute particles from infinite separation to a distance R , it is sufficient to study the solute-solute pair correlation function $g_{ss}(R)$. The question can now be stated as follows. Having a system with two *free* solute particles, what is the probability density of finding these particles at a distance $R \approx \sigma$, and is this probability density notably larger in water than in other solvents?

It is important to realize that the two formulations of the problem of the $H\phi O$ interaction apply to two different systems. In the first we have two solute particles at *fixed* positions in the system, and we search for the Helmholtz energy of the whole system as a function of R . In the second the two solute particles are assumed to be *free* so that they can wander about in the system, and the relevant question involves the probability of finding the two particles at some distance $R \approx \sigma$.¹³

Relation (4.3.12) shows how to separate the direct and the indirect contributions to $g_{ss}(R)$. Suppose that we compare two solvents l and f , and we are interested in the pair correlation functions $g_{ss}^l(R)$ and $g_{ss}^f(R)$ for the same solute in the two solvents. From (4.3.12), we obtain

$$\frac{g_{ss}^l(R)}{g_{ss}^f(R)} = \frac{y_{ss}^l(R)}{y_{ss}^f(R)} \quad (4.3.13)$$

Therefore, instead of studying the ratio of the g_{ss} , we can equivalently study the ratio of the y_{ss} . The latter is more convenient since this function is well behaved in the entire region $0 < R < \infty$, even for hard spheres.¹⁴

Finally, from (4.3.9), (4.3.10), and (4.3.12) we obtain

$$y_{ss}(R) = \exp[-\beta\delta A(R)] \quad (4.3.14)$$

¹³Note that $g_{ss}(R)$ is not a probability. The ratio of $g_{ss}(R)$ in two solvents having the same density of the solute is equal to the ratio of probabilities.

¹⁴For more details, see Ben-Naim (1974).

In the following sections, we will find it more convenient to study the function $\delta A(R)$, or equivalently the function $\gamma_{ss}(R)$, to obtain a measure of $H\phi O$ interactions.

4.4. A Simple Measure of the Strength of the “Pure” $H\phi O$ Interaction

Consider the quantity $\delta A(\mathbf{R}_1, \mathbf{R}_2)$ defined in (4.3.9), which we shall refer to as a measure of the strength of the $H\phi O$ interaction at the configuration $\mathbf{R}_1, \mathbf{R}_2$:

$$\begin{aligned}\delta A(\mathbf{R}_1, \mathbf{R}_2) &= A_{N+2}^l(\mathbf{R}_1, \mathbf{R}_2) - A_{N+2}^l(R = \infty) - U(\mathbf{R}_1, \mathbf{R}_2) \\ &= [A_{N+2}^l(\mathbf{R}_1, \mathbf{R}_2) - A_N^l - A_2^g(\mathbf{R}_1, \mathbf{R}_2)] \\ &\quad - [A_{N+2}^l(R = \infty) - A_N^l - A_2^g(R = \infty)] \\ &= \Delta A^*(\mathbf{R}_1, \mathbf{R}_2) - \Delta A^*(R = \infty)\end{aligned}\quad (4.4.1)$$

In the second form on the right-hand side, we have added and subtracted A_N^l , and we have also used relation (4.3.6). The last form on the right-hand side of (4.4.1) employs the definition of ΔA^* in (4.3.6).

Relation (4.4.1) suggests an interesting possibility for a connection between a measure of the $H\phi O$ interaction and experimental quantities. Suppose, for concreteness, that $R = |\mathbf{R}_2 - \mathbf{R}_1| = \sigma$. Thus, $\Delta A^*(R = \infty)$ is the Helmholtz energy change when transferring two solute particles from fixed positions in the gas phase to fixed positions in the liquid. In both phases, the separation between the two particles is infinite. Similarly, $\Delta A^*(R = \sigma)$ is the Helmholtz energy change for transferring the pair of particles at distance σ , as a single entity, into the liquid. Figure 4.5 shows a cyclic process relevant to the above

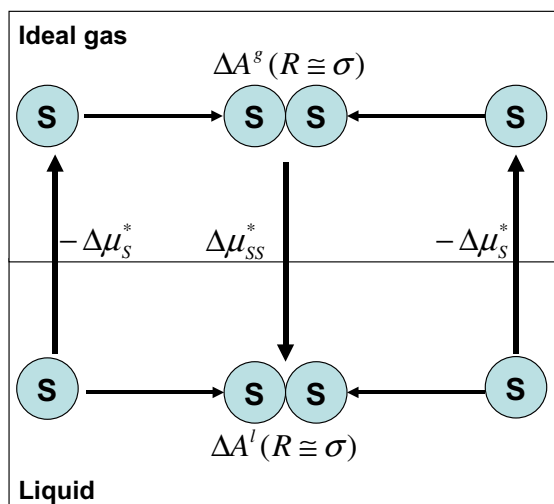


Fig. 4.5 A cyclic process relating the Gibbs (or Helmholtz) energy of “dimerization” in two phases to the solvation Gibbs (or Helmholtz) energies of the monomer s and the “dimer.”

discussion.¹⁵ We consider two solutes a and b at fixed positions in the liquid, but far apart brought to contact distance within the liquid. We denote the pair of solute particles at this separation by $a+b$. The corresponding total work associated with this process is $\Delta A^l(R)$ defined in (4.3.10). Alternatively, we may choose the “round trip” process as indicated in Fig. 4.5. First, we take the two solutes from the liquid into the gaseous phase, then we bring the two solutes to the distance σ , and finally we introduce the pair $a+b$ as a unit into the liquid. The total balance of work in the two routes is

$$\Delta A^l(\sigma) = \Delta A^g(\sigma) + \Delta\mu_{a+b}^* - \Delta\mu_a^* - \Delta\mu_b^* \quad (4.4.2)$$

or equivalently

$$\delta A(\sigma) = \Delta\mu_{a+b}^* - \Delta\mu_a^* - \Delta\mu_b^* \quad (4.4.3)$$

¹⁵In Fig. 4.5, we show the process for two solutes of the same kind, denoted s . The conclusions apply for any two molecules.

Thus, the study of the $H\phi O$ interaction is equivalent to the study of the difference in solvation Gibbs energies.

We now develop a convenient measure for $\delta A(R)$. We rewrite (4.3.9) for two solutes of the same type as

$$\begin{aligned} & \exp[-\beta\delta A(\mathbf{R}_1, \mathbf{R}_2)] \\ &= \left\langle \exp \left[-\beta U \left(\mathbf{X}^N \mid \mathbf{R}_1, \mathbf{R}_2 \right) \right] \right\rangle / \left\langle \exp \left[-\beta U \left(\mathbf{X}^N \mid R = \infty \right) \right] \right\rangle \end{aligned} \quad (4.4.4)$$

The most important aspect of this relation is the absence of the direct pair potential between the two solute particles. One may therefore envisage a hypothetical system of pure solvent subjected to an “external” field of force originating from two fixed points and given by $U(\mathbf{X}^N \mid \mathbf{R}_1, \mathbf{R}_2)$.¹⁶ In such a system, $\delta A(\mathbf{R}_1, \mathbf{R}_2)$ is the work required to move the two sources of the field of force from infinite separation to the final positions $\mathbf{R}_1$ and $\mathbf{R}_2$. This point of view will be used to obtain a measure of the $H\phi O$ interaction.

Suppose that we start with two simple solutes s and form a “dimer” D . Applying Eq. (4.4.4) for this case, we obtain

$$\delta A(R = \sigma) = \Delta\mu_D^* - 2\Delta\mu_s^* \quad (4.4.5)$$

Note that the “dimer” is not a *real* dimer but rather a virtual dimer. We simply define D as the two monomers at constant distance $R = \sigma$. If D is a real dimer, then one can measure the concentration of the dimers D in a dilute solution, hence, (4.4.5) could have been evaluated from the ratio of the equilibrium constant for dimerization in the gas and in the liquid phases,

¹⁶This “field of force” is sometimes referred to as cavities. The term “cavity” is correct only for hard-sphere solutes. In general, the “field of force” includes both repulsive and attractive parts.

namely

$$\Delta\mu_D^* - 2\Delta\mu_s^* = -k_B T \ln \left(\frac{\rho_D}{\rho_s^2} \right)_{eq}^l - k_B T \ln \left(\frac{\rho_D}{\rho_s^2} \right)_{eq}^g \quad (4.4.6)$$

Before we apply relation (4.4.6) to real molecules, we briefly discuss a similar cycle in the T, P, N ensemble. Consider the process of bringing two solute particles from fixed positions at infinite separation to some final separation R , the process being carried out at constant T, P, N . The total work is the change in the Gibbs energy:

$$\Delta G^l(R) = G_{N+2}^l(R) - G_{N+2}^l(R = \infty) = U(R) + \delta G(R) \quad (4.4.7)$$

where $\delta G(R)$ is referred to as the indirect part of the total work.

Repeating almost the same process carried out in this section, we arrive at a final expression for $\delta G(R)$:

$$\delta G(R) = \Delta\mu_{a+b}^* - \Delta\mu_a^* - \Delta\mu_b^* \quad (4.4.8)$$

Thus, the strength of the $H\phi O$ interactions from experimental quantities can be measured either by $\delta A(R)$ for a process at constant volume or by $\delta G(R)$ for the same process performed at constant pressure. The latter is advantageous for evaluating the entropy and enthalpy of the $H\phi O$ interactions from experimental quantities.

As we have noted above, neither the internal properties nor the direct solute-solute pair potential appears in (4.4.4). This fact is utilized in this and the following sections to obtain a simple and useful relation between $\delta A(R)$ and experimentally measurable quantities. To facilitate the grasping of the central idea of this section, it is useful to view (4.4.4) in a somewhat different light. Figure 4.6 shows two solute particles at $\mathbf{R}_1$ and $\mathbf{R}_2$ and a water molecule at $\mathbf{X}_w$. The only way the solvent “notices” the presence of the two solutes is through the “field of force” they produce.

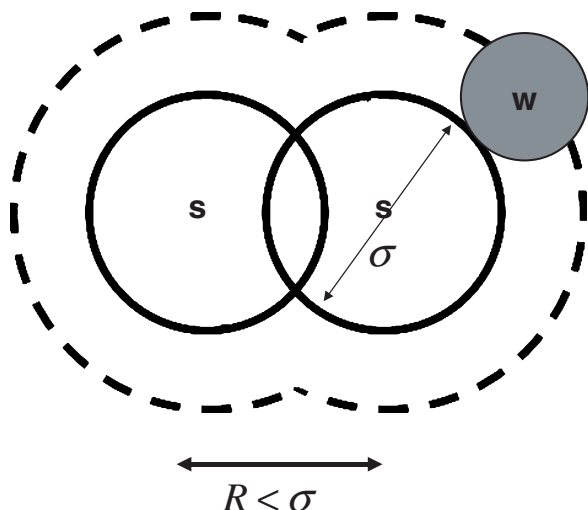


Fig. 4.6 Two solute particles s cannot penetrate into each other at distances shorter than the molecular diameter σ . However, two sources of fields of force can be moved to any distance R . In this figure, the dashed line shows the cavity produced by the two solutes. The cavity is only a part of the field of force produced by the repulsive solute-solute interaction.

Once we recognize that the presence of the solutes is revealed to the solvent only through the field of force they produce, we can forget about the real solutes and consider the following hypothetical system of N solvent molecules subjected to an “external” field of force equal to $U(\mathbf{X}^N | \mathbf{R}_1, \mathbf{R}_2)$. This point of view will prove to be quite rewarding. The main reason is that with two *real* solutes we must restrict ourselves to distances $R = |\mathbf{R}_2 - \mathbf{R}_1|$ which are larger than σ . With the two sources of fields of force, on the other hand, there are no restrictions on the distance R .

We recall that our main interest is focused on the properties of the *solvent* as a medium for the $H\phi O$ interaction. Therefore, from a theoretical point of view, since the solute diameter σ is a property of the *solutes*, there is no reason to restrict ourselves to $R \geq \sigma$ just because the two solutes repel each other at $R \leq \sigma$.

Relation (4.4.4) allows us to formulate the problem of the $H\phi O$ interaction at any distance $R \leq \sigma$.

Before elaborating on a specific example involving real solutes, it is instructive to work out a simple case. Consider a solvent of N hard spheres of diameter σ_w . The solute particles are also hard spheres of diameter σ_s . Clearly, the distance between these two solute particles cannot be smaller than σ_s . However, if we focus our attention on the function $\delta A(R)$ and since we know that this function is smooth and finite in the entire region $0 \leq R < \infty$, we can inquire about the value of $\delta A(R)$ for any distance $R \leq \sigma$. This point of view is equivalent to replacing the two solute particles by two *cavities* of appropriate size. While a system of two *HS* particles in a solvent is certainly different from a system with two cavities, from the point of view of the solvent the two systems are identical. In contrast to the two *HS* solutes, two cavities can be brought to any distance including $R = 0$. For this limiting case, expression (4.4.5) reduces to

$$\delta A(R = 0) = \Delta\mu_{HS}^* - 2\Delta\mu_{HS}^* = -\Delta\mu_{HS}^* \quad (4.4.9)$$

Thus, the indirect part of the work required to bring two *HS* particles from infinite separation $R = \infty$ to zero separation $R = 0$ is the same as the work required to eliminate a single cavity in the solvent. Equivalently, this is the work of the reversed solvation of an *HS* solute. The relevant cycle is shown schematically in Fig. 4.7.

In the aforementioned example, the field of force produced by the two *HS* solutes can be described in terms of simple cavities. With a little imagination, we can generalize this idea to real solute particles. We recall that in (4.4.4) the solvent molecules “feel” the presence of the solutes through the function

$$U(\mathbf{X}^N | \mathbf{R}_1, \mathbf{R}_2) = \sum_{k=1}^2 \sum_{i=3}^{N+2} U(\mathbf{X}_i, \mathbf{R}_k) \quad (4.4.10)$$

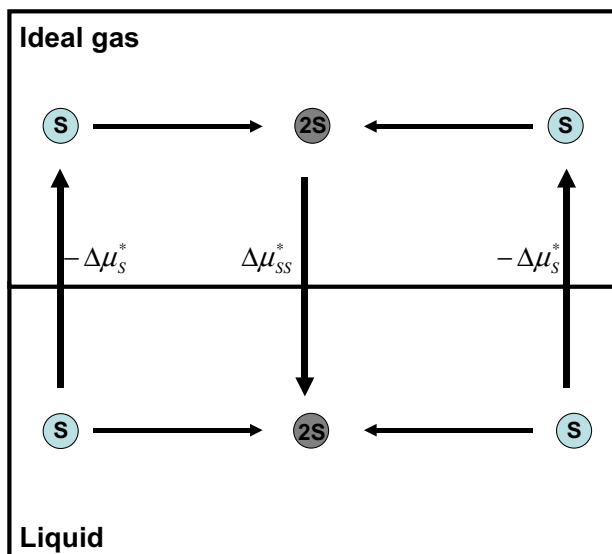


Fig. 4.7 Two real solutes brought from infinite separation to a distance $R = 0$ requires an infinite amount of work. However, two sources of fields of force can be brought to any distance, including $R = 0$. The hypothetical solute denoted "2S," is simply a solute with a field of force twice as large as the field of force of a single solute s .

We can imagine a system of pure solvent subjected to the "external" field of force defined by (4.4.10) and originating from the two sources $\mathbf{R}_1$ and $\mathbf{R}_2$. The $H\phi O$ interaction as formulated in (4.4.4) is equal to the (total) work required to move the two sources from infinite separation to the final separation R . Since now we are not dealing with real solutes, we can bring the two points $\mathbf{R}_1$ and $\mathbf{R}_2$ to any distance up to $R = 0$.

We now consider a specific example of two methane molecules. The solvation Helmholtz energy of methane $\Delta\mu_M^*$ is well known in water and in non-aqueous solutions (see Chapter 3). Suppose that we start with two methane molecules at infinite separation and replace them with the corresponding fields of force. Next, we move the centers of the fields of force from infinity to the final distance $R = \sigma_1 = 1.533 \text{ \AA}$, σ_1 being the

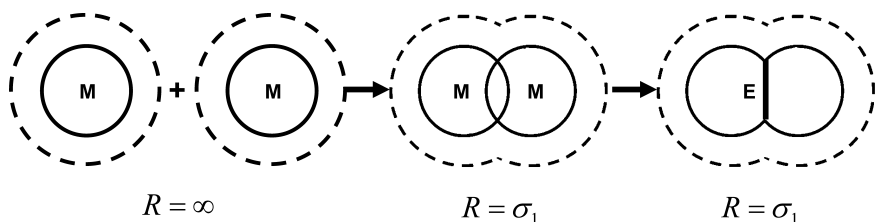


Fig. 4.8 Two methane molecules (M) are initially at infinite separation $R = \infty$. They are replaced by their fields of force (here, schematically depicted by the dashed lines) and brought to a distance $R = \sigma_1$. At this stage the two fields of force are replaced by a field of force of an ethane molecule.

carbon-carbon distance in the ethane molecule. This process is depicted in Fig. 4.8. The essential approximation introduced into the theory is that the field of force produced by the two methane molecules at $R = \sigma_1$ is approximately the same as that produced by a single ethane molecule placed at the same positions (see Fig. 4.8). Mathematically, this approximation is written as

$$U(\mathbf{X}_i, \mathbf{R}_1) + U(\mathbf{X}_i, \mathbf{R}_2) \approx U(\mathbf{X}_i | \mathbf{X}_E) \quad \text{for } i = 3, 4, \dots, N + 2 \quad (4.4.11)$$

where $\mathbf{X}_E$ is the configuration of ethane for which one carbon is placed at $\mathbf{R}_1$ and the second carbon at $\mathbf{R}_2$ such that $|\mathbf{R}_2 - \mathbf{R}_1| = \sigma_1$. If this approximation is valid for all configurations $\mathbf{X}^N$ having non-zero probability, then we can replace the average quantity in (4.4.4) by

$$\begin{aligned} \left\langle \exp \left[-\beta U \left(\mathbf{X}^N | \mathbf{R}_1, \mathbf{R}_2 \right) \right] \right\rangle &\cong \left\langle \exp \left[-\beta U \left(\mathbf{X}^N | \mathbf{X}_E \right) \right] \right\rangle \\ &= \exp[-\beta \Delta \mu_E^*] \end{aligned} \quad (4.4.12)$$

Once we have made the replacement of the two sources of the field of force by a single molecule, we identify on the right-hand side of (4.4.12) the Helmholtz energy of solvation of the *real* ethane molecule. Figure 4.9 is a modification of Fig. 4.5,

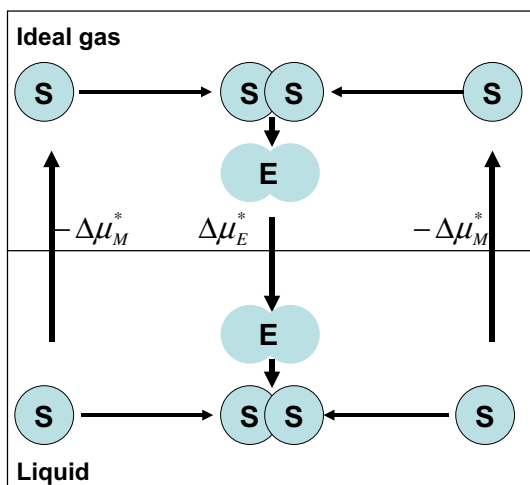


Fig. 4.9 A modification of the cyclic process in Fig. 4.5. Instead of transferring a hypothetical “dimer,” we first replace the two monomers s (here, methane molecules) by one ethane molecule, and then transfer the real ethane molecule into the liquid.

where instead of a hypothetical “dimer” we use a real “dimer,” an ethane molecule.

Perhaps the simplest and the most convincing argument for justifying the approximation (4.4.12) is to recall that this approximation becomes exact for hard-sphere solutes. An exact statement for hard spheres is likely to be a reasonable approximation for simple non-polar solutes.

Let us further elaborate on the nature of approximation (4.4.12). Figure 4.10 shows a schematic description of two methane molecules at a distance of $R = \sigma_1$. The particular configuration of the two methane molecules is such that one hydrogen atom of each molecule is directed toward the second molecule. We note also that the methane molecule, the methyl group ($-\text{CH}_3$), and the methylene group ($-\text{CH}_2-$) are assigned almost the same van der Waals radius of about $2.0 \text{ \AA}$. The C-H distance in the saturated alkanes is $1.093 \text{ \AA}$ and the van der Waals radius assigned to the hydrogen atom is about $1.2 \text{ \AA}$.

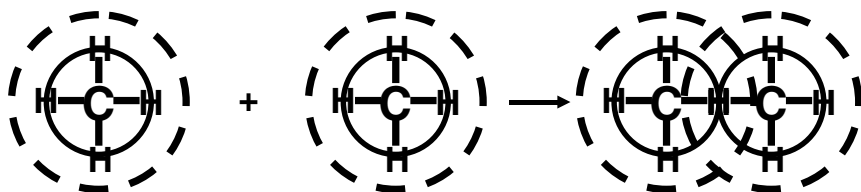


Fig. 4.10 Schematic description of the two methane molecules brought to a distance $\sigma_1 \approx 1.53 \text{ \AA}$. At this distance we replace the pair of methane molecules by one ethane molecule. The dashed line marks the excluded volume for solvent molecules.

Figure 4.10 also shows the “excluded” volume for this pair of molecules. The dashed line is roughly the closest distance that the center of a water molecule can approach. Thus, if we replace the pair of methane molecules at this specific configuration by an ethane molecule, we expect that the geometry of the excluded region will not be changed.

The above consideration on the form of the excluded region accounts for the repulsive part of the solute-solvent interaction. We now consider the attractive part of the field of force produced by the pair of methane molecules. It is convenient to separate the total field of force produced by each methane molecule into two contributions: that produced by the methyl group and that by the inner hydrogen atom. We assume that the field of force produced by the methyl group of methane is the same as that by the methyl group of ethane. Furthermore, the two hydrogen atoms that we have placed along the C-C line are assumed to make a very small contribution to the total field of force in the region beyond the excluded volume, and therefore this contribution is neglected.

It is important to stress that our replacement of the two methane molecules by one ethane has nothing to do with the *chemical reaction* $2\text{CH}_4 \rightarrow \text{C}_2\text{H}_6 + \text{H}_2$. In fact, we can imagine the process of bringing two argon molecules to a distance $R = \sigma_1$ and making the replacement by a single ethane molecule.

Although it might be possible in principle to find a different pair of solutes s so that the replacement $2s \rightarrow \text{C}_2\text{H}_6$ will be a good approximation in (4.4.12), we believe that the pair of methane molecules replaced by an ethane molecule is a particularly fortunate choice. This is so because it is known that the properties of the methyl group are almost independent of the other parts of the molecule, whether it is a hydrogen, a methyl group, or a larger alkyl group.

From (4.4.2), (4.4.4), and (4.4.12), we write the $H\phi O$ interaction between two methane molecules at a distance $\sigma_1 = 1.533 \text{ \AA}$ as

$$\delta A(\sigma_1) = \Delta\mu_E^* - 2\Delta\mu_M^* \quad (4.4.13)$$

where on the right-hand side of (4.4.3) we have measurable quantities. We shall use (4.4.13) in the next sections as a simple measure for estimating the strength of the $H\phi O$ interaction in various solvents. In all of the examples presented here, we shall be interested in the *difference* between the value of $\delta A(\sigma_1)$ in water and other solvents. Clearly, for the purpose of comparison of the quantity $\delta A(\sigma_1)$ in various solvents, we require that the replacement approximation in (4.4.12) be equally valid in the two solvents. This is a far weaker requirement than to assume the validity of (4.4.12) for each solvent separately. In Sec. 4.4.7, we show how, by the choice of bulkier solute molecules, one can improve on the approximation (4.4.12) to any required degree of accuracy.

4.4.1. *Some experimental data on the strength of $H\phi O$ interactions*

In Sec. 4.2, we surveyed some of the experimental evidence relevant to the problem of the $H\phi O$ interaction. In this section we use the quantity $\delta A(\sigma_1)$ defined in (4.4.13) as a simple and

convenient measure for comparing the strength of the $H\phi O$ interaction in various solvents.¹⁷ Our main interest will not be the absolute magnitude of $\delta A(\sigma_1)$ but rather the difference between these values in different solvents. In establishing the connection between the $H\phi O$ interaction and experimental quantities, it is sometimes more convenient to refer to the process of bringing the two solute particles from infinite separation to any distance R at constant *pressure* rather than constant volume. The total work in this case is given by

$$\Delta G^I(R) = U(R) + \delta G(R) \quad (4.4.14)$$

Thus, insofar as we are concerned with estimates of the *strength* of the $H\phi O$ interaction, we can use either $\delta A(R)$ or $\delta G(R)$. The latter is more convenient for calculating the entropy and enthalpy of $H\phi O$ interactions. All the experimental quantities referred to in this section are computed either by relation (4.4.13), or equivalently¹⁸ by

$$\delta G(\sigma_1) = \Delta\mu_E^* - 2\Delta\mu_M^* \quad (4.4.15)$$

Figure 4.11 shows the values of $\delta G(\sigma_1)$ for various solvents. There are two prominent differences between water and non-aqueous solvents which are worthwhile noting. First, the absolute magnitude of $\delta G(\sigma_1)$ is larger in water than in the other solvents. The difference, say, at 25°C, is significant and amounts to about 0.6 kcal mol⁻¹. This value is of the order of magnitude of $k_B T$ at this temperature. This finding can be reformulated in terms of the ratio of probabilities. We use relation (4.3.14) for a pair of methane molecules in water and in, say, ethanol at 25°C

¹⁷Note again the use of the term "hydrophobic interaction" for water as well as for non-aqueous solvents. A better term would be the *solvent induced part of the interaction* between the two solutes.

¹⁸No distinction is made between δA and δG . Such a distinction is important for computation of other thermodynamic quantities.

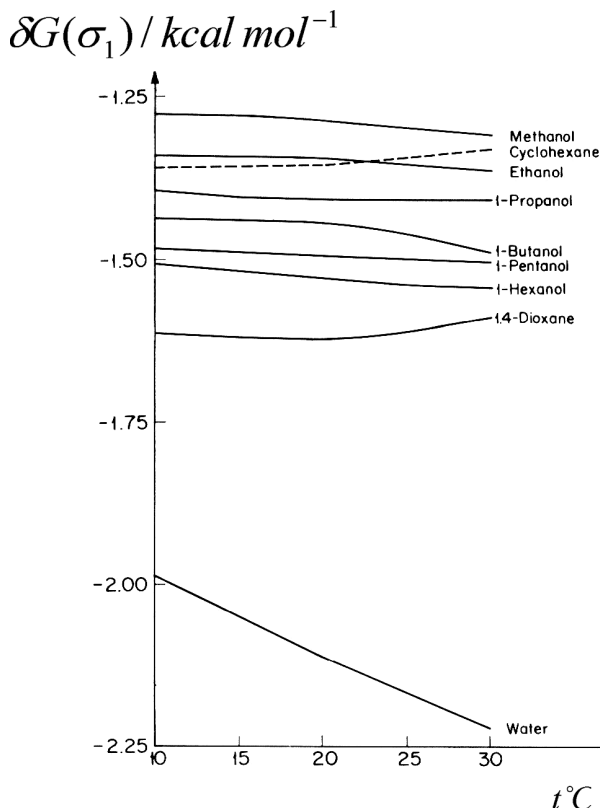


Fig. 4.11 Values of $\delta G(\sigma_1)$ as a function of temperature in different solvents.

to obtain¹⁹

$$\frac{\text{Pr}(\sigma_1, \text{in water})}{\text{Pr}(\sigma_1, \text{in ethanol})} = \frac{y(\sigma_1, \text{in water})}{y(\sigma_1, \text{in ethanol})} = \exp(1.36) = 3.9 \quad (4.4.16)$$

The interpretation of the above result is the following. The probability of finding two methane molecules with an effective diameter of $\sigma \approx 3.82 \text{ \AA}$ at a distance of about $R \approx 1.533 \text{ \AA}$ is almost zero. However, since the ratio of such probabilities in the two solvents is equal to the ratio of the quantities $y(\sigma_1)$, and

¹⁹The probability interpretation requires that the solute density be the same in the two solvents.

since the latter does not include the direct pair potential operating between the two solutes, we can assign to this ratio the meaning of the relative probability of finding the two solutes at $R = \sigma_1$ in a system for which the direct solute-solute pair potential has been “switched off.” We can see from (4.4.16) that the probability of finding the two particles at a close distance in water is about four times larger than the corresponding value in ethanol. We stress, however, that from (4.4.16) one cannot reach any conclusions regarding the relative probabilities of finding the two solutes at the contact distance $R = \sigma$. We will return to this point in Sec. 4.4.6.

The second important difference between water and other solvents is in the temperature dependence of $\delta G(\sigma_1)$. It is seen that the $H\phi O$ interaction in water becomes *stronger* as the temperature increases; in other solvents, the temperature dependence is very small and is sometimes opposite in direction to that of water. The unique temperature dependence of the $H\phi O$ interaction in water is quite remarkable, and in a sense seems contradictory to our intuition. We will return to a more detailed discussion of this subject in Sec. 4.7.

Table 4.2 presents some values of $\delta G(\sigma_1)$ for water, heavy water, and other solvents. Note that the $H\phi O$ interaction is slightly *stronger* in H_2O than in D_2O , and these values are

Table 4.2. Hydrophobic Interaction^a

t (°C)	$\delta G(\sigma_1)$ (kcal mol ⁻¹)					
	H ₂ O	D ₂ O	Methanol	Ethanol	1,4-Dioxane	Cyclohexane
10	-1.99	-1.94	-1.28	-1.34	-1.61	-1.36
25	-2.17	-2.14	-1.29	-1.36	-1.61	-1.34

^a Data from Ben-Naim *et al.* (1973) and Ben-Naim and Yaacobi (1974).

$\delta G(\sigma_1) = \Delta\mu_E^* - 2\Delta\mu_M^*$ computed for a pair of methane molecules at a final distance $\sigma_1 = 1.533$ Å in various solvents.

appreciably smaller in most of the solvents for which the relevant experimental quantities are available. Table 4.2A shows some values of δG for the addition of a methyl group to a small hydrocarbon. As can be seen in this table, the values of $\delta G(\sigma_1)$, in these polar liquids, are even larger than in water.

The finding that the strength of the $H\phi O$ interaction is weaker in D_2O compared to H_2O is as counterintuitive as the finding that the strength of the $H\phi O$ interaction is weaker, say, at $15^\circ C$ than at $25^\circ C$.

Adopting the quantity $\delta G(\sigma_1)$, as defined in (4.4.15) as a probe for the strength of the $H\phi O$ interaction in various solvents, we can follow its variation in a mixture of water and a non-aqueous solvent. Figure 4.12 shows such a variation for the water-ethanol system at two temperatures. Note that in the water-rich region, the values $\delta G(\sigma_1)$ are large (in absolute magnitude) and strongly temperature dependent. As the mole fraction of alcohol becomes larger than, say, $x \approx 0.2$, the variation of $\delta G^{HI}(\sigma_1)$ with the mole fraction becomes monotonous, and $|\delta G(\sigma_1)|$ steadily decreases to the corresponding value in pure ethanol. Note also the inversion of the temperature dependence at about $x \approx 0.5$.

The most remarkable feature of this figure is the maximum followed by a minimum in the curve at $10^\circ C$. This is similar to the behavior of the solvation Gibbs energy in this system (see Fig. 3.5). As yet, there is no explanation for this phenomenon; a partial interpretation in terms of a structural change in water is provided in Appendix H.

Another application of the quantity $\delta G(\sigma_1)$ is shown in Table 4.3, where we follow the change in $\delta G(\sigma_1)$ brought about by the addition of various solutes, a topic of considerable importance in the study of solute effects on the conformational stability of various biopolymers. Table 4.3 presents a sample of data on the variation of $\delta G(\sigma_1)$ in various aqueous solutions of

Table 4.2A Solvophobic Interaction^a

Solvent	$\delta G = \Delta\mu_E^* - 2\Delta\mu_M^*$	$\Delta\mu_{Pr}^* - \Delta\mu_E^* - \Delta\mu_M^*$	$\Delta\mu_{Bu}^* - \Delta\mu_{Pr}^* - \Delta\mu_M^*$	$\Delta\mu_{IB}^* - \Delta\mu_{Pr}^* - \Delta\mu_M^*$
Ethylene glycol 25°C	-2.85	-1.77	-1.78	-1.67
Dimethyl sulfoxide 25°C	-2.25	-1.59	-1.78	-1.32
Benzyl alcohol 25°C	-2.03	-1.50	-1.57	-1.16
Tripropyl phosphate 25°C	-1.55	-1.09	-1.14	-0.88
50°C	-1.70	-1.14	-1.21	-0.96
70°C	-1.65	-1.18	-1.25	-0.99

^a δG (kcal mol⁻¹) for several processes in polar solvents.

M = methane; E = ethane; Bu = butane; Pr = propane; IB = isobutane.

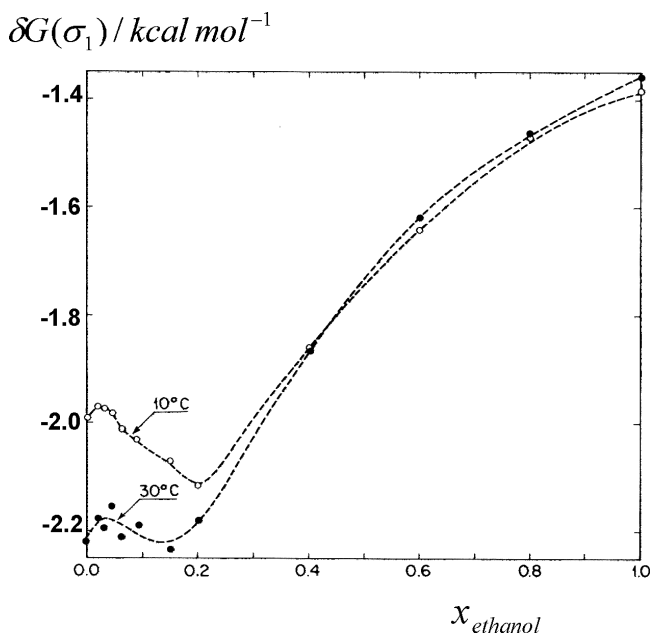


Fig. 4.12 Values of $\delta G(\sigma_1)$ in mixtures of water and ethanol at two temperatures.

electrolytes and non-electrolytes. As can be seen from the table, almost all solutes added to water at low concentration cause an increase in the $H\phi O$ interaction.

An exceptional case in this table is the aqueous solution of ethanol ($x = 0.03$ and $t = 10^\circ\text{C}$) for which the $H\phi O$ interaction is slightly weaker than in pure water. (This can also be seen from Fig. 4.12, where in the range $0 \leq x \leq 0.03$ there is a decrease in the $H\phi O$ interaction as a function of the mole fraction of ethanol.)

It is often claimed that the $H\phi O$ interaction is a “reversal of solvation.” The idea is that two (or more) non-polar solutes forming a dimer (or a cluster of molecules) are less exposed to the solvent than the same solutes dispersed in the solvent. This is true in some extreme cases, which we shall discuss in Secs. 4.4.5

Table 4.3 Value of $\delta G(\sigma_1)$ (kcal mol⁻¹) for Various Aqueous Solutions at Two Different Temperatures^a

Electrolytes								
<i>t</i> (°C)	H ₂ O	LiCl (1 M)	NaCl (1 M)	KCl (1 M)	CsCl (1 M)	NH ₄ Cl (1 M)	NaBr (1 M)	NaI (1 M)
10	-1.99	-2.11	-2.17	-2.16	-2.14	-2.09	-2.18	-2.19
25	-2.17	-2.29	-2.34	-2.33	-2.32	-2.26	-2.34	-2.33

Non-electrolytes							
<i>t</i> (°C)	Ethanol (<i>x</i> = 0.03)	1,4-Dioxane (<i>x</i> = 0.03)	Dimethyl sulfoxide (<i>x</i> = 0.03)	Sucrose (0.5 M)	Urea (1 M)	Urea (2 M)	Urea (7 M)
10	-1.97	-2.05	-2.04	-2.12	-2.04	-2.11	-2.38
25	-2.19	-2.20	-2.22	-2.30	-2.21	-2.26	-2.49

^a *x* = mole fraction. (From Ben-Naim and Yaacobi (1974).)

and 4.6, but it is not true in general. The following examples show that the values of $-\Delta\mu_s^*$ and $\delta G(\sigma_1)$ are not always compatible. Sometimes, these two quantities provide contradictory information on the $H\phi O$ effect.

Let us consider first water and ethanol. The change in solvation Gibbs energy of a methane molecule from water to ethanol at $t = 10^\circ\text{C}$ is

$$\begin{aligned}\Delta\Delta\mu_M^*(\text{water} \rightarrow \text{ethanol}) &= \Delta\mu_M^*(\text{in ethanol}) - \Delta\mu_M^*(\text{in water}) \\ &= -1.42 \text{ kcal mol}^{-1}\end{aligned}\quad (4.4.17)$$

This value can be interpreted in terms of the tendency of the methane molecules to favor the ethanol over the aqueous environment. Alternatively, we can say that methane tends to “escape” from water into ethanol. Consistent information on this tendency is obtained from the following two values of

$\delta G(\sigma_1)$ (all values are for σ_1 at 10°C):

$$\begin{aligned}\delta G(\text{in water}) &= -1.99 \text{ kcal mol}^{-1} \\ \delta G(\text{in ethanol}) &= -1.39 \text{ kcal mol}^{-1}\end{aligned}\quad (4.4.18)$$

meaning that the tendency to adhere to each other is stronger in water as compared to ethanol, i.e. the two methane molecules tend to avoid the aqueous environment more than they do the ethanol environment.

We now present a different example showing that the two measures $\Delta\mu_M^*$ and $\delta G(\sigma_1)$ lead to different conclusions. Consider a mixture of water and ethanol with a mole fraction of ethanol of $x = 0.2$ (referred to below as the “mixture”). For these solvents, we have (for methane at 10°C)

$$\begin{aligned}\Delta\mu_M^* (\text{water} \rightarrow \text{mixture}) \\ &= \Delta\mu_M^* (\text{in mixture}) - \Delta\mu_M^* (\text{in water}) \\ &= 1.58 - 1.75 = -0.17 \text{ kcal mol}^{-1}\end{aligned}\quad (4.4.19)$$

From (4.4.19) we conclude that the mixture is a slightly more favorable solvent to methane than is pure water. On the other hand,

$$\begin{aligned}\delta G(\text{in water}) &= -1.99 \text{ kcal mol}^{-1} \\ \delta G(\text{in mixture}) &= -2.11 \text{ kcal mol}^{-1}\end{aligned}\quad (4.4.20)$$

indicating that the tendency to adhere to each other is *stronger* in the mixture than in pure water.

The last example shows that $\Delta\mu_M^*$, though useful as a measure for the extreme process of transferring a non-polar group from an aqueous to a non-polar environment, is in general unsuitable for measuring the tendency of two solute particles to adhere to each other in various solvents. In Secs. 4.4.5 and 4.6,

we shall encounter two special cases for which $\Delta\mu_M^*$ and δG provide identical information.²⁰

In previous sections, we discussed the $H\phi O$ interaction between two simple solutes in various solvents. We now generalize along two directions: firstly, we study the $H\phi O$ interaction between more complex molecules, and secondly, we examine the $H\phi O$ interaction among a set of, say, m solute molecules.

4.4.2. $H\phi O$ interaction among m identical spherical non-polar solute particles

Consider the work required to bring m solute particles (which, for simplicity, are presumed to be spherical) from infinite separation to a final configuration $\mathbf{R}^m$:

$$\begin{aligned}\Delta A^l(\mathbf{R}^m) &= A_{N+M}^l(\mathbf{R}^m) - A_{N+M}^l(\mathbf{R}^m = \infty) \\ &= U_M(\mathbf{R}^m) + \delta A(\mathbf{R}^m)\end{aligned}\quad (4.4.21)$$

where $\mathbf{R}^m = \infty$ indicates a configuration of the m solute particles in the solvent, the separation between each pair being infinity, i.e.

$$|\mathbf{R}_j - \mathbf{R}_i| = \infty, \quad \text{for } i = 1, \dots, m, \quad j = 1, \dots, m \quad i \neq j \quad (4.4.22)$$

The statistical mechanical expression for $\Delta A^l(\mathbf{R}^m)$ is

$$\begin{aligned}&\exp[-\beta\Delta A^l(\mathbf{R}^m)] \\ &= \frac{\int \cdots \int d\mathbf{X}^N \exp[-\beta U_N(\mathbf{X}^N) - \beta U(\mathbf{R}^m) - \beta U(\mathbf{X}^N | \mathbf{R}^m)]}{\int \cdots \int d\mathbf{X}^N \exp[-\beta U_N(\mathbf{X}^N) - \beta U(\mathbf{R}^m = \infty) - \beta U(\mathbf{X}^N | \mathbf{R}^m = \infty)]}\end{aligned}\quad (4.4.23)$$

²⁰Koga *et al.* (2002) found a linear correlation between the PMF and the solvation Gibbs energy in a lattice model of aqueous solutions. As we have demonstrated above, such a correlation does not exist in general.

where $U(\mathbf{X}^N | \mathbf{R}^m)$ is the total interaction energy between solvent molecules at the configuration $\mathbf{X}^N$ and the solute molecules at the configuration $\mathbf{R}^m$.

The integrations in (4.4.23) extend over all the configurations of the *solvent* particles; hence, we can rewrite (4.4.23) as

$$\begin{aligned} \exp[-\beta \Delta A^l(\mathbf{R}^m)] \\ = \exp[-\beta U(\mathbf{R}^m)] \frac{\langle \exp[-\beta U(\mathbf{X}^N | \mathbf{R}^m)] \rangle}{\langle \exp[-\beta U(\mathbf{X}^N | \mathbf{R}^m = \infty)] \rangle} \end{aligned} \quad (4.4.24)$$

where we put $U(\mathbf{R}^m = \infty) = 0$. From (4.4.21) and (4.4.24), we identify the expression for the $H\phi O$ interaction among the m solute particles as

$$\exp[-\beta \delta A(\mathbf{R}^m)] = \frac{\langle \exp[-\beta U(\mathbf{X}^N | \mathbf{R}^m)] \rangle}{\langle \exp[-\beta U(\mathbf{X}^N | \mathbf{R}^m = \infty)] \rangle} \quad (4.4.25)$$

which is the generalization of relation (4.4.4).

Note again that (4.4.25) does not include any internal properties of the solutes or the direct interaction among the solute particles, $U(\mathbf{R}^m)$. Hence, we can interpret $\delta A(\mathbf{R}^m)$ as the *total* work required to move m sources of *fields of force* from the configuration $\mathbf{R}^m = \infty$ to the final configuration $\mathbf{R}^m$.

By direct generalization of the arguments in the previous subsection (either through formal statistical mechanical expressions or by using a generalization of the cyclic process shown in Fig. 4.5), we can express $\delta A(\mathbf{R}^m)$ in terms of the Helmholtz energy associated with transferring the m solute particles from a fixed configuration in the gas to a fixed configuration in the liquid:

$$\delta A(\mathbf{R}^m) = \Delta A^*(\mathbf{R}^m) - \Delta A^*(\mathbf{R}^m = \infty) \quad (4.4.26)$$

which is a generalization of (4.4.1). Clearly, the second term on the right-hand side of (4.4.26) is equal to m times the work of

transferring a single particle to a fixed position in the liquid, i.e.

$$\Delta A^*(\mathbf{R}^m = \infty) = m\Delta A^*(\mathbf{R}_1) = m\Delta\mu_s^* \quad (4.4.27)$$

where $\Delta\mu_s^*$ is the Helmholtz or Gibbs energy of the solvation of the solute s .

The next step is to find a connection between $\Delta A^*(\mathbf{R}^m)$ and experimental quantities. In order to do this, we must find a particular configuration, say, $\mathbf{R}^m$, of the m solutes and one single molecule such that the *field of force* produced by the m solute particles at $\mathbf{R}^m$ is approximately equal to that produced by the single molecule for a given configuration $\mathbf{Y}$ (here, $\mathbf{Y}$ denotes the configuration of a single molecule, including location, orientation, and conformation). Mathematically, the requirement is

$$U(\mathbf{X}^N | \mathbf{R}^m) \cong U(\mathbf{X}^N | \mathbf{Y}) \quad (4.4.28)$$

As an example, suppose we start with five methane molecules and bring them to a final configuration $\mathbf{R}^m$ ($m = 5$) in such a way that a replacement by one pentane molecule in a configuration $\mathbf{Y}$ produces approximately the same field of force. If (4.4.28) is valid for all the configurations of the solvent molecules that have non-zero probability, then (4.4.25) can be rewritten as

$$\exp[-\beta\delta A(\mathbf{R}^m)] = \left\langle \exp \left[-\beta U(\mathbf{X}^N | \mathbf{Y}) \right] \right\rangle \exp(m\beta\Delta\mu_s^*) \quad (4.4.29)$$

where $\Delta\mu_s^*$ is the solvation Gibbs or Helmholtz energy of solvation of a single solute s . In order to find a connection between δA and the relevant experimental quantities, we have to distinguish between two cases: when the replacing molecule does or does not possess internal rotations that affect the solvation Gibbs solvation energy. The second case is simpler: the average quantity on the right-hand side of (4.4.29) can be related to the solvation Gibbs energy of the single molecule, say, neopentane, and we

obtain the relation

$$\left\langle \exp \left[-\beta U \left(\mathbf{X}^N \mid \mathbf{Y} \right) \right] \right\rangle = \exp \left(-\beta \Delta \mu_{m \cdot s}^* \right) \quad (4.4.30)$$

The subscript $m \cdot s$ denotes a single molecule that replaces m solute particles of type s at the configuration $\mathbf{R}^m$.

From (4.4.29) and (4.4.30), we get

$$\delta A(\mathbf{R}^m) = \Delta \mu_{m \cdot s}^* - m \Delta \mu_s^* \quad (4.4.31)$$

where on the right-hand side we have measurable quantities. An example of a molecule in this group is neopentane or propane (although both have internal rotations, the solvation Gibbs energy will be nearly the same for all the conformations of the molecules).

The first case includes molecules that possess internal rotations, in which case (4.4.29) should be understood as an average over all the conformations of the molecule. It is convenient, in this case, to introduce an auxiliary quantity, the solvation Gibbs energy of the molecule in a specific configuration $\mathbf{Y}$,

$$\begin{aligned} & \exp[-\beta \Delta \mu_{m \cdot s}^*(\mathbf{Y})] \\ &= \frac{\int \cdots \int d\mathbf{X}^N \exp[-\beta U_N(\mathbf{X}^N) - \beta U(\mathbf{X}^N \mid \mathbf{Y})]}{\int \cdots \int d\mathbf{X}^N \exp[-\beta U(\mathbf{X}^N)]} \end{aligned} \quad (4.4.32)$$

This is the work required to transfer a single molecule, say, butane, from a fixed configuration $\mathbf{Y}$ in the gas to a fixed configuration $\mathbf{Y}$ in the liquid. [Note that $\Delta \mu_{m \cdot s}^*(\mathbf{Y})$ is actually a function of the conformation of the molecule. If no internal rotations exist, then $\Delta \mu_{m \cdot s}^*$ is independent of both the location and orientation of the molecule.]

The solvation Gibbs energy of the molecule $m \cdot s$ is obtained from (4.4.32) by averaging over all the configurations of the molecule, weighted by the internal rotation potential, which we

denote by $U_m^*(Y)$:

$$\begin{aligned} & \exp(-\beta \Delta \mu_{m.s}^*) \\ &= \frac{\int dY \exp[-\beta U_m^*(Y) - \beta \Delta \mu_{m.s}^*(Y)]}{\int dY \exp[-\beta U_m^*(Y)]} \end{aligned} \quad (4.4.33)$$

If $\Delta \mu_{m.s}^*$ and $\delta A(R^m)$ are understood as average quantities in the sense of (4.4.33), then we can apply (4.4.31) to molecules possessing internal degrees of freedom as well. [For more details, see Ben-Naim (1971a, 1972g).]

Figures 4.13 and 4.14 show the values of the $H\phi O$ interaction among a group of m methane molecules brought to the

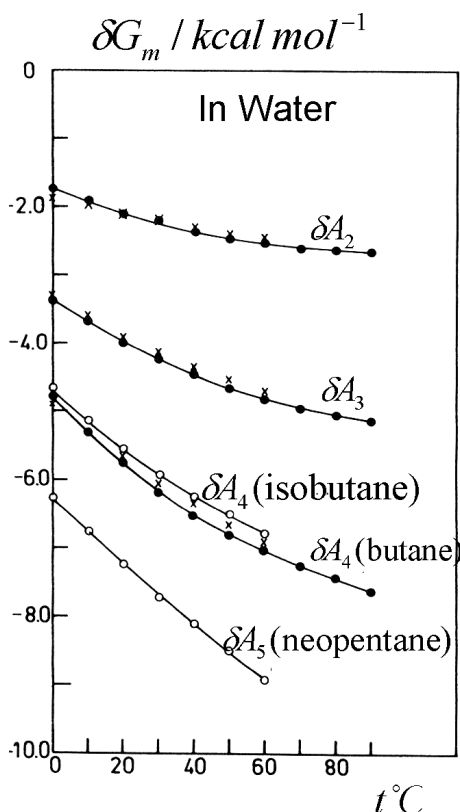


Fig. 4.13 Values of the $H\phi O$ interactions (δA_m) among m methane molecules as a function of temperature.

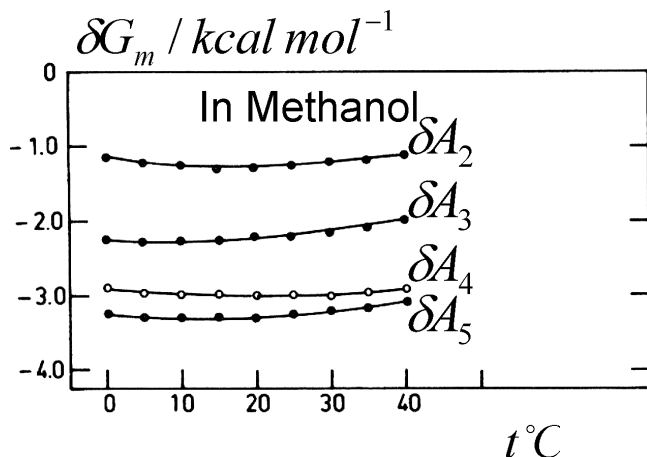


Fig. 4.14 Values of δA_m as a function of temperature in methanol.

final configuration of the molecules indicated next to each curve. (Note that in these examples only butane requires averaging over all configurations.)

As we see from these figures, the values for the $H\phi O$ in water are considerably larger (in absolute magnitude) than the corresponding values in methanol. Also, the temperature dependence is distinctly different. In water, we find a clear-cut negative temperature dependence, whereas in methanol, there is a slight positive slope which is estimated to be within the range of experimental error (Ben-Naim, 1971ab).

Tables 4.4 and 4.5 present further information on the $H\phi O$ interaction among the m methane molecules brought to a final configuration of a suitable hydrocarbon molecule. The first column shows the value of m , i.e. the number of carbon atoms in each molecule. The second column presents the $H\phi O$ interaction for the m methane molecules. The third column shows that the $H\phi O$ interaction per carbon atom *increases* with m . Note that for a given m the value of $\delta A_m/m$ is almost insensitive to the final configuration (i.e. the isomers of $m \cdot s$). The last column in

Table 4.4 Values of δA_m (in kcal mol⁻¹ at 25°C) for the interaction among m Methane Molecules brought to a Final Configuration similar to an existing molecule containing m carbon atoms^a

Hydrocarbon	m	$-\delta A_m$	$-\delta A_m/m$	$-\delta A_m/m_B$
Ethane	2	2.16	1.08	2.16
Propane	3	4.01	1.33	2.00
<i>n</i> -Butane	4	5.87	1.47	1.96
Isobutane	4	5.70	1.42	1.90
<i>n</i> -Pentane	5	7.53	1.50	1.88
Isopentane	5	7.59	1.52	1.89
2,2-Dimethylpropane	5	7.34	1.47	1.83
<i>n</i> -Hexane	6	9.43	1.57	1.88
2-Methylpentane	6	9.48	1.58	1.89
3-Methylpentane	6	9.41	1.57	1.88
2,2-Dimethylbutane	6	9.39	1.58	1.88
<i>n</i> -Heptane	7	11.34	1.62	1.89
2,4-Dimethylpentane	7	11.07	1.58	1.85
<i>n</i> -Octane	8	13.08	1.63	1.87
2,2,4-Trimethylpentane	8	13.10	1.64	1.87

^a Based on data from Wen and Hung (1970) and McAuliffe (1966).**Table 4.5** Values of δA_m (in kcal mol⁻¹ at 25°C) for the interaction between m Methane Molecules brought to the Configuration of Cyclo-hydrocarbons^a

Cycloparaffin	m	$-\delta A_m$	$-\delta A_m/m$
Cyclopropane	3	3.49	1.16
Cyclopentane	5	8.80	1.76
Cyclohexane	6	10.72	1.78
Cycloheptane	7	13.17	1.88
Cyclooctane	8	15.13	1.89
Methylcyclopentane	6	10.37	1.73
Methylcyclohexane	7	12.25	1.75
1- <i>cis</i> -2-Dimethylcyclohexane	8	14.40	1.80

^a Based on data from Ben-Naim (1972g).

Table 4.4 contains the value of $\delta A_m/m_B$, where m_B is the number of C-C bonds in the molecule. There is a clear decrease in this value for the first four members. Beyond that, the values seem to converge to an almost constant value of about $-1.88 \text{ kcal mol}^{-1}$. This remarkable fact indicates that the $H\phi O$ is almost additive insofar as we count only the number of nearest-neighbor groups in the hydrocarbon molecules. Table 4.5 shows similar results for cyclo-hydrocarbon molecules, where m is the same as m_B . Again, except for the first few cyclic molecules, the strength of the $H\phi O$ interaction per bond is almost constant.

4.4.3. *Attaching a methyl group to various hydrocarbons*

Consider a “reaction” of the form



The term “reaction” is used here to describe the process of bringing a methane molecule from infinity to a final position next to a hydrocarbon molecule denoted RH; then the pair of molecules is replaced by a single hydrocarbon denoted by R-CH₃.

For this “reaction,” we can write

$$\begin{aligned} \delta A(\text{R-CH}_3) &= \Delta\mu^*(\text{R-CH}_3) - \Delta\mu^*(\text{RH}) \\ &\quad - \Delta\mu^*(\text{CH}_4) \end{aligned} \quad (4.4.35)$$

This is the indirect work in bringing a methane molecule from infinite separation from RH to the final configuration similar to an existing molecule R-CH₃. This process is schematically shown in Fig. 4.15. As in the previous subsection, on the right-hand side of (4.4.35), we have measurable quantities. Note that in every case in which internal rotations are involved, one must interpret the appropriate solvation Gibbs or Helmholtz energy as an average over all the conformations of the molecule.

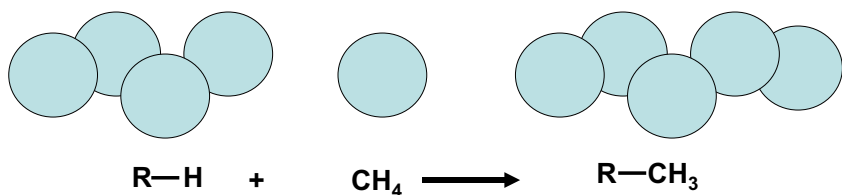


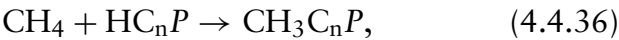
Fig. 4.15 Schematic process of adding one methane molecule to a linear hydrocarbon.

Table 4.6 Values of δA for the Interaction between Methane and various Normal Hydrocarbons [“reaction” (4.4.34)] at 25°C^a

$RH+CH_4$	RCH_3	$-\delta A$ (kcal mol ⁻¹)
C+C	C-C	2.16
C+C-C	C-C-C	1.85
C+C-C-C	C-C-C-C	1.86
C+C-C-C-C	C-C-C-C-C	1.66
C+C-C-C-C-C	C-C-C-C-C-C	1.91
C+C=C	C-C=C	2.01
C+C-C=C	C-C-C=C	1.89
C+C-C-C=C	C-C-C-C=C	1.72
C+C-C-C-C=C	C-C-C-C-C=C	2.02
C+C-C≡C	C-C-C≡C	1.68
C+C-C-C≡C	C-C-C-C≡C	1.82
C+C-C-C-C≡C	C-C-C-C-C≡C	1.69
C+C-C-C-C-C≡C	C-C-C-C-C-C≡C	1.68

^a “-”, “=”, and “≡” correspond to single, double, and triple bonds, respectively.

Table 4.6 shows δA values for some “reactions” as in Eq. (4.4.34) for normal hydrocarbon molecules. There are two kinds of information that one can obtain from “reactions” of type (4.4.34). Let P be any group attached to a linear hydrocarbon molecule, and consider the following “reaction”:



i.e. we bring a methane molecule from infinity and attach it to one side of a molecule which has n carbon atoms (denoted C_n) and is connected to a group P on its other side.

For a given group P (e.g. halogen, carboxylic, or amino acid residue), one can study the $H\phi O$ interaction as a function of the chain length n of the molecule. Such a study provides information on the *range* of influence of the group P on the medium. For a large n , one expects the $H\phi O$ interaction will be independent of P , but for small n , due to the perturbation effect of P on the solvent, the $H\phi O$ interaction may vary considerably with n .

A different kind of information may be obtained by fixing n and examining the effects of different groups P on the solvent as they are revealed in the values of the quantity δA .

4.4.4. Attaching an ethyl group to various molecules

The “reaction” given in (4.4.34) can be generalized as follows: instead of bringing a methane molecule from infinity and attaching it to various molecules, we bring an ethane molecule. The relevant “reaction” is

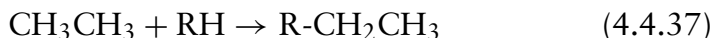


Table 4.7 shows values of δA for “reactions” of the type (4.4.37), for which

$$\begin{aligned} \delta A(\text{R-CH}_2\text{CH}_3) &= \Delta\mu^*(\text{R-CH}_2\text{CH}_3) - \Delta\mu^*(\text{RH}) \\ &\quad - \Delta\mu^*(\text{CH}_3\text{CH}_3) \end{aligned} \quad (4.4.38)$$

Note here that the study of “reactions” of the type (4.4.37) provides new and independent information on the $H\phi O$ interaction which is not contained in the study of “reactions” of the type (3.4.34). Table 4.7 shows that the values of δA for “reactions” in this class are systematically smaller than the corresponding values for “reactions” of the type (4.4.34). These

Table 4.7 Values of δA for the Interaction between Ethane and Various Hydrocarbons at 25°C^a

$\text{CH}_3-\text{CH}_3+\text{RH}$	$\text{R}-\text{CH}_2-\text{CH}_3$	$-\delta A(\text{kcal mol}^{-1})$
C-C+C	C-C-C	1.85
C-C+C-C	C-C-C-C	1.55
C-C+C-C-C	C-C-C-C-C	1.36
C-C+C-C-C-C	C-C-C-C-C-C	1.40
C-C+C-C-C-C-C	C-C-C-C-C-C-C	1.66
C-C+C=C	C-C-C=C	1.73
C-C+C-C=C	C-C-C-C=C	1.45
C-C+C-C-C=C	C-C-C-C-C=C	1.58
C-C+C-C-C-C=C	C-C-C-C-C-C=C	1.28
C-C+C≡C	C-C-C≡C	1.85
C-C+C-C≡C	C-C-C-C≡C	1.34
C-C+C-C-C≡C	C-C-C-C-C≡C	1.36
C-C+C-C-C-C≡C	C-C-C-C-C-C≡C	1.21
C-C+C-C-C-C-C≡C	C-C-C-C-C-C-C≡C	1.45

^a From Ben-Naim (1972g).

findings are in accord with theoretical expectations that will be discussed in Sec. 4.4.6.

4.4.5. *The hydrophobic interaction at zero separation*

This section presents some information of a more theoretical nature on the problem of $H\phi O$ interaction. In the next section, we also show how such considerations can be used to extract information on the $H\phi O$ interaction at “real” distances, but for the moment we focus our attention on the formal aspect of the problem.

Consider first the case of two simple solute particles such as argon, methane, or even hard-sphere particles. We recall the general expression for the indirect part of the work required to bring the two solute particles from infinite separation to the final configuration $\mathbf{R}_1, \mathbf{R}_2$ (the process being carried out at

constant T, V, N):

$$\delta A(\mathbf{R}_1, \mathbf{R}_2) = -k_B T \ln \left\langle \exp \left[-\beta U \left(\mathbf{X}^N \mid \mathbf{R}_1, \mathbf{R}_2 \right) \right] \right\rangle - 2\Delta\mu_s^* \quad (4.4.39)$$

From a practical point of view, the interesting question concerning the $H\phi O$ interaction is for $R = |\mathbf{R}_2 - \mathbf{R}_1| \approx \sigma$, with σ being the diameter of the solute. However, since we are interested in the solvent properties, and since the expression in (4.4.39) does not include the direct solute-solute pair potential, we can ask for the value of δA at any distance $R < \sigma$. This section is devoted to one particular distance, $R = 0$.

We can apply a cyclic process similar to the one depicted in Fig. 4.7 and obtain $\delta A(0)$, expressed as a difference between the work required to bring the two real solutes to $R = 0$ in the liquid and in the gas. We will avoid such a cyclic process, however, since it compels us to subtract two quantities of the order of infinity to obtain a finite quantity. Instead, we regard $\delta A(0)$ as the *total* work required to bring the two *fields of force* from infinity to zero separation. In such a process, we do not encounter any repulsive forces that originate from the direct solute-solute interaction.

Suppose the solutes are hard-sphere particles. Clearly, two hard spheres of diameter σ_{HS} cannot be brought to a distance $R < \sigma_{HS}$. However, in (4.4.39), we need only be concerned with the field of force produced by two hard spheres; the latter may be referred to as two cavities in the solvent.²¹

Applying (4.4.39) to two cavities at zero separation, we get

$$\begin{aligned} \delta A(R = 0) &= -k_B T \ln \left\langle \exp \left[-\beta U \left(\mathbf{X}^N \mid R = 0 \right) \right] \right\rangle - 2\Delta\mu_{HS}^* \\ &= \Delta\mu_{HS}^* - 2\Delta\mu_{HS}^* = -\Delta\mu_{HS}^* \end{aligned} \quad (4.4.40)$$

²¹If σ_w is the effective diameter of the solvent molecule, then the radius of the cavity is $(\sigma_{HS} + \sigma_w)/2$. However, if the solvent molecule is not spherical, the geometric form of the cavity depends on the orientation of the solvent molecule. We refer to a "cavity" in both cases to mean the actual field of force produced by the hard sphere.

The second form on the right-hand side of (4.4.40) follows from the fact that the field of force produced by one cavity at some fixed point in the solvent is exactly the same as the field of force produced by a "double cavity" at the same point. In other words, a cavity is a stipulation on the centers of all solvent molecules to be excluded from a certain region. A double stipulation for the same region is the same as a single one, hence the equality (4.4.40). This result is also clear on intuitive grounds; the total work of bringing two equal cavities from infinite separation to zero separation is equal to the work required to eliminate one cavity. This is exactly the content of the third equality on the right-hand side of (4.4.40).²²

Relation (4.4.40) for a system of hard spheres is known in the form²³

$$\ln \gamma(0) = \beta \Delta \mu_{HS}^* \quad (4.4.41)$$

In the following, we elaborate on two generalizations of (4.4.40), one for two real solutes and the second for any number of either real or hard-sphere solutes. Before doing that, we note that relation (4.4.40) means that the $H\phi O$ interaction at zero separation is equivalent to the reversal of the solvation process. This is one example of the exact relation between the $H\phi O$ interaction and the solvation Gibbs energy.

Relation (4.4.40) suggests a novel application of the scaled particle theory to the problem of $H\phi O$ interactions. In spite of some serious reservations that one may have regarding the application of the scaled particle theory to fluids such as water, the results computed by the *SPT* show the same trends as those for $H\phi O$ interactions. [A more detailed examination of the application of the scaled particle theory for this problem was

²²Relation (4.4.40) is slightly more general since it is concerned with two hard spheres in *any* solvent, provided we assign a proper hard-core diameter σ_w to the solvent molecules.

²³See, for instance, Meeron and Siegert (1968) and Rowlinson (1968).

reported by Wilhelm and Battino (1972). An extension of the scaled particle theory to particles of arbitrary shape was given by Gibbons (1969).]

We now proceed to obtain two generalizations of (4.4.40). For the process of bringing m hard-sphere solutes from infinite separation to zero separation, we have

$$\exp[-\beta\delta A(\mathbf{R}^m=0)] = \frac{\langle \exp[-\beta U(\mathbf{X}^N | \mathbf{R}^m=0)] \rangle}{\langle \exp[-\beta U(\mathbf{X}^N | \mathbf{R}^m=\infty)] \rangle} \quad (4.4.42)$$

Here, $\delta A(\mathbf{R}^m=0)$ is the total work required to bring m cavities from infinite separation ($\mathbf{R}^m=\infty$) to zero separation ($\mathbf{R}^m=0$). Following arguments similar to those made above, we can rewrite (4.4.42) as

$$\delta A(\mathbf{R}^m=0) = \Delta\mu_{HS}^* - m\Delta\mu_{HS}^* = (1-m)\Delta\mu_{HS}^* \quad (4.4.43)$$

which is a generalization of (4.4.40) for any m .

The second generalization involves *real* solutes at zero separation. Let us first elaborate on the case of two simple solutes s . From (4.4.40), we get at $R = |\mathbf{R}_2 - \mathbf{R}_1| = 0$

$$\begin{aligned} \delta A(R=0) &= -k_B T \ln \langle \exp[-\beta U(\mathbf{X}^N | R=0)] \rangle - 2\Delta\mu_s^* \\ &= \Delta\mu_{2,s}^* - 2\Delta\mu_s^* \end{aligned} \quad (4.4.44)$$

In the first form on the right-hand side, we recognize the first term as the solvation Gibbs energy of a hypothetical solute, the field of force of which is “twice” the field of force of a single solute s . By “twice” we mean the following. The field of force $U(\mathbf{X}^N | \mathbf{R}_1, \mathbf{R}_2)$ has the form

$$U(\mathbf{X}^N | \mathbf{R}_1, \mathbf{R}_2) = \sum_{i=3}^{N+2} U(\mathbf{X}_i, \mathbf{R}_1) + \sum_{i=3}^{N+2} U(\mathbf{X}_i, \mathbf{R}_2) \quad (4.4.45)$$

where each term on the right-hand side is the field of force produced by a single solute. If $\mathbf{R}_1 = \mathbf{R}_2$, i.e. if the centers of the two fields of force coincide, then we have²⁴

$$U(\mathbf{X}^N | R = 0) = 2 \sum_{i=3}^{N+2} U(\mathbf{X}_i, \mathbf{R}_1) \quad (4.4.46)$$

which is the meaning of field of force assigned to the hypothetical solute, designated in (4.4.44) by $2 \cdot s$. The question arises whether we can find a *real* molecule for which the solvation Gibbs energy is equal to $\Delta\mu_{2 \cdot s}^*$. In principle, it is possible to find a solute which has almost the same diameter as s , but the attractive part of the potential of which is twice as strong as that of s .

Let us denote such a solute by $\bar{s}$. Then (4.4.44) can be written as

$$\delta A(R = 0) = \Delta\mu_{\bar{s}}^* - 2\Delta\mu_s^* \quad (4.4.47)$$

Now suppose we take two solutes, say, a and b , which differ appreciably in their diameters. For such solutes at zero separation, we have

$$\begin{aligned} \delta A(R = 0) &= -k_B T \ln \left\langle \exp \left\{ -\beta \sum_{i=3}^{N+2} [U^{wa}(\mathbf{X}_i, \mathbf{R}) + U^{wb}(\mathbf{X}_i, \mathbf{R})] \right\} \right\rangle \\ &\quad - \Delta\mu_a^* - \Delta\mu_b^* \end{aligned} \quad (4.4.48)$$

where we have denoted by U^{wa} and U^{wb} the solvent-solute pair potentials, and $\mathbf{R}$ is any location in the solvent. Suppose that a and b are simple spherical molecules such that the diameter of a is much larger than that of b . At zero separation, the field of force produced by a will dominate the total field of force produced by the pair of solutes. A solvent molecule w approaching the combined field of force will be repelled from the excluded

²⁴Note that for hard-sphere solutes, $2 \cdot s$ and s are indistinguishable.

volume of a before it has a chance to approach the excluded region of b . Thus, insofar as we are concerned with the hard-core part of the solute-solvent interaction, this is taken care of by the larger molecule a . Furthermore, since b is buried deeply in the excluded region of a , the attractive part of the field of force of b will be very weak in those regions accessible to the solvent molecules. Hence, we can neglect this part of the field of force of b as well. Mathematically, the approximation is

$$U^{wa}(\mathbf{X}_i, \mathbf{R}) + U^{wb}(\mathbf{X}_i, \mathbf{R}) \cong U^{wa}(\mathbf{X}_i, \mathbf{R}) \quad (4.4.49)$$

which is valid for all configurations $\mathbf{X}_i$ that have non-zero probability. Using (4.4.49) in (4.4.48), we get

$$\delta A(R=0) = \Delta\mu_a^* - \Delta\mu_a^* - \Delta\mu_b^* = -\Delta\mu_b^* \quad (4.4.50)$$

This means that the $H\phi O$ interaction at zero separation between two solutes a and b , with b much smaller than a , is determined by the solvation Gibbs energy of the solute b . This relation is useful for small solutes that are absorbed by large solutes such as proteins.

4.4.6. *The hydrophobic interaction at contact distance between the two solutes*

In the previous subsections, we devised a measure of the $H\phi O$ interaction at some distance $R < \sigma$ (σ being the solute diameter), which was found to be useful for a comparison of various solvents. We also discussed the case $R = 0$. In both cases, it was argued that since our primary interest is the solvent rather than the solute, we can study the problem of the $H\phi O$ interaction at any convenient distance for which we get a connection with experimental quantities.

In this section, we turn to a more practical question: What is the strength of the $H\phi O$ at contact, or approximately contact distance, for a pair of solute particles? We outline here two

possible routes for obtaining such information. The first is more theoretical, and it is based on the form of the function $y_{ss}(R)$. We recall the relation (Sec. 4.3)

$$y_{ss}(R) = \exp[-\beta\delta A(R)] \quad (4.4.51)$$

where $y_{ss}(R)$ is the indirect part of the correlation function between the two solutes.

It is well known that the function $y(R)$ is a monotonically decreasing function of R in the range $0 \leq R \leq \sigma$.²⁵ We write here the form of $y(R)$ from the exact solution of the Percus-Yevick equation for hard spheres in the region $0 \leq R \leq \sigma$:

$$y(R) = -(1 - \eta)^{-4} \left[-(1 + 2\eta)^2 + 6\eta \left(1 + \frac{1}{2}\eta\right)^2 \left(\frac{R}{\sigma}\right) - \frac{1}{2}\eta \left(1 + \frac{1}{2}\eta\right)^2 \left(\frac{R}{\sigma}\right)^3 \right] \quad (4.4.52)$$

where $\eta = \pi\rho\sigma^3/6$, with σ being the diameter of the particles and ρ being the number density. Figure 4.16 shows the function $y(R^*)$ where $R^* = R/\sigma$ for (a) the regular close-packed density $\eta = \sqrt{2}\pi/6$, and (b) the density of water at 4°C, $\rho = 0.03346 \text{ \AA}^{-3}$. Clearly, this function is a monotonically decreasing function of R . If this form of the function is valid for real solutes in water, then one can use the information on $y(R)$ in the range $0 \leq R \leq \sigma$ to extract information on $y(\sigma)$ [and hence on $\delta A(\sigma)$] from estimates of $y(R)$ at distances $R \leq \sigma$. Because of the uncertainty of this procedure, we shall not pursue it here. For details, see Ben-Naim (1974). In the next subsection, we discuss a more practical measure of the $H\phi O$ interaction at realistic distances.

²⁵For more details, see Wertheim (1963), Thiele (1963), Percus (1964), and Ben-Naim (1974).

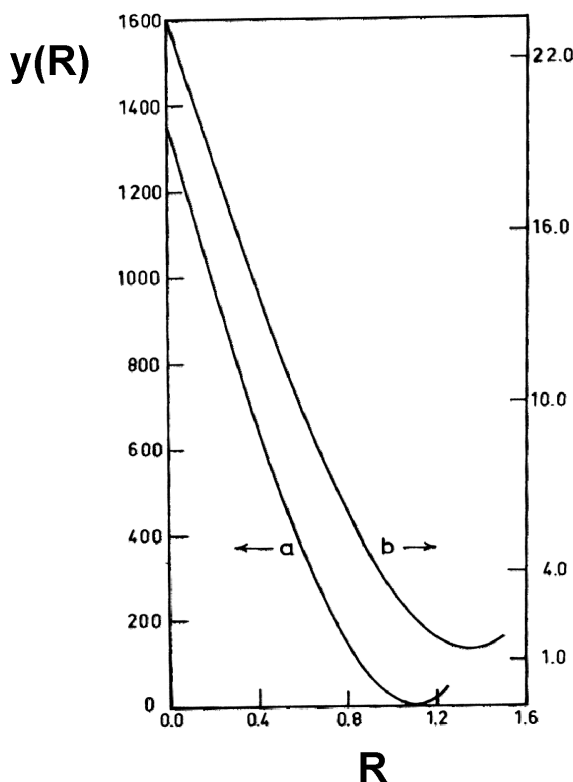


Fig. 4.16 The form of the function $y(R)$ for hard spheres at two densities (Sec. 4.4.6). (See text for details.)

4.4.7. *An improved approximate measure of the $H\phi O$ interaction*

In Sec. 4.4.1, we presented an approximate measure of the $H\phi O$ interaction between two methane molecules at a distance of $R \approx 1.53 \text{ \AA}$. We noted also that the distance $R \approx 1.53 \text{ \AA}$ is not accessible to real solutes. Therefore, little can be inferred about the $H\phi O$ interaction at more realistic distances.

In this section, we present a modified measure of the $H\phi O$ interaction which is based on essentially the same type of arguments as in Sec. 4.4.1 but can, in principle, provide improved

information. The improvement is in both the nature of the approximation and in the reality of the final configuration of the solutes.

As a prototype of the new measure, we choose the neopentane molecule. Using the same arguments as in Sec. 4.41, we consider the process of bringing *five* methane molecules from infinite separation to the final configuration of a neopentane molecule (see Fig. 4.17a). The solvent induced part of the interaction in this case is

$$\delta G_5(\text{process } a) = \Delta\mu^*(\text{neopentane}) - 5\Delta\mu^*(\text{methane}) \quad (4.4.53)$$

This measure involves the same kind of approximation as discussed in Sec. 4.4.1, i.e. the *five* methane molecules are brought to a very close distance ($\sigma_1 \approx 1.53 \text{ \AA}$).

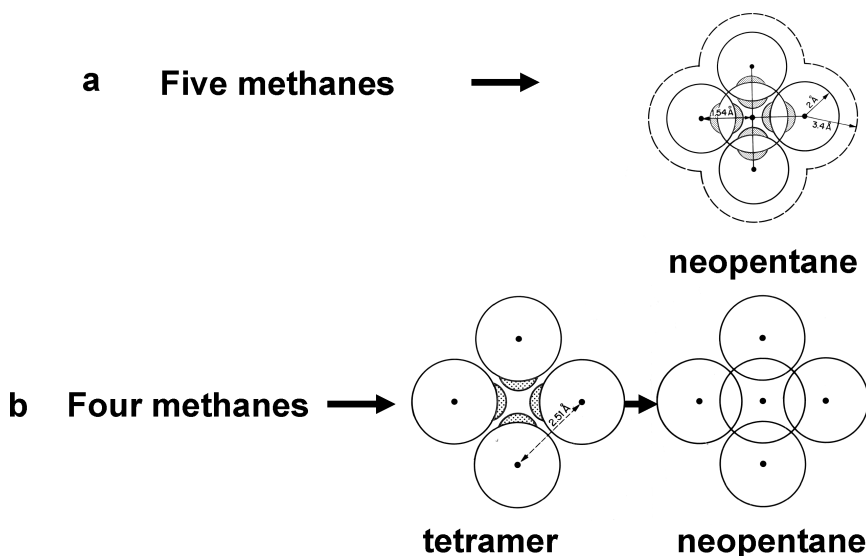


Fig. 4.17 (a) The process of bringing five methanes to the final configuration of neopentane. (b) The process of bringing four methanes to the final configuration of the “tetramer,” and replacing by a real neopentane molecule.

Next, we consider a different process. We start with *four* methane molecules at fixed positions at infinite separation from each other. These solutes are brought to the final configuration of the four peripheral methyl groups in neopentane. We shall refer to this configuration as the tetramer (Fig. 4.17b). At this configuration, we have the relation

$$\delta G_4(\text{process } b) = \Delta\mu^*(\text{tetramer}) - 4\Delta\mu^*(\text{methane}) \quad (4.4.54)$$

where $\Delta\mu^*(\text{tetramer})$ is the solvation Gibbs energy of the tetramer viewed as a single entity. Clearly, this is not a measurable quantity. The statistical mechanical expression for $\Delta\mu^*(\text{tetramer})$ is

$$\Delta\mu^*(\text{tetramer}) = -k_B T \ln \langle \exp(-\beta B_{\text{tetramer}}) \rangle_0 \quad (4.4.55)$$

where B_{tetramer} is the total binding energy of the tetramer to the solvent molecules; more explicitly:

$$B_{\text{tetramer}} = \sum_{j=1}^4 \sum_{i=1}^N U(\mathbf{R}_j, \mathbf{X}_i) \quad (4.4.56)$$

where $U(\mathbf{R}_j, \mathbf{X}_i)$ is the solute-solvent pair potential between the j th solute at $\mathbf{R}_j$ and the i th solvent molecule at the configuration $\mathbf{X}_i$.

Since the tetramer has a compact structure, no solvent molecule can penetrate into the interior of this aggregate. (Note, however, that the average $\langle \cdot \rangle$ is over *all* possible configurations of the solvent molecules. This also includes configurations for which solvent molecules do penetrate into the region occupied by the solute molecules. However, for each of the configurations in which a solvent molecule penetrates into this region, B_{tetramer} becomes very large and positive; hence, $\exp[-\beta B_{\text{tetramer}}]$ becomes practically zero). In Fig. 4.17a, we

indicate with the dashed line the boundary of the excluded volume (assuming that the solvent is water, with a molecular diameter of 2.8 Å).

Clearly, the average in (4.4.55) gets non-zero contributions only from those configurations for which no solvent molecules penetrate into the excluded region produced by the four solute molecules. Therefore, if we insert in the center of this aggregate any particle or a group that produces a short-range field of force, such that it is not felt outside the excluded volume, the value of the average in (4.4.55) will not be affected. We exploit this fact by introducing into the center of the aggregate an “agent” that binds the four solute molecules in such a way that a *real* molecule is formed and for which the solvation Gibbs energy is measurable.

Specifically, we replace the *tetramer* in the process *b* of Fig. 4.17 by one neopentane molecule. The approximation of the binding energy is

$$B(\text{tetramer}) \approx B(\text{neopentane}) \quad (4.4.57)$$

If this approximation is valid for all the configurations of the solvent molecules that have non-zero contributions to the average in (4.4.55), then we can write the approximate expression for $\Delta\mu^*(\text{tetramer})$ as

$$\Delta\mu^*(\text{tetramer}) \approx \Delta\mu^*(\text{neopentane}) \quad (4.4.58)$$

Using (4.4.58) in (4.4.54), we get the final expression for the solvent induced interaction:

$$\delta G_4(\text{process } b) = \Delta\mu^*(\text{neopentane}) - 4\Delta\mu^*(\text{methane}) \quad (4.4.59)$$

This should be compared with (4.4.53), which is a measure of the *H ϕ O* interaction among *five* solute particles. Here, we have a measure of the *H ϕ O* interactions among *four* solutes at

a configuration that is more realizable than the one we have treated in Sec. 4.4.1. Furthermore, the nature of the approximation involved in (4.4.59) is different from the one used in Sec. 4.4.1. Here, we have replaced the four inner hydrogens of the four methane molecules by one carbon center. In a sense, we have partially compensated for the loss of the field of force produced by these hydrogens on the solvent. It is clear that had we started with four bulkier molecules, say, four benzene molecules, and used the same procedure as above, we would have reached the relation

$$\delta G_4 = \Delta G^*(\text{TPM}) - 4\Delta G^*(\text{benzene}) \quad (4.4.60)$$

which measures the $H\phi O$ interaction among four benzene molecules holding the positions of the four benzyl radicals in tetraphenylmethane (TPM). In this case, the boundaries of the excluded volume are quite far from the center of the aggregate. The effect of any replacement made at the center of this aggregate on the solvent becomes negligible. Clearly, the bulkier the four molecules are, the better the replacement approximation that is used in process *b*.

Figure 4.18 presents some values of δG_5 and δG_4 defined in (4.4.53) and (4.4.59) as a function of temperature. Note that values of δG_5 are systematically more negative than the corresponding values of δG_4 . This is probably a result of the fact that the $H\phi O$ interaction becomes larger as the particles come closer together in the final configuration. This is the same behavior we observed for two particles (see Sec. 4.4.6).

The quantity δG_4 (process *b*) in (4.4.59) measures the $H\phi O$ interaction among *four* methane molecules; the closest distance between any pair of molecules is about 2.51 Å, as compared to 1.5 Å between some of the pairs of methane molecules in Fig. 4.17a. Clearly, this is a more realistic configuration than the one for five methane molecules as in process *a*. One can

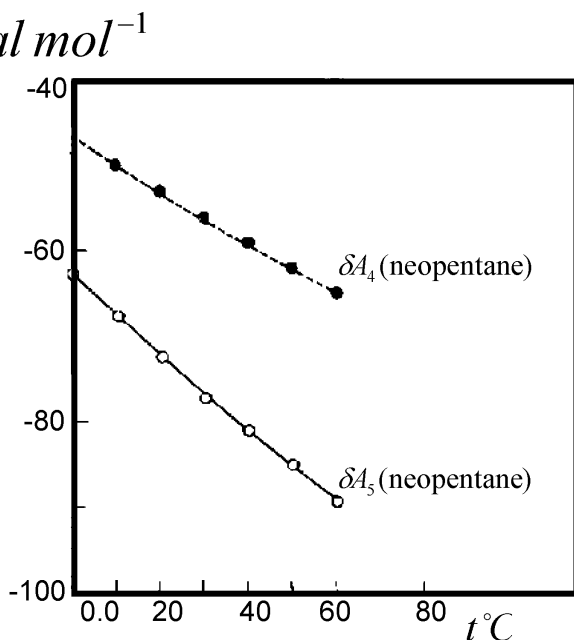


Fig. 4.18 Values of δA_4 [Eq. (4.4.60)] and δA_5 [Eq. (4.4.53)].

make further improvements in this direction by taking four bulkier molecules, such as benzene or long-chain hydrocarbon molecules, to form tetraalkyl or tetraphenyl methane. In such cases, the final configuration is very similar to an actually realizable configuration.

To conclude, Eqs. (4.4.53) and (4.4.59) are approximate relations between a molecular quantity δG and measurable quantities. These relations were obtained not for a real process, but for theoretical (on-paper) processes. The main trick is to manipulate the field of force produced by different sets of solute particles in such a way that changes in the field of force are unnoticed by the solvent. The larger and bulkier the molecules are, the better the approximation.

Finally, a comment on the relevance of the quantity δG and the standard Gibbs energy of dimerization is in order.

The standard Gibbs energy of dimerization is pertinent to the formation of a *real* dimer. It includes the solute-solute intermolecular interactions as well as the change in the translational, rotational, and vibrational degrees of freedom involved in the processes of dimerization.

As was emphasized several times in the original publication,²⁶ the quantity δG is not related to the formation of a *real* dimer. It is simply the change in Gibbs energy in the process of bringing two “fields of force” from infinite separation to the final specific configuration. Unfortunately, this was misunderstood in the literature. First, the “things” that are brought to a close distance are not “cavities” but sources of “fields of force.” Second, I have never “incorrectly interpreted” the quantity δG in terms of the “physical association” of pairs of real molecules as claimed by Pratt and Chandler (1977).

4.5. Intramolecular $H\phi O$ Interactions

As we noted in the introduction of this chapter, the problem of $H\phi O$ interaction was “extracted” from the problem of protein folding (see Fig. 4.1). We noted that there are several effects that together are referred to as the $H\phi O$ effect. One, is the transfer of a $H\phi O$ group from water to the interior of the protein. Another is the approaching of two $H\phi O$ groups, initially independently solvated, to close separation, hence correlated. We also noted that Kauzmann’s idea of studying the first process by using the transfer of a $H\phi O$ group from water to an organic liquid might not be a good model for the process of transferring the same group when it is attached to the backbone of the protein. This has led to the study of the *conditional* solvation energy

²⁶See, for example, Ben-Naim (1974).

(see Sec. 3.3). Likewise, the study of the problem of two-solutes-in-a-solvent, instead of studying the same two groups attached to a protein, might miss an important effect of the protein backbone. Therefore, all the studies of the pair correlation function between two solutes in water might be interesting as an aspect of the properties of water but might be totally irrelevant to the problem of protein folding.

In this section, we examine the question of the *conditional* correlation between the two $H\phi O$ groups — conditional in the sense that the two groups are not solvated by “pure” water but water perturbed by a backbone. The backbone might alter the properties of the solvent in its immediate vicinity, hence also affect the correlation between the groups in the vicinity of the backbone.

In Sec. 4.4, we defined the $H\phi O$ interaction as the indirect work required to bring two $H\phi O$ groups from infinite separation to some close distance, say, $R = |\mathbf{R}_2 - \mathbf{R}_1| \approx \sigma$:

$$\exp[-\beta\delta G(R = \sigma)] = \frac{\langle \exp[-\beta U(\mathbf{X}^N | R \approx \sigma)] \rangle_0}{\langle \exp[-\beta U(\mathbf{X}^N | R \approx \infty)] \rangle_0} \quad (4.5.1)$$

where the quantity $U(\mathbf{X}^N | R)$ is the total binding energy of two solutes at a distance R , to all solvent molecules at some specific configuration $\mathbf{X}^N$.

We have also seen that $\delta G(R)$ is related to the indirect (or the solvent induced) correlation between the two solutes:

$$y_{ss}(R) = \exp[-\beta\delta G(R)] \quad (4.5.2)$$

The *conditional* $H\phi O$ interaction, or the conditional correlation between the two solutes, is defined in the same way as in (4.5.1), but the averaging over all solvent molecules is now replaced by a *conditional* average over all solvent molecules given a backbone (BB) molecule at some fixed location in the

solvent. Thus, instead of (4.5.1) we write

$$\exp[-\beta\delta G(R)] = \frac{\langle \exp[-\beta U(\mathbf{X}^N|R)] \rangle_{BB}}{\langle \exp[-\beta U(\mathbf{X}^N|R = \infty)] \rangle_{BB}} \quad (4.5.3)$$

$\delta G(R)$ in (4.5.3) is the indirect part of the work required to bring two $H\phi O$ groups from infinite separation, near or attached to the BB , to some close distance R , still near or attached to the BB .

In general, the groups do not have to be attached to the BB : all that is required is that the $H\phi O$ groups be in some region close to the BB so that the distribution of the solvent configurations is affected by the BB . In practice, we use (4.5.3) for the case where the $H\phi O$ groups are *attached* to the BB . Figure 4.19 shows three cases: (a) $H\phi O$ interaction in a solvent, (b) conditional $H\phi O$ interaction *near* a BB , and (c) conditional $H\phi O$ interaction when the groups are attached to the BB .

The BB can be the same molecule for the two $H\phi O$ groups or different molecules. In the former case we can also refer to the conditional $H\phi O$ interaction as an *intramolecular* $H\phi O$ interaction. This is the most common case, e.g. in protein folding, where the two groups are attached to the same protein. On

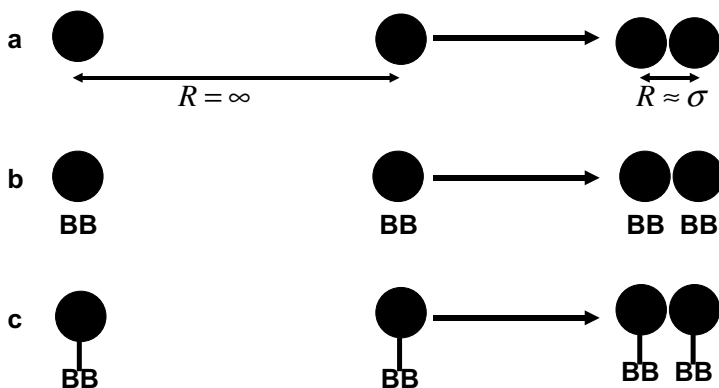


Fig. 4.19 The process of $H\phi O$ interaction between two solutes (a) in a solvent, (b) near a BB , and (c) attached to a BB .

the other hand, in protein-protein association we can refer to the conditional $H\phi O$ interaction as the *intermolecular* $H\phi O$ interaction.

Of course, it is not possible to study the intramolecular $H\phi O$ interaction on a protein. It is not even feasible to calculate the average quantities in (4.5.3) in the presence of a protein. Fortunately, the theory comes to our aid in this case, much as it did in the case of the conditional solvation, or the measure of the $H\phi O$ interaction between two methane molecules studied in Sec. 4.4.

In the next subsection, we shall describe an approximate method of estimating the conditional or the intramolecular $H\phi O$ interaction. As in the previous section, the derivation of this measure relies on statistical mechanical arguments. Without statistical mechanics it is doubtful that such a measure could ever be devised.

4.5.1. A simple measure of the intramolecular $H\phi O$ interaction

Consider a general backbone (BB) having two attached alkyl groups (A). The BB could be a protein or a small molecule; the alkyl group A is a $H\phi O$ group such as methyl or ethyl. We denote by Φ_∞ the isomer of the BB when the two alkyl groups are far apart ("infinity"), so that their solvation spheres do not overlap. In this case, the two groups are said to be independently solvated.

Suppose that we "cut" this molecule into four groups as indicated schematically in Fig. 4.20. The exact location of the "cut" is of no importance since in our final expression we shall deal with the whole molecule. For convenience, however, we assume that the "cut" is done in the middle of the C-C and of the C-H bonds. Also, for simplicity we assume that the molecule as a whole is rigid.

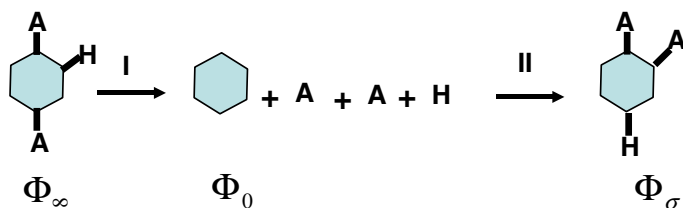


Fig. 4.20 The process of “cutting” a molecule into four radicals and “pasting” the radical to form a new isomer (only one hydrogen that is exchanged is shown explicitly).

We now consider the following process. We start with a single molecule, represented in the figure by the symbol Φ_{∞} , at some fixed location and orientation in a solvent at a given temperature T , pressure P , and total number of molecules N . We “cut” the molecule into four radicals and remove them to fixed locations but at infinite separation from each other. This process is indicated by I in Fig. 4.20. The “bare” BB is denoted by Φ_0 .

The Gibbs energy change for this process is written in the T, P, N ensemble as

$$\Delta G(I) = k_B T \ln \left[\frac{\Delta(T, P, N; \Phi_{\infty})}{\Delta(T, P, N; \Phi_0, H, A, A)} \right] \quad (4.5.4)$$

where in the numerator and in the denominator we have the partition functions of the system at the initial and the final states considered above. Dividing the numerator and the denominator by the partition function of the pure solvent $\Delta(T, P, N)$, we obtain

$$\Delta G(I) = k_B T \ln \frac{\langle \exp[-\beta B(\Phi_{\infty})] \rangle_0 \exp[-\beta U(\Phi_{\infty})]}{\langle \exp[-\beta B(\Phi_0) - \beta B(H) - \beta B(A) - \beta B(A)] \rangle_0} \quad (4.5.5)$$

where $B(\alpha)$ represents the “binding energy” of the solute (or radical) α to the rest of the system which is at a fixed configuration $\mathbf{X}^N$. More specifically, the binding energy of any solute α is

defined as

$$B(\alpha) = \sum_{i=1}^N U(\mathbf{X}_\alpha, \mathbf{X}_i) \quad (4.5.6)$$

where $(\mathbf{X}_\alpha, \mathbf{X}_i)$ represents the configuration of the solute α and of the i th solvent molecule. By $U(\Phi_\infty)$ we denote the total *direct* interactions between the four radicals at the configuration of the molecule Φ_∞ . Alternatively, $-U(\Phi_\infty)$ is the total work required to perform the same process, as described above, but in the absence of a solvent. The two alkyl groups A are identical (e.g. methyl, ethyl, etc.). However, in (4.5.5) they are understood to be at finite separation from each other.

Since we have assumed that the radicals Φ_0, H, A, A are at infinite separation from one another, we may factor the average in the denominator on the right-hand side of (4.5.5) into a product of four average quantities, namely

$$\begin{aligned} & \langle \exp[-\beta B(\Phi_0) - \beta B(H) - \beta B(A) - \beta B(A)] \rangle_0 \\ &= \langle \exp[-\beta B(\Phi_0)] \rangle_0 \langle \exp[-\beta B(H)] \rangle_0 \langle \exp[-\beta B(A)] \rangle_0^2 \end{aligned} \quad (4.5.7)$$

Using this factorization we rewrite (4.5.5) as

$$\begin{aligned} \Delta G(I) &= -U(\Phi_\infty) - \Delta\mu^*(\Phi_\infty) + \Delta\mu^*(H) \\ &\quad + \Delta\mu^*(\Phi_0) + 2\Delta\mu^*(A) \end{aligned} \quad (4.5.8)$$

where $\Delta\mu^*(\alpha)$ is the solvation Gibbs energy of the solute α . In (4.5.8), the only directly measurable quantity is $\Delta\mu^*(\Phi_\infty)$. All of the other terms can be eliminated by the following considerations. First, we define the indirect part of the total work $\Delta G(I)$ by

$$\delta G(I) = \Delta G(I) + U(\Phi_\infty) \quad (4.5.9)$$

From (4.5.8) and (4.5.9) we have

$$\delta G(I) = -\Delta\mu^*(\Phi_\infty) + \Delta\mu^*(H) + \Delta\mu^*(\Phi_0) + 2\Delta\mu^*(A) \quad (4.5.10)$$

Similarly, for the process indicated as *II* in Fig. 4.20 we write the indirect part of the total work as

$$\delta G(II) = \Delta\mu^*(\Phi_\sigma) - \Delta\mu^*(H) - \Delta\mu^*(\Phi_0) - 2\Delta\mu^*(A) \quad (4.5.11)$$

Adding (4.5.10) and (4.5.11) we obtain

$$\delta G(\infty \rightarrow \sigma) = \delta G(I) + \delta G(II) = \Delta\mu^*(\Phi_\sigma) - \Delta\mu^*(\Phi_\infty) \quad (4.5.12)$$

In (4.5.11) and (4.5.12), Φ_σ denotes the configuration of the *BB* with the two alkyl groups at some close separation σ .

What we have done in the two processes *I* and *II* in Fig. 4.20 is essentially to “cut” and “paste” the four groups of Φ_∞ . If we assume that all the direct interactions between the groups (including chemical bonds) are the same in the two configurations Φ_∞ and Φ_σ , the network in the combined processes *I* and *II* is $\Delta G(I) + \Delta G(II)$, but the indirect, or the solvent induced, part of the work is given in (4.5.12).

In principle, on the right-hand side of (4.5.12) we have measurable quantities: the solvation Gibbs energies of two isomers of the same molecule. However, if the *BB* is a protein, then the two solvation Gibbs energies on the right-hand side of (4.5.12) cannot be measured. Fortunately, we can find small *BBs* for which (4.5.12) applies and for which the two quantities on the right-hand side of (4.5.12) can be measured.

The following experimental system was studied.²⁷ The *BB* is the benzene ring, and the two alkyl groups are either methyl or ethyl groups.

For this system, Eq. (4.5.12) is rewritten as

$$\delta G(a) = \delta G[(1,4) \rightarrow (1,2)] = \Delta\mu_{1,2}^* - \Delta\mu_{1,4}^* \quad (4.5.13)$$

²⁷Ben-Naim and Wilf (1979).

Table 4.8 The Indirect Part of the Work required to Transfer an Alkyl Group from Position 4 to Position 2 at Two Temperatures, Process *a* in Fig. 4.21a (in cal mol⁻¹)

Alkyl Group	<i>t</i> (°C)	$\delta G[(1, 4) \rightarrow (1, 2)]$	$\delta G[(1, 4) \rightarrow (1, 2)]$	$\delta G[(1, 4) \rightarrow (1, 2)]$
		H ₂ O	D ₂ O	<i>n</i> -hexane
Methyl	10	-238		70
	20	-300	-280	-28
Ethyl	10	-603		360
	20	-616	-430	445

where $\Delta\mu_{1,2}^*$ and $\Delta\mu_{1,4}^*$ are the solvation Gibbs energies of the 1,2- and 1,4-dialkylbenzene, respectively. These are two measurable quantities. The difference between the two is the indirect work of transferring one alkyl group from position 4 to position 2.

Table 4.8 shows some values of δG relevant to process *a* in Fig. 4.20. Several points should be noted: (i) the values of $\delta G(a)$ in water are negative, compared with the same quantity in *n*-hexane. In *n*-hexane, the values of $\delta G(a)$ are either small or positive. This clearly indicates that the larger the $H\phi O$ interaction in water is larger than the corresponding “solvophobic” effect in *n*-hexane. (ii) The values of $\delta G(a)$ for ethyl are larger than the values for methyl. This is in accordance with the expectation that the $H\phi O$ interaction between hydrocarbons is stronger, the larger the size of the hydrocarbon molecule. (iii) The $H\phi O$ interaction as measured by $\delta G(a)$ is larger (in absolute magnitude) at higher temperatures. This is in agreement with what we have found in Sec. 4.4, namely that the *strength* of the $H\phi O$ interaction increases with the increase in temperature, at least in the range of temperatures around 25°C.

The values of $\delta G(a)$ in Table 4.8 correspond to the process of bringing a group from position 4 to position 2 relative to

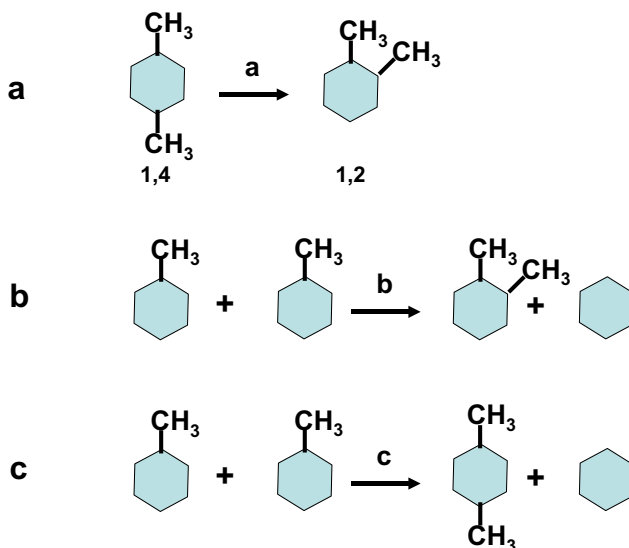


Fig. 4.21 Processes in model compounds used to measure intramolecular $H\phi O$ interactions. The processes (a), (b), and (c) are described in Sec. 4.5.1.

position 1, which is occupied by an alkyl group. As can be seen from Fig. 4.21, the two groups at (1,4) configuration looks quite “far” from each other, and therefore one can reasonably assume that they are independently solvated.

To test this assumption, we examine a new process in Fig. 4.21b. Here, we start with two mono alkylbenzene molecules at *infinite* separation and transfer one alkyl group from one molecule to another. The relevant indirect work is denoted by $\delta G(b)$.

$\delta G(b)$ is defined similarly to (4.5.13) by

$$\delta G(b) = \Delta\mu_B^* + \Delta\mu_{1,2}^* - 2\Delta\mu_T^* \quad (4.5.14)$$

where $\Delta\mu_B^*$ and $\Delta\mu_T^*$ are the solvation Gibbs energies of benzene and toluene, respectively. Table 4.9 shows some values of $\delta G(b)$ for methyl and ethyl groups at two different temperatures. The fact that these values are almost the same within

Table 4.9 Values of $\delta G(b)$ and $\delta G(c)$ (in cal mol⁻¹) for Processes *b* and *c* in Fig. 4.21, respectively

Alkyl Group	<i>t</i> (°C)	In water		In <i>n</i> -hexane	
		$\delta G(b)$	$\delta G(c)$	$\delta G(b)$	$\delta G(c)$
Methyl	10	-205	+33	+7	-62
	20	-276	+24	+40	+68
Ethyl	10	-619	-16	-160	-411
	20	-609	+7	+304	-141

experimental error as the values of $\delta G(a)$ reported in Table 4.8 confirms the assumption that the two groups at positions 1 and 4 are nearly independent. A further confirmation is obtained from the values of $\delta G(c)$, relevant to the process in Fig. 4.21c. Note that all the values of $\delta G(c)$ in water are very small and probably within the experimental error.

Exercise E.4.1: Repeat the argument leading to Eq. (4.5.13) for the processes *b* and *c* in Fig. 4.21.

Finally, we note that the intramolecular $H\phi O$ interaction as measured by $\delta G(a)$ is larger in H₂O compared with D₂O.²⁸ This is consistent with the conclusion we have arrived at in Sec. 4.4.

4.5.2. Mixed $H\phi O$ – $H\phi I$ interactions

We discuss here some aspects of solvent-induced interactions between $H\phi O$ and $H\phi I$ molecules or groups. The simplest example is a simple non-polar atom, say, neon or argon, and a water molecule. These are “pure” $H\phi O$ and $H\phi I$ molecules. The more common cases are molecules that contain both $H\phi O$ and $H\phi I$ groups, such as alcohols, fatty acids, and proteins.

²⁸Wilf and Ben-Naim (1979).

First, consider the case of a simple LJ solute, say, neon or argon, denoted A , very diluted in water w . The solute-solvent pair correlation function should have a first peak at about $R_1 \approx (\sigma_A + \sigma_w)/2$, mainly due to the solute-solvent direct interaction. This is indeed observed in simulations by both Monte Carlo and molecular dynamics methods. We consider here the orientational dependence of the pair correlation function at contact distance R_1 . Simulations of aqueous solutions of simple solutes indicate that at contact distance none of the four arms of the water molecule point to the center of the non-polar solute (see Sec. 3.11).

A qualitative reason for this particular orientation can be easily understood. Water molecules tend to form a hydrogen-bonded network, leaving empty, cage-like spaces in which the solute can be accommodated. In such cages, there are no HB directions (or arms) that point toward the solute molecule.

For a simple solute A diluted in water w , we assume that the direct solute-solvent interaction is spherically symmetrical, that is, $U_{Aw}(R)$ is a function of R only. Therefore, the solute-solvent pair correlation function for this pair is written as

$$g_{Aw}(1, 2) = \exp[-\beta U_{LJ}(R)] \exp[-\beta \delta G(1, 2)] \quad (4.5.15)$$

Within this assumption, all the orientational dependence of g_{Aw} is attributed to $\delta G(1, 2)$.

If a solute A approaches a water molecule w in the gaseous phase, it has the same probability of attaching to any region on the surface w . (This is not precisely the case for real water molecules. However, we make this assumption to highlight the new effect of the solvent-induced interaction in producing the orientational preference discussed below.)

In water, the situation is quite different. We distinguish between two regions on the “surface” of a water molecule. One region consists of the four regions $\Delta X_1, \Delta X_2, \Delta X_3$, and ΔX_4

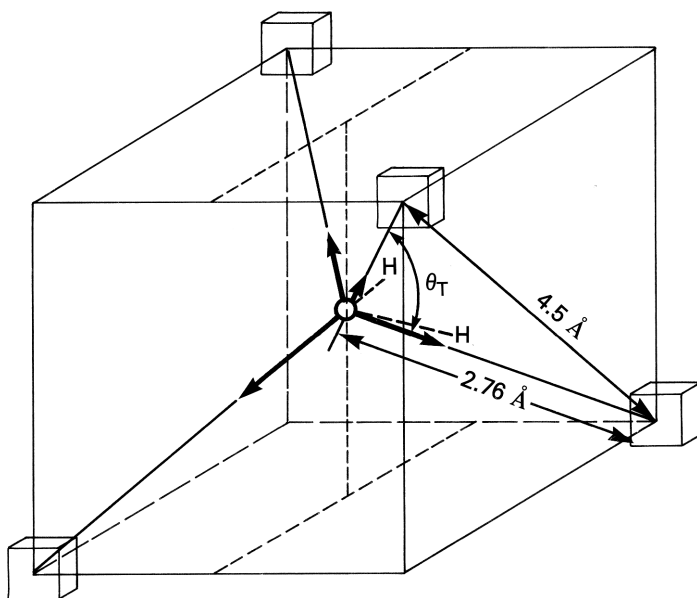


Fig. 4.22 The four squares at the corners of a regular tetrahedral symbolize the regions $\Delta X_1, \Delta X_2, \Delta X_3$, and ΔX_4 from which a water molecule can hydrogen-bond to the central water molecule.

(indicated by four boxes in Fig. 4.22) from which the water molecule can form an *HB* with another water molecule. These regions will be referred to as the hydrogen-bonding regions. All the rest is referred to as the non-hydrogen-bonding region.

When a solute *A* approaches a water molecule near the hydrogen-bonding-region, it blocks the capacity of *w* to form *HBs* with other water molecules. This configuration is denoted by *a'* in Fig. 4.23. The other preferential configuration is denoted by *a*. We write the indirect work required to bring a water molecule to the configurations *a'* and *a* near a solute *A* as

$$\delta G(\infty \rightarrow a') = \Delta G_{Aw}^*(a') - \Delta G_{Aw}^*(\infty) \quad (4.5.16)$$

$$\delta G(\infty \rightarrow a) = \Delta G_{Aw}^*(a) - \Delta G_{Aw}^*(\infty) \quad (4.5.17)$$

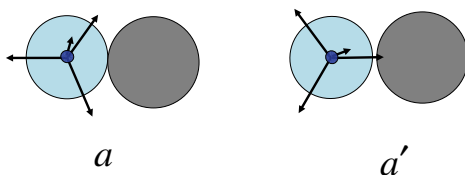


Fig. 4.23 (a) Preferable and (a') unpreferable orientation of a water molecule near a spherical solute.

Since in the configuration *a* all arms of *w* are free to form HBs to the solvent, the solvation Gibbs energy of the pair at configuration *a* must be more negative than in the configuration *a'* by an amount of approximately $-2.25 \text{ kcal mol}^{-1}$. In other words, rotating the water molecule from configuration *a* to *a'* involves the loss of the solvation Gibbs energy of one arm (see Sec. 2.7.6); hence

$$\delta G(a \rightarrow a') = \Delta G_{Aw}^*(a') - \Delta G_{Aw}^*(a) \approx 2.25 \text{ kcal mol}^{-1} \quad (4.5.18)$$

This is the Gibbs energy “penalty” for orienting an arm of a water molecule toward a solute.

In terms of probability, the difference between the two cases can be stated as follows. The ratio of the frequency of observing the two configurations *a* and *a'* is about

$$\begin{aligned} \frac{\text{Pr}(a)}{\text{Pr}(a')} &= \frac{\exp[-\beta \Delta G_{Aw}^*(a)]}{\exp[-\beta \Delta G_{Aw}^*(a')]} \\ &= \exp[-\beta \delta G(a' \rightarrow a)] \approx \exp\left[\frac{+2.25}{0.6}\right] \approx 43 \end{aligned} \quad (4.5.19)$$

This means that configuration *a* is much more probable than configuration *a'*.

Note that in (4.5.19) we compared two discrete (or “point”) events: *a* and *a'*. Since the total hydrogen-bonding region is

considerably smaller than the non-hydrogen-bonding region, the ratio would have been much larger had we taken *any* of the events of type *a* and *any* events of type *a'*.

Similar considerations apply to the prediction of the most likely location of the second minimum in the potential of mean force for the pair of $H\phi O$ solute molecules.²⁹ Consider two methane molecules (or neon, argon, etc.) in water. We have already noted that the first peak of $g_{AA}(R)$ is expected at $R_1 \approx \sigma_A$. The main reason is that $R_1 \approx \sigma_A$ corresponds to the minimum of the direct pair potential between two solute molecules. For two spherical solutes in a normal solvent, the location of the second peak is expected at about $R_2 \approx \sigma_A + \sigma_w$.³⁰ In Sec. 4.11, we shall see that the simulated curve of the potential of mean force for methane in water has a second minimum either at $R_2 \approx 6 \text{ \AA}$ or at $R_2 \approx 7 \text{ \AA}$ (with a choice of molecular diameters of $4.4 \text{ \AA}$ and $2.8 \text{ \AA}$ for methane and water, respectively).

We recall that at the distances between $6 \text{ \AA}$ and $7 \text{ \AA}$, the direct methane-methane interaction is negligible. Therefore, the main contribution to $g_{AA}(R_2)$ should come from the indirect interaction, i.e.

$$g_{AA}(R_2) \approx \exp[-\beta \delta G(R_2)] \quad (4.5.20)$$

$\delta G(R_2)$ is the indirect part of the work of bringing two simple solutes from infinite separation to the final separation R_2 . We have found that the preferential orientation of a water molecule relative to the solute is such that no “arm” is sacrificed. We can assume that this will be true as we move the two solutes from infinity to any short separation R_2 .

In the solvent-separated configuration shown in Fig. 4.24a, the distance between the methane groups is about $7 \text{ \AA}$. On

²⁹For more details, see Ben-Naim (1989).

³⁰See Ben-Naim (2006).

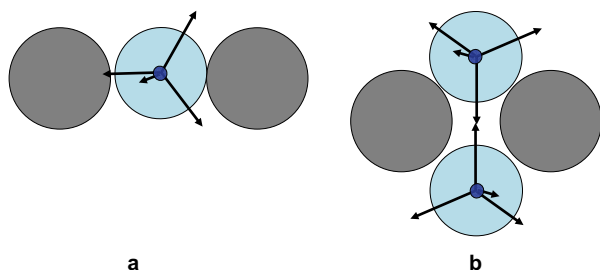


Fig. 4.24 (a) “Water separated” and (b) “water-bridged” configurations near a pair of solute molecules.

the other hand, at a distance of about $6 \text{ \AA}$, the two methane molecules can be “bridged” by a water molecule (Fig. 4.24b). Using the same argument as for the preferential orientation, we can conclude that the configuration of a water-bridge is more probable than the solvent separated configuration.

We now turn to the case of the intramolecular $H\phi O-H\phi I$ interaction. We present here one example of the solvent-induced interaction between a $H\phi O$ group, say, methyl, and an $H\phi I$ group, say, hydroxyl, on a benzene ring. Consider the formation of 2-methylphenol from toluene and phenol (Fig. 4.25a). The relevant “reaction” is



Using the same arguments as in Sec. 4.5.1, we can estimate δG by

$$\begin{aligned} \delta G &= \Delta G_{\text{2-methylphenol}}^* + \Delta G_{\text{benzene}}^* - \Delta G_{\text{toluene}}^* - \Delta G_{\text{phenol}}^* \\ &= 0.76 \text{ kcal mol}^{-1} \end{aligned} \quad (4.5.22)$$

The fact that δG in this case is positive indicates that the methyl group, brought to within very close proximity of the hydroxyl group, *interferes* with the solvation of the latter and hence makes this configuration less stable than the corresponding 4-methylphenol isomer. Another “reaction”

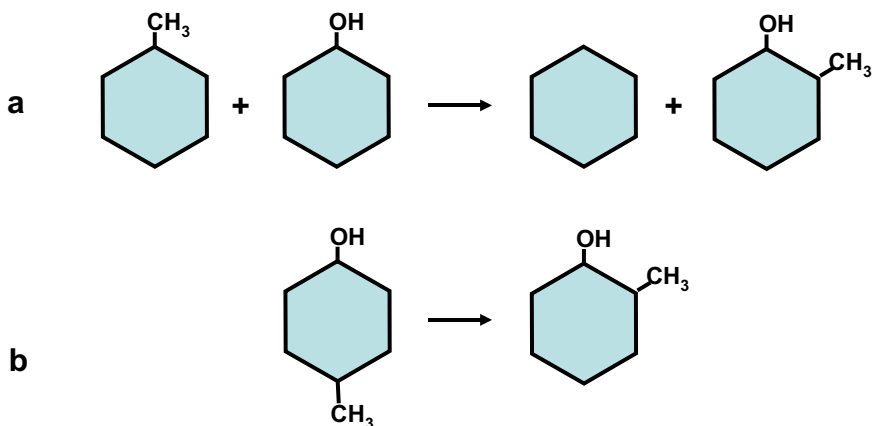


Fig. 4.25 Two processes used to estimate the $H\phi O-H\phi I$ interaction.

relevant to the $H\phi O-H\phi I$ interaction is shown in Fig. 4.25b. The relevant solvent induced contribution to the Gibbs energy change of this process is

$$\delta G = \Delta G_{2\text{-methyphenol}}^* - \Delta G_{4\text{-methyphenol}}^* = 1.09 \text{ kcal mol}^{-1} \quad (4.5.23)$$

which is slightly larger than in the previous case.

4.6. Application of the Scaled Particle Theory

In the previous sections, we presented several measures of the $H\phi O$ interaction in which we made use of experimental data. In this section, we shall use a combined theoretical and experimental input to obtain information on the $H\phi O$ interaction. The basic process is the same as before. We start with m solute particles at fixed positions but at infinite separation from each other in a solvent at some given temperature T and pressure P . We then bring these particles to a close-packed configuration. More specifically, we require that the centers of all the particles be confined to a spherical regions S_A , the radius of which is

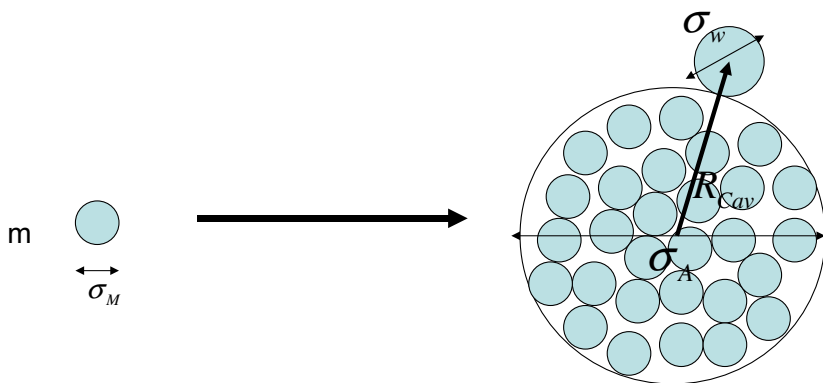


Fig. 4.26 The process of bringing m solute molecules of diameter σ_M to form a spherical aggregate of diameter σ_A .

chosen as described below. The process is schematically shown in Fig. 4.26 and written as

$$(\mathbf{R}^m = \infty) \rightarrow (\mathbf{R}^m \in S_A) \quad (4.6.1)$$

and the corresponding Gibbs energy change is

$$\Delta G_m = U_m + \delta G_m \quad (4.6.2)$$

where U_m and δG_m are the direct and the indirect parts of the work required to carry out the process indicated in (4.6.1). Using the same argument as in the previous sections, we write, for the indirect part of the interaction, the exact relation

$$\delta G_m = \Delta G_A^* - m\Delta G_M^* \quad (4.6.3)$$

where ΔG_M^* is the experimental solvation Gibbs energy of the monomer M , and ΔG_A^* is the solvation Gibbs energy of the close-packed aggregate A , viewed as a single entity.

In the previous sections, we sought approximations for ΔG_A^* using experimental sources. Here, we use the scaled particle theory (SPT) to estimate ΔG_A^* . The procedure of estimating

ΔG_A^* by the *SPT* is the following. First, we split ΔG_A^* into two terms:

$$\Delta G_A^* = \Delta G_A^*(\text{cav}) + \Delta G_A^*(\text{soft}) \quad (4.6.4)$$

where the first term on the right-hand side of (4.6.4) is the work required to create a cavity of a suitable size (see below) in the solvent. The second term is due to the turning on of the soft (or attractive) part of the interaction between the aggregate A and the solvent.

We further assume that m is a large number, that the solute monomers are simple (e.g. argon, methane), and that the aggregate A has a spherical shape and consists of closely packed monomers. With these assumptions, we expect that the soft part of the field of force A will originate only from those molecules that are in direct contact with the solvent, i.e. the molecules that form the surface of the aggregate A . If the number of monomers m is large, the contribution of $\Delta G_A^*(\text{soft})$ to ΔG_A^* becomes small compared to $\Delta G_A^*(\text{cav})$. Thus, for sufficiently large m , we use the approximation

$$\Delta G_A^* \approx \Delta G_A^*(\text{cav}) \quad (4.6.5)$$

where $\Delta G_A^*(\text{cav})$ may be computed from the *SPT*. Note that for a hard-sphere solute, $\Delta G_A^*(\text{soft})$ is zero, and (4.6.5) is an equality. We therefore expect that for a simple solute such as methane, (4.6.5) is a good approximation.

To proceed, we need to estimate the size of the cavity created by the aggregate of m molecules. Let σ_M be the effective hard-core diameter of methane, which we take as equal to the Lennard-Jones diameter of methane, $\sigma_M = 3.82 \text{ \AA}$. If m solutes of diameter σ_M are packed in a compact manner in such a way that they form a sphere of diameter σ_A , the ratio of the actual volume of the m particles to the volume of the sphere S_A is

about

$$\frac{m\pi\sigma_M^3/6}{\pi\sigma_A^3/6} \approx 0.7405 \quad (4.6.6)$$

From (4.6.6), we can estimate the diameter of the sphere S_A :

$$\sigma_A = \left(\frac{m\sigma_M^3}{0.7405} \right)^{1/3} \quad (4.6.7)$$

If the diameter of the solvent molecules is σ_w , then the radius of the cavity produced by the aggregate A is given by

$$R_{\text{cav}} = \frac{\sigma_A + \sigma_w}{2} \quad (4.6.8)$$

The situation is schematically depicted in Fig. 4.26. Once we have the radius R_{cav} , the molecular diameter, and the number density of the solvent, we can use the *SPT* to estimate $\Delta G_A^*(\text{cav})$.

Thus, in essence, we have replaced the exact result in (4.6.3) by the approximate relation

$$\delta G_m \approx \Delta G_A^*(\text{cav}) - m\Delta G_M^* \quad (4.6.9)$$

Here, ΔG_M^* is taken from experimental data and $\Delta G_A^*(\text{cav})$ is computed from the *SPT*. For the following numerical examples, we use methane with a molecular diameter of $\sigma_M = 3.82 \text{ \AA}$ as our monomer. The solvents used in these illustrations are water (and heavy water) with $\sigma_w = 2.90 \text{ \AA}$, methanol with $\sigma_M = 3.69 \text{ \AA}$, ethanol with $\sigma_E = 4.34 \text{ \AA}$, and cyclohexane with $\sigma_C = 5.63 \text{ \AA}$. These are effective hard-core diameters of the molecules that have been used in the application of the *SPT*.

In addition to the effective molecular diameter, the solvents are characterized by their number densities at the given temperature and pressure. This information is sufficient for the calculation of the Gibbs energy change associated with the formation of

a cavity $\Delta G_A^*(\text{cav})$, and hence the computation of δG_m through relation (4.6.9).³¹

Once we have calculated δG_m , we can proceed to calculate the corresponding entropy and enthalpy of the process (4.6.1):

$$\delta S_m = -\frac{\partial \delta G_m}{\partial T} = \Delta S_A^*(\text{cav}) - m\Delta S_M^* \quad (4.6.10)$$

and

$$\delta H_m = \delta G_m + T\delta S_m = \Delta H_A^*(\text{cav}) - m\Delta H_M^* \quad (4.6.11)$$

where again we use the *SPT* to compute $\Delta S_A^*(\text{cav})$ and $\Delta H_A^*(\text{cav})$ but using experimental data for ΔS_M^* and ΔH_M^* .

Note that δS_m as defined in (4.6.10) is the same as the total entropy change for the process (4.6.1). On the other hand, δH_m is only the indirect part of the enthalpy change that corresponds to this process. The relationship between the total and the indirect enthalpy changes is

$$\Delta H_m[(R^m = \infty) \rightarrow (R^m \in S_A)] = U_m + \delta H_m \quad (4.6.12)$$

In Fig. 4.27, we present some computed values of δG_m , δS_m , and δH_m as functions of the number of monomers m . It is clear that as m becomes large enough (say, $m \geq 100$), the values of δG_m in water (and heavy water) become large and negative. In methanol, ethanol, and cyclohexane, the corresponding values are either positive or slightly negative. These results may be translated into the language of probability. Suppose we take two solvents, say, water and methanol, both at the same temperature T and pressure P . Also, we assume that the solute M forms a very dilute solution in these two solvents, in such a way that the number density ρ_M is the same in the two solvents, i.e. $\rho_M(\text{in water}) = \rho_M(\text{in methanol})$ (ρ_M is the number of solute molecules per unit volume of the solvent). In such a solution,

³¹For details, see Ben-Naim and Tenne (1977).

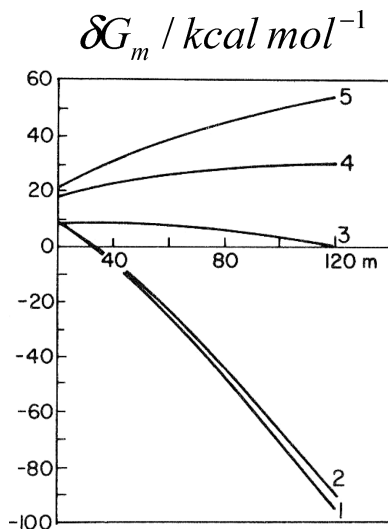


Fig. 4.27 Values of δG_m as a function of the number of monomers m . The solute is methane and the solvents are: (1) H₂O, (2) D₂O, (3) methanol (4) ethanol, and (5) cyclohexane. The calculations were made at 30°C and 1 atm.

we may ask for the probability of finding a close-packed aggregate containing m solute molecules. Clearly, if we choose an exact configuration of the aggregate, then the probability of its occurrence is nearly zero. However, the ratio of such probabilities in two solvents is a finite quantity. This ratio is given by

$$\eta = \frac{P_m(\text{water})}{P_m(\text{methanol})} = \exp[-\beta\delta G_m(\text{water}) - \beta\delta G_m(\text{methanol})] \quad (4.6.13)$$

As an example, we choose $m = 100$ and compute the ratio η at three temperatures. The results are

$$\begin{aligned} \eta(t = 10^\circ\text{C}) &\approx 4 \times 10^{32}, & \eta(t = 30^\circ\text{C}) &\approx 5 \times 10^{53}, \\ \eta(t = 60^\circ\text{C}) &\approx 2 \times 10^{57} \end{aligned} \quad (4.6.14)$$

These results indicate that in a dilute solution of $m = 100$ monomers M , as described above, the probability of finding a close-packed aggregate in water is far larger than the corresponding probability in methanol. Furthermore, this ratio becomes larger as the temperature *increases* in the range of temperatures of, say, $0^\circ\text{C} \leq t \leq 80^\circ\text{C}$.

It should be noted that these ratios of the probability of aggregation is much larger than the ratios calculated for a pair or a small number of solute molecules. One should bear in mind these results when arguing about the role of the $H\phi O$ interaction in processes such as protein folding or micelle formation. In the latter, a large number of $H\phi O$ groups are brought into contact, and hence, the $H\phi O$ effect is expected to be large. On the other hand, in processes such as protein folding and protein-protein association, only a few $H\phi O$ groups are brought into contact. Therefore, it is not expected that the $H\phi O$ effect will dominate the driving force for such processes.

We have seen in Sec. 4.4.1 that the pairwise $H\phi O$ interaction between methane molecules is stronger in H_2O as compared to D_2O . From Fig. 4.27, we see that the $H\phi O$ interaction among m solute particles in H_2O is stronger than in D_2O , in conformity with the behavior of the pairwise $H\phi O$ interaction.

Figure 4.28 shows the variation with m of the three quantities involved in (4.6.9). We see that for small m , values of $\Delta G_A^*(\text{cav})$ and $m\Delta G_M^*$ are of comparable magnitude. As m increases, the term $m\Delta G_M^*$ becomes the dominant one. This means that for large values of m , our computed results are determined by the experimental rather than by the theoretical calculation based on the *SPT*. This conclusion may also be understood on intuitive grounds. To see this, we make a distinction between two kinds of monomers that build up the aggregates. Let m_s be the number of solute monomers that form the surface of the aggregate (i.e. those that are in contact with the

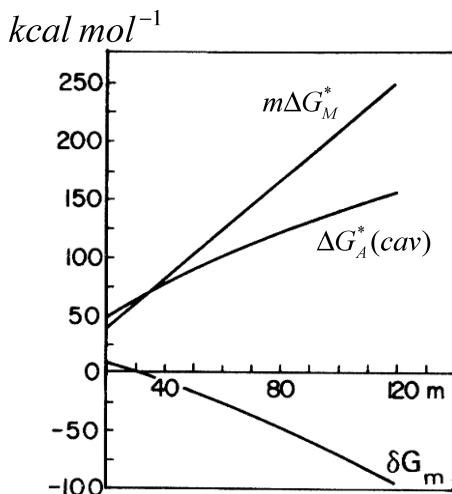


Fig. 4.28 Values of δG_m , $\Delta G_A^*(\text{cav})$, and $m\Delta G_M^*$ (in kcal mol^{-1}) n as a function of m in water at 30°C and 1 atm.

solvent) and m_I be the number of solute monomers that are in the interior of the aggregate (i.e. those that are surrounded by other solute monomers only). Thus, the overall process of aggregation depicted in Fig. (4.26) may be split into two parts:

$$m_s \text{ monomers} \rightarrow \text{surface of the aggregate} \quad (4.6.15)$$

$$m_I \text{ monomers} \rightarrow \text{interior of the aggregate} \quad (4.6.16)$$

Clearly, for very large aggregates, the number of surface particles may be neglected with respect to the number of interior particles. Hence, the Gibbs energy change of the overall process will be determined by the Gibbs energy of transferring m_I monomers from the solvent into the interior of the aggregate. Furthermore, since we have eliminated the direct solute-solute interaction in the definition of δG_m , the process in Fig. 4.26 is the same as transferring m_I solutes from the liquid to the gas. Hence, this process is approximately represented by $-m\Delta G_M^*$.

The above considerations are valid for very large m , in which case δG_m becomes essentially equal to m times $-\Delta G_M^*$. As we see from Fig. 4.28, for m of the order of 100, both terms on the right-hand side of (4.6.3) contribute to δG_m ; hence, for such a size of aggregate, we are still far from the limiting behavior that we mentioned above. This means that δG_m , with m of the order of 100, is more relevant to an aggregation process than to a mere reversal of the solvation of the m monomers.

Figure 4.29 presents the values of δS_m and δH_m as functions of the number of monomers m . These computations were based on the assumption that the diameter of the solvent molecules is temperature independent.³² These results indicate that both the entropy and the enthalpy changes associated with the process of aggregation in water are larger than the corresponding values in methanol, ethanol, and cyclohexane. These results are in complete agreement with the results obtained for $\delta G_2(\sigma_1)$ discussed in Sec. 4.4.1.

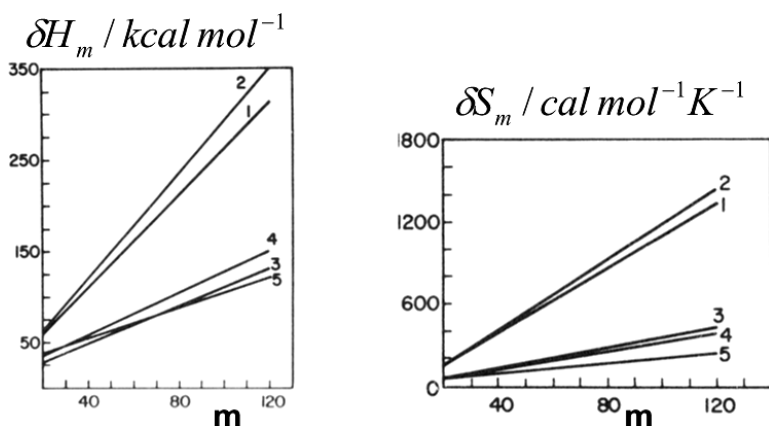


Fig. 4.29 Values of δH_m (in kcal mol^{-1}) and δS_m (in kcal mol^{-1}) as a function of the number of monomers in different liquids. The labels are as in Fig. 4.27.

³²Ben-Naim and Tenne (1977).

It should be noted that the question of which temperature dependence for the molecular diameter one should employ in these computations has not yet been settled. Only for hard spheres is the diameter of the particles a well-defined quantity and temperature independent. For simple fluids, say, argon or methane, one may reasonably argue that the effective hard-core diameter should be a decreasing function of the temperature. The physical idea is that as one increases the temperature, the average kinetic energy of the particles also increases. Hence, on average, inter-particle collisions would lead to more extensive penetration into the repulsive region of the pair potential. Indeed, it has been demonstrated that if such a negative temperature dependence of σ_s is adopted, then one can obtain a good agreement between the prediction from the *SPT* and experimental results.

The situation is far more complicated for non-spherical or more complex solvent molecules. In the first place, the very concept of a hard-core diameter is not a well-defined quantity. For water, for instance, one may conveniently choose the effective diameter of the water molecule as the location of the first peak of the radial distribution function $g(R)$ for pure water. If we adopt this definition, we find that there exists a small positive temperature dependence of the molecular diameter of water. The rationale for this behavior is quite simple. In liquid water at room temperature, most of the water molecules are engaged in hydrogen bonds. The optimal distance for a hydrogen bond is about $2.76 \text{ \AA}$, well within the effective hard-core diameter assigned to a water molecule, about $2.8 \text{ \AA}$. As the temperature increases, one should consider at least two competing effects. On the one hand, we have the kinetic energy effect that was described above, which tends to decrease the effective diameters of the free water molecules. On the other hand, hydrogen-bonded pairs are broken as we increase the temperature; hence,

fewer pairs of molecules will be found at the relatively short distance of 2.76 Å. This calls for an increase in the effective diameters of the bonded molecules.

4.7. Temperature and Pressure Dependence

In the previous sections, we have characterized the *strength* of the $H\phi O$ interaction by either $\delta A(R)$ or $\delta G(R)$. We now consider the entropy and the enthalpy changes associated with the process of bringing two solutes from infinite separation to a final distance R . We refer to this process as the $H\phi O$ process and make a distinction between $H\phi O$ processes in T, V, N and T, P, N ensembles.

The Helmholtz energy change for the $H\phi O$ process is given by

$$\Delta A^l(R) = A_{N+2}^l(R) - A_{N+2}^l(R = \infty) = U(R) + \delta A(R) \quad (4.7.1)$$

The entropy change associated with this process is

$$-\Delta S^l(R) = \left(\frac{\partial \Delta A^l(R)}{\partial T} \right)_{V,N} = \left(\frac{\partial \delta A(R)}{\partial T} \right)_{V,N} = -\delta S(R) \quad (4.7.2)$$

where we have assumed that the direct pair potential $U(R)$ is temperature independent. We can thus obtain $\Delta S^l(R)$ from the temperature dependence of $\delta A(R)$.

Since we shall derive most of the information on the temperature and pressure dependence of the $H\phi O$ interaction from experimental data, we shall discuss in the following only the $H\phi O$ process in the T, P, N ensemble.

The Gibbs energy change for the $H\phi O$ process is defined as

$$\begin{aligned}\Delta G^l(\mathbf{R}_1, \mathbf{R}_2) &= G_{N+2}^l(\mathbf{R}_1, \mathbf{R}_2) - G_{N+2}^l(R = \infty) \\ &= U(\mathbf{R}_1, \mathbf{R}_2) + \delta G(\mathbf{R}_1, \mathbf{R}_2)\end{aligned}\quad (4.7.3)$$

and the statistical mechanical expression for $\delta G(\mathbf{R}_1, \mathbf{R}_2)$ is

$$\delta G(\mathbf{R}_1, \mathbf{R}_2) = -k_B T \ln \langle \exp[-\beta U(\mathbf{X}^N | \mathbf{R}_1, \mathbf{R}_2)] \rangle - 2\Delta\mu_s^* \quad (4.7.4)$$

Here, $\langle \cdot \rangle$ indicates an average in the T, P, N ensemble. $\Delta\mu_s^*$ is the Gibbs energy of solvation of the solute s .

In Sec. 4.4.1, we used an approximate measure for the $H\phi O$ between two methane molecules at the distance $R = \sigma_1 = 1.53 \text{ \AA}$:

$$\delta G(\sigma_1) = \Delta\mu_E^* - 2\Delta\mu_M^* \quad (4.7.5)$$

Here, the subscripts E and M denote ethane and methane, respectively. In (4.7.5), we view each quantity as a function of T and P ; hence, the corresponding entropy change for this particular process is

$$-\delta S(\sigma_1) = \left(\frac{\partial \delta G(\sigma_1)}{\partial T} \right)_P = \left(\frac{\partial \Delta\mu_E^*}{\partial T} \right)_P - 2 \left(\frac{\partial \Delta\mu_M^*}{\partial T} \right)_P \quad (4.7.6)$$

We now identify the two derivatives on the right-hand side of (4.7.6) as the entropies of solvation. Hence

$$\delta S(\sigma_1) = \Delta S_E^* - 2\Delta S_M^* \quad (4.7.7)$$

Similarly, the enthalpy of the $H\phi O$ process is obtained from (4.7.3) by differentiation with respect to temperature:

$$\begin{aligned}\Delta H^l(\mathbf{R}_1, \mathbf{R}_2) &= -T^2 \partial [\Delta G^l(\mathbf{R}_1, \mathbf{R}_2) / T] / \partial T \\ &= U(\mathbf{R}_1, \mathbf{R}_2) + \delta H(\mathbf{R}_1, \mathbf{R}_2)\end{aligned}\quad (4.7.8)$$

For the particular distance $R = \sigma_1$, we get the approximate expression

$$\delta H(\sigma_1) = -T^2 \partial[\delta G(\sigma_1)/T]/\partial T = \Delta H_E^* - 2\Delta H_M^* \quad (4.7.9)$$

For the volume change, we have

$$\Delta V^l(\mathbf{R}_1, \mathbf{R}_2) = \frac{\partial \Delta G^l(\mathbf{R}_1, \mathbf{R}_2)}{\partial P} = \frac{\partial \delta G(\mathbf{R}_1, \mathbf{R}_2)}{\partial P} \quad (4.7.10)$$

Therefore, the approximate measure of the volume change for the particular distance $R = \sigma_1$ is

$$\delta V(\sigma_1) = \Delta V_E^* - 2\Delta V_M^* \quad (4.7.11)$$

4.7.1. *Some experimental values of the entropy, enthalpy, and volume changes associated with the $H\phi O$ interaction*

Table 4.10 gives some values of $\delta G(\sigma_1)$, $\delta S(\sigma_1)$, $\delta H(\sigma_1)$, and $\delta V(\sigma_1)$ when bringing two methanes to the final configuration of ethane in various solvents. Note that both the entropy and the enthalpy values in water (and heavy water) are positive and large compared with the corresponding values in other solvents.

It is instructive to estimate the difference between the enthalpy change $\delta H(\sigma_1)$ and the corresponding energy change $\delta E(\sigma_1)$, which for water at 10°C and 1 atm is

$$\delta H(\sigma_1) - \delta E(\sigma_1) = P\delta V(\sigma_1) = -0.55 \text{ cal mol}^{-1} \quad (4.7.12)$$

Thus, the difference between $\delta H(\sigma_1)$ and $\delta E(\sigma_1)$ in water is considered to be negligibly small when compared with their individual values.

Figure 4.30 shows the variation of $\delta S(\sigma_1)$ and $\delta H(\sigma_1)$ as a function of the mole fraction of ethanol in water-ethanol mixtures. The most prominent feature of these two curves is the steep decrease in δS and δH in the water-rich region

Table 4.10 Values of $\delta G(\sigma_1)$, $\delta S(\sigma_1)$, $\delta H(\sigma_1)$, and $\delta V(\sigma_1)$ in bringing two Methane Molecules to the Distance $\sigma_1=1.533 \text{ \AA}$ at 10°C^a

Solvent	$\delta G(\sigma_1)$, (kcal mol ⁻¹)	$\delta S(\sigma_1)$, (cal mol ⁻¹ K ⁻¹)	$\delta H(\sigma_1)$, (kcal mol ⁻¹)	$\delta V(\sigma_1)$ (cm ³ mol ⁻¹)
Water	-1.99	12	1.60	-22.3
Heavy water	-1.94	13	1.70	—
Methanol	-1.28	0	-1.4	—
Ethanol	-1.34	0	-1.3	—
1-Propanol	-1.39	2	-0.6	—
1-Butanol	-1.44	-1	-1.9	—
1-Pentanol	-1.49	0	-1.3	—
1-Hexanol	-1.51	2	0.7	—
1,4-Dioxane	-1.61	3	-0.8	—
Cyclohexane	-1.36	1	-1.2	—
CCl ₄				-34.8
<i>n</i> -hexane				-46.7
Benzene				-38.6

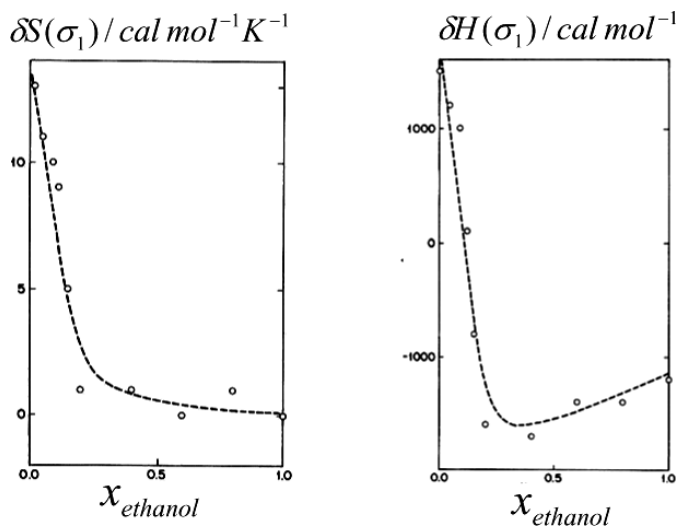
^aBased on data from Yaacobi and Ben-Naim (1974).**Fig. 4.30** Values of $\delta S(\sigma_1)$ and $\delta H(\sigma_1)$ as functions of the mole fraction of ethanol at 15°C .

Table 4.11 Volume Change Associated with the “Dimer” Formation of α , ω -Alcohols from Monoalcohols in Water at 25°C^a

Monomer	“Dimer”	δV
C–OH	HO–C–C–OH	–19.87
C ₂ –OH	HO–C ₄ –OH	–20.57
C ₃ –OH	HO–C ₆ –OH	–19.47
C ₄ –OH	HO–C ₈ –OH	–19.47
C ₅ –OH	HO–C ₁₀ –OH	–19.47

^aValues of δV (cm³ mol^{–1}) computed from data from Edwards *et al.* (1977). Similar data have also been reported by Jolicœur and Lacroix (1976).

($0 \lesssim x_{\text{ethanol}} \lesssim 0.2$) followed by an almost constant value in the entire region of composition $x_{\text{ethanol}} \gtrsim 0.2$.

In Tables 4.10 and 4.11, we also present some values of the volume change corresponding to the $H\phi O$ process. Note that all the values of δV are negative, meaning that the strength of the $H\phi O$ interaction decreases with the increase in pressure.

It is of interest to note also that the volume change in adding a methyl group to an n -alcohol is about -20 cm³ mol^{–1} and is nearly independent of n .³³

4.7.2. Formal statistical mechanical expressions for δG , δS , δH , and δV for the $H\phi O$ process

We have already discussed the statistical mechanical expression for δG in Sec. 4.4. For the process of bringing two simple solutes s from infinite separation to some close distance R we have

$$\begin{aligned} \delta G(R) &= -k_B T \ln \frac{\langle \exp[-\beta B(R)] \rangle_0}{\langle \exp[-\beta B(\infty)] \rangle_0} = -k_B T \ln \frac{\langle \exp[-\beta B_D] \rangle_0}{\langle \exp[-\beta B_s] \rangle_0^2} \\ &= \Delta \mu_D^* - 2\Delta \mu_s^* \end{aligned} \quad (4.7.13)$$

³³Terasawa *et al.* (1975).

where $B(R)$ and $B(\infty)$ are the binding energies of the two solutes at a distance R and at infinite distance from each other, respectively. The average in the denominator may be factorized into a product of two averages each of which is pertinent to the solvation Gibbs energy of one solute s . We have also denoted the “dimer,” consisting of two solutes at a distance R , by D . The entropy, enthalpy, and volume changes associated with the $H\phi O$ processes may be obtained by the direct differentiation of $\delta G(R)$ in (4.7.13) with respect to temperature and pressure. The results are

$$\begin{aligned} \delta S(R) = \Delta S_D^* - 2\Delta S_s^* &= k_B \ln \left\{ \frac{\langle \exp[-\beta B(R)] \rangle_0}{\langle \exp[-\beta B(\infty)] \rangle_0} \right\} \\ &\quad - \frac{1}{T} [\langle B(R) \rangle_R - \langle B(\infty) \rangle_\infty + \langle U_N \rangle_R - \langle U_N \rangle_\infty \\ &\quad + P\langle V \rangle_R - P\langle V \rangle_\infty] \end{aligned} \quad (4.7.14)$$

$$\begin{aligned} \delta H(R) = \Delta H_D^* - 2\Delta H_s^* &= \langle B(R) \rangle_R - \langle B(\infty) \rangle_\infty + \langle U_N \rangle_R \\ &\quad - \langle U_N \rangle_\infty + P\langle V \rangle_R - P\langle V \rangle_\infty \end{aligned} \quad (4.7.15)$$

$$\delta V(R) = \langle V \rangle_R - \langle V \rangle_\infty \quad (4.7.16)$$

$$\delta E(R) = \langle B(R) \rangle_R - \langle B(\infty) \rangle_\infty + \langle U_N \rangle_R - \langle U_N \rangle_\infty \quad (4.7.17)$$

where $\langle \cdot \rangle_R$ and $\langle \cdot \rangle_\infty$ stand for the conditional averages over all the configurations of the solvent molecules given that the two solutes are at fixed positions at a distance R and at infinite distance, respectively. Thus, for example, the energy change associated with the $H\phi O$ process consists of two terms. $\langle B(R) \rangle_R - \langle B(\infty) \rangle_\infty$ is the change in the binding energy of the pair of solutes when they are brought from infinity to the distance R . The averages are conditional averages with different conditions in each case. The second term $\langle U_N \rangle_R - \langle U_N \rangle_\infty$ is the change in the average potential energy of interaction among the solvent molecules caused by the process of bringing the two solute molecules from infinity to R . This quantity may be reinterpreted

in terms of structural changes in the solvent induced by the process of the $H\phi O$. This interpretation will be further discussed in the next subsection.

Finally, we note that the temperature dependence of the $H\phi O$ interaction has two sources. We write for any δG the relation

$$\delta G = -k_B T \ln y$$

Here, δG is the indirect part of the Gibbs energy change in the process of bringing two (or more) real particles (or sources of fields of forces) from infinite separation to some final configuration. y is the indirect part of the pair (or higher-order) correlation function.

As we have done in Sec. 3.2, the temperature dependence of δG can be written as

$$\frac{\partial \delta G}{\partial T} = -\delta S = \frac{\delta G}{T} - \frac{\delta H}{T}$$

Since the values of both δG and $-\delta H$ are negative, we can conclude that both of these contribute to the negative temperature dependence of the $H\phi O$. In conjunction with this, it is instructive to mention an erroneous conclusion which appeared quite frequently in the literature. Pratt and Chandler (1977) used approximate integral equations to calculate the $H\phi O$ and its temperature dependence. They found that $\ln y$ actually *decreases* with temperature. They claimed that the temperature dependence of δG is “trivial” and arises from the $k_B T$ factor in $-k_B T \ln y$.

In my opinion, the temperature dependence of $-k_B T \ln y$ is far from trivial and arises from the two contributions mentioned above. Regarding the overall temperature dependence of the $H\phi O$ interaction, Pratt and Chandler (1977) wrote:

“Viewed on a microscopic level this conclusion appears paradoxical. If the hydrophobic interaction is a result

of the peculiar nature of liquid water, then one would expect that the hydrophobic interaction strength should decrease as the temperature is raised and liquid water becomes less peculiar.”

This erroneous reasoning also appeared in the literature in connection with the temperature dependence of the solvation Gibbs energy as well as in discussing the Gibbs energy of transferring a solute from H_2O to D_2O (see Sec. 3.6). It is true that the $H\phi O$ interaction, as well as the solvation Gibbs energy of a simple solute, is related to the “peculiar nature of liquid water.” It is not true, however, that this dependence is a monotonous function of whatever one chooses to measure the extent of the peculiarity of water. In other words, one cannot conclude that the more structured the system is, the larger the $H\phi O$ interaction.

The fact that Pratt and Chandler (1977) got the wrong temperature dependence of the $H\phi O$ does not render the experimental facts “paradoxical”; it only proves that the approximation used in their calculations is inadequate. More specifically, they used in their theory the experimental, *spatial* pair correlation function of liquid water. As we have seen, the sign of δH and δS depend on the *structural changes induced* by the process of $H\phi O$. Clearly, by using the experimental, angle-averaged pair correlation function of water, one cannot obtain any result that depends on the subtle structural changes in the water. The inevitable conclusion is that the Pratt and Chandler theory fails to capture phenomena that depend on the “peculiar structure of liquid water.”

4.7.3. *Hydrophobic interaction and structural changes in the solvent*

This section is concerned with the interpretation of the large, positive values of $\delta S(\sigma_1)$ and $\delta H(\sigma_1)$ found for water, as

compared with the corresponding values in other solvents, for which relevant experimental results are available.

Consider the two contributions to $\delta G(\sigma_1)$ in water and in ethanol (in kcal mol^{-1} at $t = 10^\circ\text{C}$ ³⁴):

$$\delta H(\sigma_1) \cong 1.6, \quad T\delta S(\sigma_1) \cong 3.4, \quad (4.7.18)$$

$$\delta G(\sigma_1) \cong -1.99 \text{ (water)}$$

$$\delta H(\sigma_1) \cong -1.3, \quad T\delta S(\sigma_1) \approx 0, \quad (4.7.19)$$

$$\delta G(\sigma_1) \cong -1.34 \text{ (ethanol)}$$

It is evident that the main contribution to the large negative value of $\delta G(\sigma_1)$ in water comes from the entropy term. This fact provides the basis for the traditional interpretation of the large negative value of δG in water based on the following two statements: (i) the large, positive value of δS in water is due to the breakdown of the structure of water, and (ii) the large negative value of δG is mainly due to the entropy change and not to the enthalpy change. Hence, it is very tempting to conclude that structural changes in the solvent are responsible for the strong $H\phi O$ interaction in water. However, because of the exact compensation effect, the structural changes associated with the $H\phi O$ process may affect the values of δS and δH but not the values of δG .

One quick argument on the independence of δG on structural changes in the solvent can be given on the basis of Eq. (4.7.13), which relates $\delta G(\sigma_1)$ to the solvation Gibbs energies of the monomers and “dimers.” We already know from Chapter 3 that these solvation Gibbs energies are independent of structural changes in the solvent. Therefore, this must also be true for $\delta G(\sigma_1)$. Because of the importance of this question, we present a direct argument here, valid for any process of bringing two

³⁴ $\delta G(\sigma_1)$ is as defined in (4.4.15).

(or more) solutes from infinite separation to a final distance R . For simplicity, we use a two-structure model for the solvent. The generalization for any mixture model is quite straightforward.

Within the two-structure model, we express the relaxation part of $\delta H(R)$ as

$$\delta H^r = \Delta H_D^r - 2\Delta H_M^r = (\bar{H}_L - \bar{H}_H) \left(\frac{\partial N_L}{\partial N_D} - 2 \frac{\partial N_L}{\partial N_M} \right) \quad (4.7.20)$$

In order to determine the sign of the contribution to the enthalpy change associated with the $H\phi O$ process, we need to know the difference in the stabilization effects of M and D on the structure of the solvent.

Using the results of Sec. 3.7, we rewrite the difference of the stabilization effects due the dimer and the monomer as

$$\begin{aligned} \frac{\partial N_L}{\partial N_D} - 2 \frac{\partial N_L}{\partial N_M} = \rho_w x_L x_H [& - (G_{wH} - G_{wL}) \\ & + (G_{LD} - G_{HD}) - 2(G_{LM} - G_{HM})] \end{aligned} \quad (4.7.21)$$

Relation (4.7.21) is very general and applies to any two-component system. As in Sec. 3.7, we now specialize to a particular two-structure model for water, where L and H are the components with low and high local density, respectively. With this choice, we immediately have one negative term in (4.7.21), namely

$$-(G_{wH} - G_{wL}) < 0 \quad (4.7.22)$$

The reason for this inequality follows directly from the definition of the two components and has been discussed in detail in Sec. 3.7.

Next, we consider the two terms $G_{LD} - G_{HD}$ and $G_{LM} - G_{HM}$, both of which are expected to be positive, the arguments being essentially the same as those presented in Sec. 3.7. We

recall that $\rho_D(G_{LD} - G_{HD})$ can be interpreted as the average excess of dimers D in the neighborhood of L relative to H . The primary reason for assuming that this excess is positive is the relative difference in the local densities of L and H . Therefore, we conclude that $G_{LD} - G_{HD}$ and $G_{LM} - G_{HM}$ are roughly of the same order of magnitude, and therefore the term $(G_{LD} - G_{HD}) - 2(G_{LM} - G_{HM})$ is expected to be negative. Hence, we can conclude that

$$\frac{\partial N_L}{\partial N_D} - 2 \frac{\partial N_L}{\partial N_M} < 0 \quad (4.7.23)$$

In Sec. 3.7, we presented some arguments showing that the large stabilization effect induced by inert solutes is probably a unique phenomenon of liquid water. The same arguments hold here as well. Furthermore, we have stressed that a unique feature of the structure of water is the correlation between the low local density and strong binding energy. Therefore, if L is chosen to be a species with relatively low local density (say, all molecules with coordination numbers less than five), then the quantity $\bar{H}_L - \bar{H}_H$ is expected to be negative.

We can now conclude that as two solutes are brought from infinite separation to the final distance $R \approx \sigma$, the net effect is a destabilization of the L form. Furthermore, this destabilization is associated with a negative $\bar{H}_L - \bar{H}_H$, so that the whole term in (4.7.20) becomes positive.

The above arguments are the basis of the interpretation of the large *positive* enthalpy change associated with the $H\phi O$ process. Because of the exact entropy-enthalpy compensation law $\Delta H^r = T\Delta S^r$ (for both solutes M and D), we can write

$$\delta G = \delta H - T\delta S = \delta H^f - T\delta S^f \quad (4.7.24)$$

i.e. the strength of the $H\phi O$ interaction does not depend on the structural changes induced in the solvent by the process. δG may

depend on the *structure* of water, but it is not affected by the *structural changes* induced by the $H\phi O$ process.³⁵

We now briefly apply a continuous mixture-model approach to demonstrate the general aspect of the contribution of structural changes in the solvent. For simplicity, we refer to the energy change associated with the $H\phi O$ process. Following Sec. 3.5, we write

$$\delta E = \Delta E_D^* - 2\Delta E_M^* = (\langle B_D \rangle_0 - 2\langle B_M \rangle_0) + \frac{1}{2} \int v \left[\frac{\partial N_w(v)}{\partial N_D} - 2 \frac{\partial N_w(v)}{\partial N_M} \right] dv \quad (4.7.25)$$

where $\langle B_D \rangle_0$ and $\langle B_M \rangle_0$ are the average binding energies (at infinite dilution) of D and M , respectively, and the second term on the right-hand side is the difference in the contributions due to structural changes induced by D and two M s.

The average binding energy of D (to the solvent) is expected to be smaller than twice the average binding energy of a single monomer M — simply because the “contact” area between D and the solvent is smaller than twice the contact area between a monomer and the solvent. Therefore, the first term on the right-hand side of (4.7.25) is expected to be positive for any solvent. For hard-sphere solutes this term is zero, and for simple non-polar solutes it is likely to have a small absolute value.

In a “normal” solvent, we expect structural changes in the solvent to be small, for reasons discussed in Chapter 3. Therefore, the second term on the right-hand side of (4.7.25) is likely to be small. In water, the large, positive enthalpy or energy of the $H\phi O$ process can be attributed to a structural change in the solvent, such that the average interaction energy between water molecules *decreases*, an effect which can also be ascribed to a net breaking of hydrogen bonds.

³⁵For further details, see Ben-Naim (1975b).

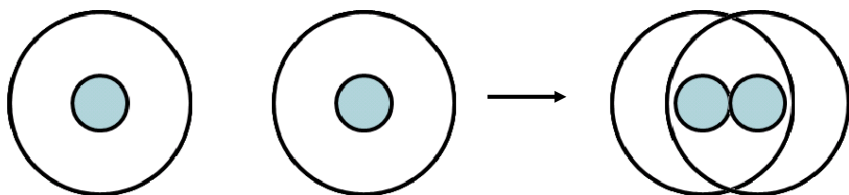


Fig. 4.31 Two solutes brought to contact distance. The “spheres of influence” that were initially separated are now overlapping.

The qualitative argument is also simple. We know that each monomer enhances the structure of water in some “sphere of influence” around it. When two monomers form a dimer D , the two spheres of influence will overlap to a large extent (Fig. 4.31). Therefore, the enhancement of the structure of water in the combined regions of influence is expected to be less than twice the enhancement in one sphere of influence. The net effect is a breakdown of the structure of water in the $H\phi O$ process.

4.7.4. *A measure of the amount of structural changes in the solvent*

In this section, we use the approximation from Sec. 3.7.5 to estimate how much structural change is involved in the process of $H\phi O$. The process for which we make the estimation is that discussed in Sec. 4.41, namely the one for which the indirect part of the free energy change is given by

$$\delta G(\sigma_1) = \Delta\mu_E^* - 2\Delta\mu_M^* \quad (4.7.26)$$

where $\Delta\mu_E^*$ and $\Delta\mu_M^*$ are the solvation Gibbs energies of ethane and methane, respectively. The corresponding isotope effect on the strength of the $H\phi O$ interaction, as measured by the quantity

(4.7.26) is given by

$$\begin{aligned}
 \delta G(\text{D}_2\text{O}) - \delta G(\text{H}_2\text{O}) &= \Delta\mu_E^*(\text{D}_2\text{O}) - \Delta\mu_E^*(\text{H}_2\text{O}) - 2[\Delta\mu_M^*(\text{D}_2\text{O}) - \Delta\mu_M^*(\text{H}_2\text{O})] \\
 &\cong \{\langle N_{HB} \rangle_E - \langle N_{HB} \rangle_0 - 2[\langle N_{HB} \rangle_M - \langle N_{HB} \rangle_0]\} (\varepsilon_D - \varepsilon_H)
 \end{aligned}
 \tag{4.7.27}$$

where ε_D and ε_H are the *HB* energies of D_2O and H_2O , respectively (see Sec. 3.7.5).

Let us denote by $\langle N_{HB} \rangle_{2M} - \langle N_{HB} \rangle_0$ the structural change in the solvent induced by the process of placing *two* methane molecules at *fixed* positions and at infinite separation from each other. Since the structural change occurs in the close vicinity of each of the solutes, the total amount of structural change produced by this process is exactly twice the structural change produced by placing *one* methane molecule at a fixed position in the liquid. Hence, we have

$$\langle N_{HB} \rangle_{2M} - \langle N_{HB} \rangle_0 = 2[\langle N_{HB} \rangle_M - \langle N_{HB} \rangle_0] \tag{4.7.28}$$

Substituting (4.7.28) in (4.7.27) we obtain

$$\delta G(\text{D}_2\text{O}) - \delta G(\text{H}_2\text{O}) \cong [\langle N_{HB} \rangle_E - \langle N_{HB} \rangle_{2M}] (\varepsilon_D - \varepsilon_H) \tag{4.7.29}$$

Thus, from the isotope effect on the quantity δG , we may estimate the structural change induced by the process of bringing two methane molecules from infinite separation to a small separation $R \approx \sigma_1$.

Table 4.12 presents some values of $\langle N_{HB} \rangle_E - \langle N_{HB} \rangle_{2M}$ estimated from relation (4.7.29). We see from Table 4.12 that the *H ϕ O* process induces a net decrease in the average structure (measured in terms of an average number of *HBs* in the system). This is consistent with the qualitative conclusion arrived at in the previous subsection.

Table 4.12 The Amount of Structural Change Induced by the Process of Bringing Two Methane Molecules from Fixed Positions at Infinite Separation to a Separation $R = \sigma_1 = 1.53 \text{ \AA}$ ^a

t (°C)	5	10	15	20	25
$\langle N_{HB} \rangle_E - \langle N_{HB} \rangle_{2M}$	-0.23	-0.23	-0.22	-0.18	-0.12

^aFrom Ben-Naim (1975a).

4.8. Solvent Induced Interactions Between Two Hydrophilic $H\phi I$ Groups

In the previous sections of this chapter we have considered the solvent induced interactions between $H\phi O$ groups. We now discuss the solvent induced interactions between two hydrophilic ($H\phi I$) groups or molecules.

By hydrophilic group or molecule, one usually means either a charged or a polar group. The charge-charge direct interaction is well described by the Coulomb interaction of the form

$$U_C(R) = \frac{z_i z_j e^2}{R} \quad (4.8.1)$$

where z_i and z_j are the number of electrons of charge e on particles i and j , respectively.

Any interaction between two polar molecules can be described in terms of the superposition of charge-charge interactions. In a solvent, these interactions are modified by introducing the dielectric constant of the medium ε . Thus, the solvent-induced interaction can be defined as the difference between the modified interaction and the vacuum interaction, i.e.

$$\delta W_C(R) = \frac{z_i z_j e^2}{\varepsilon R} - \frac{z_i z_j e^2}{R} = \frac{z_i z_j e^2}{R} \left(\frac{1 - \varepsilon}{\varepsilon} \right) \quad (4.8.2)$$

Since the dielectric constant is always larger than one, the medium will always reduce the absolute magnitude of the

charge-charge interaction. This is a well-known phenomenon. The polarization induced by the charged particles on the molecules of the solvent is always such that the net interaction between the charges is weakened compared with the interaction between the same charges in vacuum. This is, of course, not a molecular theory of the dielectric constant. In principle, one should be able to express the dielectric constant in terms of molecular parameters such as the dipole moments, polarizability, etc., of the solvent molecules. We shall not need this theory here.

There exists an important group of molecules that can interact either between themselves or with water molecules through hydrogen bonding. These interactions are ubiquitous and of fundamental importance in biochemical processes.

The polar groups which we shall refer to as *HBing* groups are groups such as hydroxyl (OH), carbonyl (C=O), amine (NH), etc. We shall refer to these as functional groups (*FG*). Two molecules that contain such *FGs* will be assumed to interact through a pair potential of the form

$$U(\mathbf{X}_i, \mathbf{X}_j) = U^{H,S}(\mathbf{X}_i, \mathbf{X}_j) + U^{HB}(\mathbf{X}_i, \mathbf{X}_j) \quad (4.8.3)$$

where $U^{H,S}$ includes the hard (*H*) and soft (*S*) parts of the interaction, and U^{HB} will be referred to as the *HB* part of the interaction. The latter will have a form similar to the one described in Chapter 2 for the water-water pair interaction.

Solutes that possess such polar groups will usually be hydrophilic in the sense that their solubility will be relatively large in water as compared with similar molecules with no *HB* capability. Formally, we can think of particles for which the U^{HB} part can be switched on and off. Experimentally, we may compare two molecules for which a polar group has been replaced by a non-polar group, say, ethanol and propane, or cyclohexanol and methyl-cyclohexane. Such a replacement will

always cause a *decrease* in the solubility of that molecule in water.

We now turn to examining the question of the potential of mean force (*PMF*), or the solvent-induced interaction between two *H ϕ I* molecules or groups that interact either between themselves or with the solvent by a pair potential of the form (4.8.3). The simplest and the most important *H ϕ I* molecules are water molecules themselves. We next consider the *H ϕ I* interactions between two water molecules at some specific configurations.

4.8.1. The *H ϕ I* interaction at $R_1 \approx 2.76 \text{ \AA}$

We recall that the radial distribution function for water has a peak at about $R_1 \approx 2.8 \text{ \AA}$, closely reminiscent of the oxygen-oxygen distance $2.76 \text{ \AA}$ in the ice lattice. The direct *HBing* between two water molecules is probably the most important interaction that determines the properties of liquid water. Likewise, the direct *HBing* between *H ϕ I* groups is of crucial importance in determining the structure and function of biomolecules such as proteins and nucleic acids.

The height of the first peak of the $g(R)$ of water at $R_1 \approx 2.8 \text{ \AA}$ is about 2 (see Fig. 1.35). This corresponds to a minimum of the potential of mean force (*PMF*) of about

$$W(R_1) = -k_B T \ln g(R_1) \approx -0.4 \text{ kcal mol}^{-1} \quad (4.8.4)$$

This is quite an unimpressive minimum well. However, remember that the value of either $g(R_1)$ or of $W(R_1)$ is an average value over all possible orientations. In considering the contribution of *HBing* between two *H ϕ I* groups in biomolecules, we must deal with two groups that have *fixed* orientations relative to each other and also take into account the fact that they are attached to some carrier or backbone (*BB*).

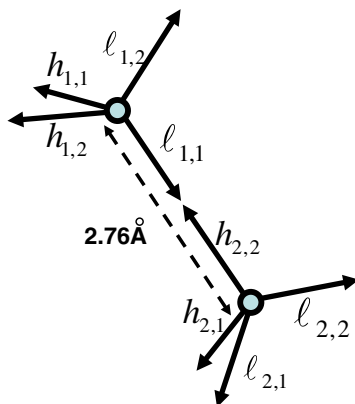


Fig. 4.32 Two water molecules at a correct configuration to form a hydrogen bond.

Consider first two water molecules brought from fixed positions and orientations at infinite separation to the final distance of $R_1 \approx 2.76 \text{ \AA}$ and a configuration which we denote by $\Omega_{HB}^{(1)}$ favorable to the formation of a *HB*, as in Fig. 4.32. The corresponding Gibbs energy change for this process is

$$\Delta G(R_1, \Omega_{HB}^{(1)}) = \Delta U(R_1, \Omega_{HB}^{(1)}) + \delta G(R_1, \Omega_{HB}^{(1)}) \quad (4.8.5)$$

where the direct interaction is mainly due to the *HB* energy ε_{HB} .

We are interested here in the solvent-induced contribution δG . Following similar reasoning as in Sec. 2.7.6, we can write the total Gibbs energy change as

$$\Delta G = \Delta G_{LJ} + \Delta G_{HB/LJ} = \Delta U + \delta G_{LJ} + \delta G_{HB/LJ} \quad (4.8.6)$$

Here, we have split the Gibbs energy change into two parts: the direct ΔU and the indirect δG . The indirect part is further split into two contributions: the first due to the process of bringing two *LJ* particles to the final configuration (i.e. the solvent-induced interaction when the *HB* part of the potential is “switched off”), and the second due to turning

on the HB part of the water-water interaction given that the LJ part of the potential has already been “turned on” (see Sec. 2.7.6 for more details). Because of the choice of the specific configuration $(R_1, \Omega_{HB}^{(1)})$, ΔU in (4.8.6) can be identified with the HB energy ε_{HB} . δG_{LJ} can be estimated from what we have already learned about the $H\phi O$ interaction between two LJ particles; here, the appropriate LJ particles are two neon atoms.

The more important term which we shall be concerned with here is the third part on the right-hand side of (4.8.6). We write this part as

$$\begin{aligned} \delta G_{HB/LJ}(R_1, \Omega_{HB}^{(1)}) &= -k_B T \ln \frac{\langle \exp[-\beta B_{ww}^{HB}(R_1, \Omega_{HB}^{(1)})] \rangle_{LJ}}{\langle \exp(-\beta B_w^{HB}) \rangle_{LJ}^2} \\ &= \Delta G_{ww}^{*HB/LJ}(R_1, \Omega_{HB}^{(1)}) - 2\Delta G_{ww}^{*HB/LJ} \end{aligned} \quad (4.8.7)$$

where $B_{ww}^{HB}(R_1, \Omega_{HB}^{(1)})$ is the HB part of the binding energy of a *pair* of water molecules in the specific configuration $(R_1, \Omega_{HB}^{(1)})$, and B_w^{HB} is the HB part of the binding energy of a *single* water molecule. Note that both averages in (4.8.7) are conditional averages. Here, the condition is: given the LJ part of the interaction is “turned on.” If the $H\phi I$ groups are attached to a protein, then we must add the condition of the BB .

In order to estimate the quantity on the right-hand side of (4.8.7), all we need is the difference between the conditional solvation Gibbs energies of the pair at $(R_1, \Omega_{HB}^{(1)})$ and at infinite separation. Figure 4.32 shows that in the configuration $(R_1, \Omega_{HB}^{(1)})$ only six arms of the pair of water molecules are exposed to the solvent, whereas at infinite separation each water molecule is fully solvated. The conditional solvation Gibbs (or Helmholtz) energy per *arm* has already been estimated in Sec. 2.7.6 to be

about $-2.25 \text{ kcal mol}^{-1}$; hence

$$\begin{aligned}\delta G_{HB/LJ}(R_1, \Omega_{HB}^{(1)}) &\cong 6 \times (-2.25) - 2 \times 4 \times (-2.25) \\ &= 4.5 \text{ kcal mol}^{-1}\end{aligned}\quad (4.8.8)$$

We conclude that the conditional solvent-induced interaction due to *HBing* with the solvent is of the order of $4.5 \text{ kcal mol}^{-1}$. The reason for this large and positive value is qualitatively clear. Two water molecules at infinite separation are fully solvated. When they are brought to the configuration $(R_1, \Omega_{HB}^{(1)})$ to form a direct *HB*, each of the water molecules loses one solvated arm. Since the conditional solvation Gibbs energy per arm is about $-2.25 \text{ kcal mol}^{-1}$, the loss of these two arms involves a net positive change in Gibbs energy of about $4.5 \text{ kcal mol}^{-1}$.

Repeating the same arguments for two functional groups attached to a polymer, we can reach the same conclusion; namely, the solvent-induced interaction between two functional groups at $(R_1, \Omega_{HB}^{(1)})$ is large and positive, of the order of $4.5 \text{ kcal mol}^{-1}$.

We can now estimate the total change in Gibbs energy ΔG in (4.8.6). We assume that the direct interaction is due to *HBing*, and hence we can take $\Delta U \approx \varepsilon_{HB} \approx -6.5 \text{ kcal mol}^{-1}$. δG_{LJ} is the same as the indirect part of the potential of average force between two LJ particles at contact. From what we have learned about the *H ϕ O* interaction, we estimate that $\delta G \approx -0.6 \text{ kcal mol}^{-1}$, and for $\delta G_{HB/LJ}$ we take the value in (4.8.8).³⁶ Altogether, we have

$$\Delta G = W(R_1, \Omega_{HB}^{(1)}) \approx -6.5 - 0.6 + 4.5 \approx -2.6 \text{ kcal mol}^{-1}\quad (4.8.9)$$

³⁶Recently, Ben-Tal *et al.* (1997) estimated the dimerization energy of N-methylacetamide in vacuum to be $-6.6 \text{ kcal mol}^{-1}$. In water, the Gibbs energy of dimerization was found to be about -1 kcal mol^{-1} .

This value may be translated into a pair correlation function at this configuration, which at 25°C is

$$g(R_1, \Omega_{HB}^{(1)}) = \exp[-\beta\Delta G] \approx 80 \quad (4.8.10)$$

This is a very large number compared with the experimental value of about 2 for the radial distribution function $g(R_1)$. This drastic reduction from $g(R_1, \Omega_{HB}^{(1)})$ to $g(R_1)$ is brought about by the averaging over all orientations of the pair of water molecules, i.e.

$$g(R_1) = \frac{1}{(8\pi^2)^2} \int g(R_1, \Omega_1, \Omega_2) d\Omega_1 d\Omega_2 \approx 2 \quad (4.8.11)$$

Note that the average in (4.8.11) gives equal weight to each configuration, i.e. $d\Omega_1 d\Omega_2 / (8\pi^2)^2$. Clearly, since the region of HB ing is very small compared to the entire range of relative orientations of the two molecules, the result of the averaging process is a diminished value of the pair correlation function. Another possible cause for the diminished value of $g(R_1)$ is the effect of non-additive interactions among water molecules.

4.8.2. The $H\phi I$ interaction at $R_2 = 4.5 \text{ \AA}$

The second configuration of importance is the distance of the second-nearest neighbor configuration of water molecules in ice. We recall that the radial distribution function of water has a second peak at $R_2 = 4.5 \text{ \AA}$. The height of this peak is about 1.15, corresponding to a minimum value of the potential of average force of about $W(R_2) \approx -0.084 \text{ kcal mol}^{-1}$. This is even less impressive than the minimum we found at R_1 . However, recalling that the experimental radial distribution function is an average over all orientations and having seen that this averaging process has a significant diminishing effect on the value of the correlation function at R_1 , we can expect to find

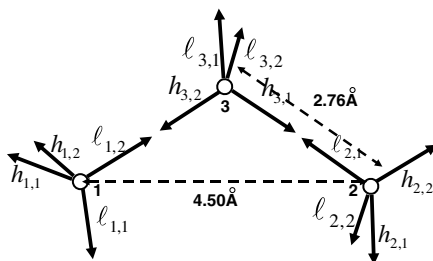


Fig. 4.33 Two water molecules (1) and (2) at a configuration such that a third water molecule (3) can form an *HB* bridge between them.

large correlations at some *specific* orientations of the two water molecules at a distance R_2 .

Consider again two water molecules (or *H ϕ I* groups attached to some *BB*) at fixed positions and orientations at infinite separation. We bring them to a distance of 4.5 Å and orientations such that an *HB* bridge can be formed by a third water molecule (Fig. 4.33). This is essentially the same configuration as for the two next-nearest neighbors of water molecules in ice. We shall denote this configuration by $(R_2, \Omega_{HB}^{(2)})$ or, for short, simply by $R_2 = 4.5$ Å. The change in the Gibbs energy for this process, say, with P, T constant is

$$\Delta G(R_2, \Omega_{HB}^{(2)}) = U(R_2, \Omega_{HB}^{(2)}) + \delta G(R_2, \Omega_{HB}^{(2)}) \quad (4.8.12)$$

Here, in contrast to the previous configuration, we can assume that the direct interaction at $R_2 \approx 4.5$ Å is quite weak and the main contribution to ΔG comes from the solvent-induced part δG . As in the previous subsection, we divide δG into two parts as in (4.8.6) but here we can neglect the quantity δG_{LJ} and focus on the *HB*ing contribution. The latter can be written as

$$\delta G_{HB/LJ} = -k_B T \ln \frac{\langle \exp[-\beta B_{ww}^{HB}(4.5)] \rangle_{LJ}}{\langle \exp(-\beta B_w^{HB}) \rangle_{LJ}^2} \quad (4.8.13)$$

where B_{ww}^{HB} (4.5) is the same as in Eq. (4.8.7) but at the new configuration $R_2, \Omega_{HB}^{(2)}$. The conditional average indicated by $\langle \cdot \rangle_{LJ}$ is the same as in (4.8.7) if we are dealing with two water molecules, but LJ and BB if we are dealing with two FG s attached to a backbone.

A theoretical estimate of $\delta G_{HB/LJ}$ in (4.8.13) is quite involved. It is essentially the same as the calculation carried out in Sec. 2.7.6. The details are presented in Appendix I, and in Ben-Naim (1989). We shall present here one estimate based on experimental data. Before doing that, we introduce two qualitative arguments that suggest that this quantity is quite large.

First, we recall that the averaging process carried out over the full pair correlation function $g(R_1, \Omega_1, \Omega_2)$ has reduced the very high value of $g(R_1, \Omega_{HB}^{(1)})$ to a much smaller value of about 2. We expect that a similar reduction would occur for $g(R_2, \Omega_{HB}^{(2)})$. Two differences should be noted between the two cases. In the case of $g(R_1)$, we have large contributions from both the direct and the indirect interactions, whereas in the case of $g(R_2)$ the direct water-water interaction is probably very weak. The second difference is that in the case of $g(R_1, \Omega_{HB}^{(1)})$ there are eight HB ing configurations (i.e. each arm of one water molecule can form an HB with two of the arms of the second water molecule). In the case of $g(R_2, \Omega_{HB}^{(2)})$, there are 16 configurations favoring the formation of an HB ed bridge with a third molecule, as in Fig. 4.33 [i.e. any arm of a water molecule (1) and any arm of the water molecule (2) can point to the third molecule (3)]. These two considerations will affect the relative values of $g(R_2, \Omega_{HB}^{(2)})$ and $g(R_2)$. Qualitatively, however, we expect that by “reversing the average process” — i.e. taking a fixed configuration $(R_2, \Omega_{HB}^{(2)})$ — we should enhance the peak at R_2 by a factor of about 40. This corresponds to a considerable deepening of the minimum of $W(R)$ at $(R_2, \Omega_{HB}^{(2)})$. A very rough estimate: If the

reduction of the height of the second peak from $g(R_2)$ to 1.15 is the same as at R_1 , i.e. by a factor of about 40, then we can estimate that $W(R_2) \approx -k_B T \ln(40 \times 1.15) \approx -2.2 \text{ kcal mol}^{-1}$.

The second qualitative argument can be obtained by rewriting (4.8.13) in the form

$$\begin{aligned}
 \delta G_{HB/LJ} &= -k_B T \ln \frac{\langle \exp[-\beta B_{ww}^{HB}(1, 2; 4.5)] \rangle_{LJ}}{\langle \exp(-\beta B_w^{HB}) \rangle_{LJ}^2} \\
 &= -k_B T \ln \frac{\langle \exp[-\beta B_w^{HB}(1)] \rangle_{LJ} \langle \exp[-\beta B_w^{HB}(2; 4.5)] \rangle_{LJ,1}}{\langle \exp(-\beta B_w^{HB}) \rangle_{LJ}^2} \\
 &= -k_B T \ln \frac{\langle \exp[-\beta B_w^{HB}(2; 4.5)] \rangle_{LJ,1}}{\langle \exp(-\beta B_w^{HB}) \rangle_{LJ,1}} \quad (4.8.14)
 \end{aligned}$$

The average in the numerator is written as a product of two averages. First, we have the solvation Gibbs energy of one molecule (1) (with the condition LJ) and a conditional solvation Gibbs energy of the second water molecule (2) at a distance of 4.5 Å from the first and orientation $\Omega_{HB}^{(2)}$. (Here, we have both the condition LJ and the presence of the first molecule indicated by 1.) In the last form on the right-hand side of (4.8.14), we have essentially a difference in the conditional solvation Gibbs energy of a water molecule with different conditions. In one case, the condition is LJ ; in the second the condition is $LJ, 1$. Clearly, because of the presence of the additional condition “1,” the conditional density of water molecules at X_3 (see Fig. 4.33) will be larger than in the absence of this condition. Therefore, the solvation Gibbs energy of molecule 2, given that molecule 1 is $HBed$, is expected to be more negative than the solvation Gibbs energy of a water molecule. The net result is a negative value of $\delta G_{HB/LJ}$.

In Appendix I, we present an approximate estimate of the strength of the $H\phi I$ interactions based on the pair potential

introduced in Chapter 2. We also note here that simulations of the $H\phi I$ between two water molecules have supported the conclusion that the strength of these interactions are of the order of -2.5 to -3.0 kcal mol $^{-1}$.³⁷

In discussing the dynamics of protein folding, the important quantity that “guides” the protein to fold along a preferred pathway is not the *PMF* but the *mean force* itself. A qualitative argument regarding the strength of the solvent-induced $H\phi I$ force has been given,³⁸ and was supported by simulated calculations.³⁹

4.8.3. Intramolecular $H\phi I$ interactions

In the previous subsections, we discussed the $H\phi I$ interaction between two water molecules at some fixed distances and relative orientations, as in Fig. 4.33. It is clear that the same arguments also apply to two functional groups that are connected to a backbone (*BB*). The *BB* could be the same or a different molecule for the two functional groups. An example is two methanol molecules (Fig. 4.34). The configuration shown in

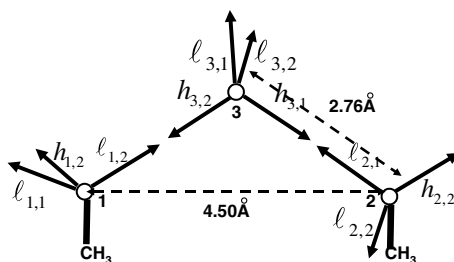


Fig. 4.34 As in Fig. 4.33 but now one hydrogen “arm” is replaced by a methyl group. The water molecule (3) forms an *HB* bridge between two hydroxyl groups.

³⁷Mezei and Ben-Naim (1990a, 1991).

³⁸Ben-Naim (1990a, 1991).

³⁹Durell *et al.* (1994).

Fig. 4.34 is the same as that of Fig. 4.33 except that one hydrogen atom in each of molecules 1 and 2 has been replaced by a methyl group.

In this specific example the *BB* is a methyl group, and it is a different *BB* for each of the functional groups, in this case the hydroxyl group OH. In other cases, the two functional groups could be attached to the same *BB*, say, two side-chains of a protein.

Because of the relatively large distance of 4.5 Å between the two functional groups, we can neglect both the direct interaction between the two groups as well as the indirect part associated with the *LJ* part of the interaction. What is left is an expression similar to (4.8.13). Therefore, we expect that the strength of the *HφI* interaction would not differ much from the strength of the conditional *HφI* interaction. Also, because of the relatively large distance between the *BB* and the water molecules in the solvent in the region from which they can form an *HB*-bridge between the two functional groups, we expect that the conditional *HφI* would not depend very much on the type of the *BB*.

We now turn to an estimate of the *HφI* interactions based on experimental data. The methodology is the same as that discussed in Sec. 4.5. Consider two isomers of a molecule having two *FGs* as in Fig. 4.35. In reaction *I*, we bring one functional group from position 4 to position 3 relative to a given *FG* at position 1. The indirect contribution to the Gibbs energy change for this reaction is

$$\delta G[(1, 4) \rightarrow (1, 3)] = \Delta G_{1,3}^* - \Delta G_{1,4}^* \quad (4.8.15)$$

Thus, having the solvation Gibbs energies of the 1,3 and the 1,4 isomers, we could have estimated δG in (4.8.15). However, these data are not available. Instead, we have the differences in the solvation Gibbs energies of these compounds between

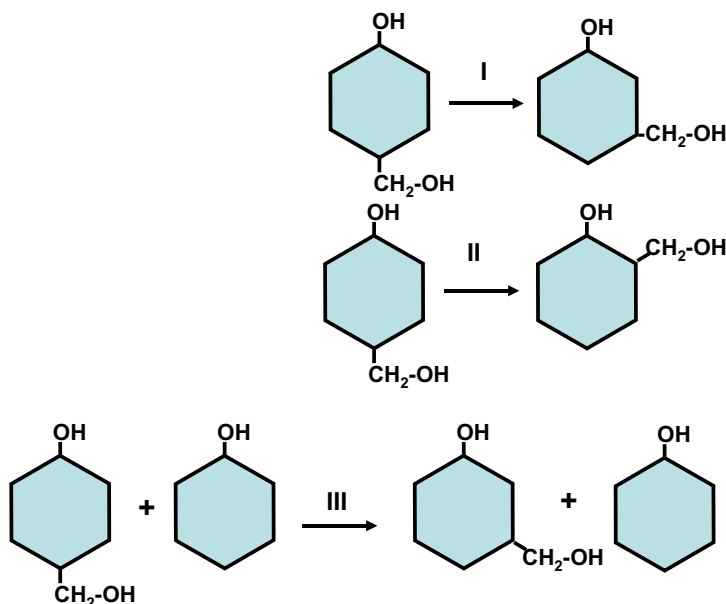


Fig. 4.35 Model processes for estimating the strength of the intramolecular $H\phi I$ interactions.

water (w) and toluene (t). From the available data, we can estimate the difference:

$$\begin{aligned}
 & \delta G[(1, 4) \rightarrow (1, 3)]^{(w)} - \delta G[(1, 4) \rightarrow (1, 3)]^{(t)} \\
 &= \Delta G_{1,3}^{*w} - \Delta G_{1,4}^{*w} - [\Delta G_{1,3}^{*t} - \Delta G_{1,4}^{*t}] \\
 &= -3.15 \text{ kcal mol}^{-1}
 \end{aligned} \tag{4.8.16}$$

and similarly for reaction *II* we have

$$\begin{aligned}
 & \delta G[(1, 4) \rightarrow (1, 2)]^{(w)} - \delta G[(1, 4) \rightarrow (1, 2)]^{(t)} \\
 &= -1.55 \text{ kcal mol}^{-1}
 \end{aligned} \tag{4.8.17}$$

Assuming that the difference in the solvation Gibbs energies of the two isomers in toluene (t) is small, we can attribute

the major part of the result (4.8.16) to the $H\phi I$ interaction in water.⁴⁰

In order to confirm that the two FG s at positions 1,4 are far enough apart so that they may be considered independently solvated, we also examine reaction *III* in Fig. 4.35. For the conversion reaction *III*, we have

$$\delta G(III)^{(w)} - \delta G(III)^{(t)} = -3.23 \text{ kcal mol}^{-1} \quad (4.8.18)$$

Similarly, for the formation of the (1,2) isomer in a process similar to *III*, we have

$$\delta G(IV)^{(w)} - \delta G(IV)^{(t)} = -1.63 \text{ kcal mol}^{-1} \quad (4.8.19)$$

Thus, the formation of the (1,3) isomer involves about $-3.23 \text{ kcal mol}^{-1}$, almost the same as the value in (4.4.16). The formation of the (1,2) isomer involves about half of this quantity, (4.8.17). The reason for this difference is clear. In the (1,3) position the two FG s are at a distance of about $4.9 \text{ \AA}$ (Fig. 4.36), and therefore they can form a water bridge; hence, there is an indirect contribution of about $\delta G \approx -3 \text{ kcal mol}^{-1}$. In the (1,2) isomer, the distance between the two FG s is

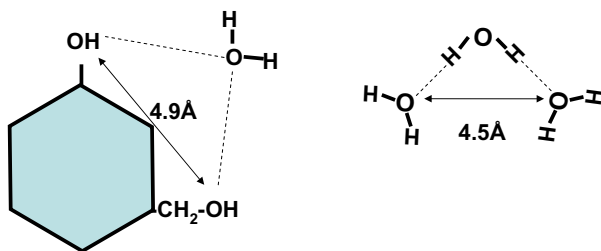


Fig. 4.36 The distance between the oxygen atoms in the model compound is similar to the “ideal” distance of the second nearest neighbors in ice.

⁴⁰Similar, but less dramatic results were obtained for cyclohexane and hexane (Wilf and Ben-Naim, 1994).

smaller, and there is partial interference between the two FG s leading to a much lower value of δG . Note again that as in (4.8.16) and (4.8.19), the values in (4.8.18) and (4.8.19) pertain to the *difference* between water and toluene. A proper estimate of the $H\phi I$ interaction should be based on the solvation Gibbs energies of the same compounds in pure water. Unfortunately, these data are not yet available.⁴¹ We present some more data on the intramolecular $H\phi I$ interaction in Appendix J.

From the above considerations, we conclude that there are two configurations for a pair of water molecules (or pair of $H\phi I$ groups) at which we expect large $H\phi I$ effects. At $(R_1, \Omega_{HB}^{(1)})$, the solvent-induced part δG is positive. However, in combination with a direct HB , the overall Gibbs energy change might be negative and of the order of -1.5 to -2 kcal mol⁻¹. (This is true provided that only one arm per FG is lost in the formation of the direct HB .) On the other hand, at $(R_2, \Omega_{HB}^{(2)})$, the solvent-induced part δG is negative and of the order of about -3.0 kcal mol⁻¹. Since the direct interaction is relatively small at this distance, δG is essentially equal to the potential of mean force. We can conclude that the $H\phi I$ interaction at $(R_2, \Omega_{HB}^{(2)})$ might be as important as, if not more important than, the total Gibbs energy change for the formation of a direct HB at $(R_1, \Omega_{HB}^{(1)})$. We therefore expect that both of these two $H\phi I$ effects will play important roles in biochemical processes. See also Sec. 4.12.

⁴¹Sun and Kollman (1996) did some calculations of the solvation Gibbs energies of the three isomers of hydroxymethylphenol and found no significant difference among the three isomers. They concluded that their results are inconsistent with the "water-bridge" hypothesis. I disagree with their conclusion. First, because it is not clear how reliable their calculations are. Second, and more importantly, the hypothesis of the water-bridge was supported by experimental, theoretical, and simulated results.

4.9. Application of One-Dimensional Models to Study Hydrophobic Interactions

The first application of a 1-D model to study $H\phi O$ interactions was carried out by Elkoshi and Ben-Naim (1979). The model used in this study was a generalized 1-D lattice model for water proposed by Bell (1969). Although it was not stated explicitly by Bell, it was noted by Elkoshi and Ben-Naim that the success of the Bell model in exhibiting some of the outstanding behavior of liquid water was due to the implementation of the *principle*, namely that water molecules strongly bound to their environment (by “hydrogen bonds”) are also those which experience a relatively low local density.

Elkoshi and Ben-Naim (1979) attempted to study the problem of the $H\phi O$ interaction within this model, hoping that the fact that the *principle* is a built-in feature of Bell’s model would be helpful in clarifying the molecular reasons for the phenomenon of the $H\phi O$ interaction. At that time it was not known whether or not the $H\phi O$ interaction was a result of the *principle*. As we noted in Sec. 3.9, the hydrophobic interaction is nothing but the difference in solvation Gibbs energies. Therefore, since the solvation Gibbs energy is not a result of the *principle*, we can also expect that the $H\phi O$ interaction will not depend on the principle.

Without going into the details of the model, we note here that the study of Elkoshi and Ben-Naim focused on the function y_{ss} at contact distance (i.e. when two solutes s become nearest neighbors). This function is related to the solvent-induced part of the change in the Gibbs energy for the process of bringing the two solutes from infinite separation to the distance of nearest neighbors:

$$y_{ss} = \exp[-\delta G/k_B T] \quad (4.9.1)$$

Two results of this study are worth noting here. First, the values of γ_{ss} increase with the increase in the solvent-solvent interaction energy. This is similar to the results we have shown in Sec. 3.9 for the solvation Gibbs energy of a simple solute in a one-dimensional model of water-like particles. The second is the temperature dependence of γ_{ss} . As pointed out in Sec. 3.7 and 3.9, the temperature dependence of the solvation Gibbs energy relies on the *principle*. It is not surprising to find that the strength of the $H\phi O$ interaction increases with temperature even in such a simple 1-D model.

A more detailed study of the $H\phi O$ was carried out recently by Widom and his collaborators⁴² using a similar 1-D model that was originally described by Ben-Naim (1992). The general idea is that particles placed on lattice points have different orientations (relative to the 1-D axis) and that in one of these states the particles can form a “hydrogen bond” (HB). A simple solute can occupy only the interstitial sites between two molecules that are in the HB ing state.

Unlike the Ben-Naim model (1992, 2008c), this model was designed to study aqueous solutions rather than the properties of pure liquid water. From the very description of the model, it is clear that the *principle* has not been implemented. Therefore, one cannot expect to obtain any result that depends on the *principle* (see Sec. 2.5). On the other hand, since a solute interacts only with two neighboring water molecules in the HB ing state, it is expected that the solute would stabilize the formation of HB s. Recall that in the primitive model (Sec. 2.5), only nearest-neighbor interactions are reckoned. Therefore, when a solute enters between two solvent molecules in the primitive model, it precludes the formation of an HB “across the solute.”

⁴²Kolomeisky and Widom (1999), Bedeaux *et al.* (2001), Widom *et al.* (2001, 2003), and Schutz *et al.* (2001).

This deficiency of the primitive model was eliminated in the cluster model (see Sec. 2.5). Similarly, in Widom's model a solute molecule entering between two solvent molecules not only allows an *HB* "across the solute" but actually enhances the formation of *HBs*.

With a choice of energy parameters for the solvent-solvent molecules (in the different states) and the solute-solvent interaction, one can write the exact partition function as well as the potential of mean force (*PMF*) for the case of dilute solutions in the solvent. Note that in Widom's model as well as in Elkoshi and Ben-Naim's model, the focus was on the *solvent-induced* part of the *PMF*. As was emphasized a long time ago (Ben-Naim, 1974), it is only this part that is of interest in connection with the problem of hydrophobic interactions. The direct solute-solute interaction (the parameter ν in Widom's model) is irrelevant to this problem.

As in the model of Elkoshi and Ben-Naim, this model also shows that the strength of the $H\phi O$ (as measured by the *PMF*) increases with the increasing temperature. An interesting new result shown by Widom and his collaborators was that the *range* (in units of the lattice spacing) of the $H\phi O$ attraction *decreases* with the *increase* in temperature. Further work on a 1-D model for the study of the hydrophobic effect was published by Koga (2004). Not surprisingly, this model exhibits some of the characteristic trends in the temperature dependence of both the solvation and the $H\phi O$ interaction.

We next describe some results which may or may not be relevant to the "hydrophobic interaction" problem. We use the 1-D model described in Sec. 2.5. In contrast to the lattice models described above, here we use a continuous primitive model. Specifically, we study the *PMF*, $W(R)$, for solute-solute pairs in two solvents. One consists of particles interacting via a square-well potential (*SW*) (Fig. 2.10b), and the second is the

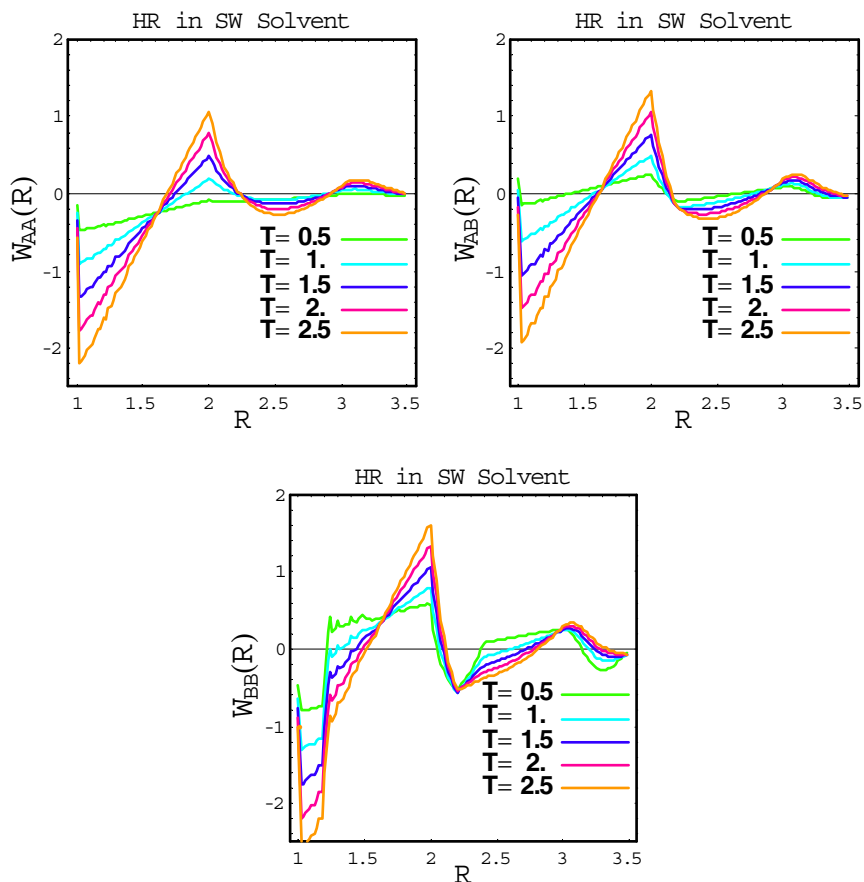


Fig. 4.37 The potential of mean force (PMF) between solute-solute (AA), solute-solute (AB), and solvent-solute (BB) molecules in (a) a 1-D mixture of hard rods and (b) in a square-well solvent. The parameters are as in Eq. (4.9.2). The various temperatures are indicated.

“hydrogen-bonding” (HB) solvent with interaction potential, as described in (Fig. 2.10d).

Figure 4.37 shows the PMF for the pairs solute-solute (AA), solute-solute (AB), and the solvent-solute (BB). The molecular parameters chosen for this SW solvent are

$$\sigma_{AA} = \sigma_{AB} = \sigma_{BB} = 1, \quad \varepsilon_{AA} = \varepsilon_{AB} = 0, \quad \varepsilon_{BB} = -1 \quad (4.9.2)$$

The total density is $\rho = 0.6$ and the mole fraction of A in B is very small, $\rho_A \rightarrow 0$. ($k_B = 1$, the unit of length is σ_{AA} , and ε_{ij} are measured in units of dimensionless temperature.) As can be seen from Fig. 4.37, the first minimum of $W_{AA}(R)$ becomes lower as we increase the temperature. This strengthening of the *PMF* is not a result of the increase in the height of the pair correlation function,⁴³ but simply because of the “ $-k_B T$ ” factor in the relation $W(R) = -k_B T \ln g(R)$. What is more important is the *range* of the *PMF*, which is quite large at lower temperatures and becomes shorter as we increase the temperature. This is similar to the range of W_{AA} found by Widom (though in Widom’s model W_{AA} refers only to the indirect part of the solute-solute *PMF*).

Since the *SW* solvent is the “normal” solvent (compared with the *HB* solvent discussed below), we believe that the *range* of the *PMF* is not a feature relevant to the hydrophobic interactions. A similar range effect can be observed for *LJ* particles in the 3-D model (see Sec. 4.11).⁴⁴

In Fig. 4.38, we show the same set of functions but now for the *HB* solvent. The molecular parameters in this case are

$$\sigma_{AA} = \sigma_{AB} = 1, \quad \sigma_{BB} = 2, \quad \varepsilon_{AA} = \varepsilon_{BB} = 0, \quad \varepsilon_{HB} = -1 \quad (4.9.3)$$

In this case, we also have $\rho = 0.6$ and A is very dilute in B . As can be seen from Fig. 4.38, the depth of the *PMF* increases considerably as we increase the temperature. Again, this lowering of the depth in $W_{AA}(R)$ is not a result of the increase in the pair correlation function $g_{AA}(R)$. We can conclude that the strength of the *PMF* for the solute-solute increases considerably as we increase the temperature, and more dramatically than in the *SW* solvent. However, it is not clear whether these findings

⁴³See Ben-Naim (2008c).

⁴⁴Ben-Naim and Shen (2008).

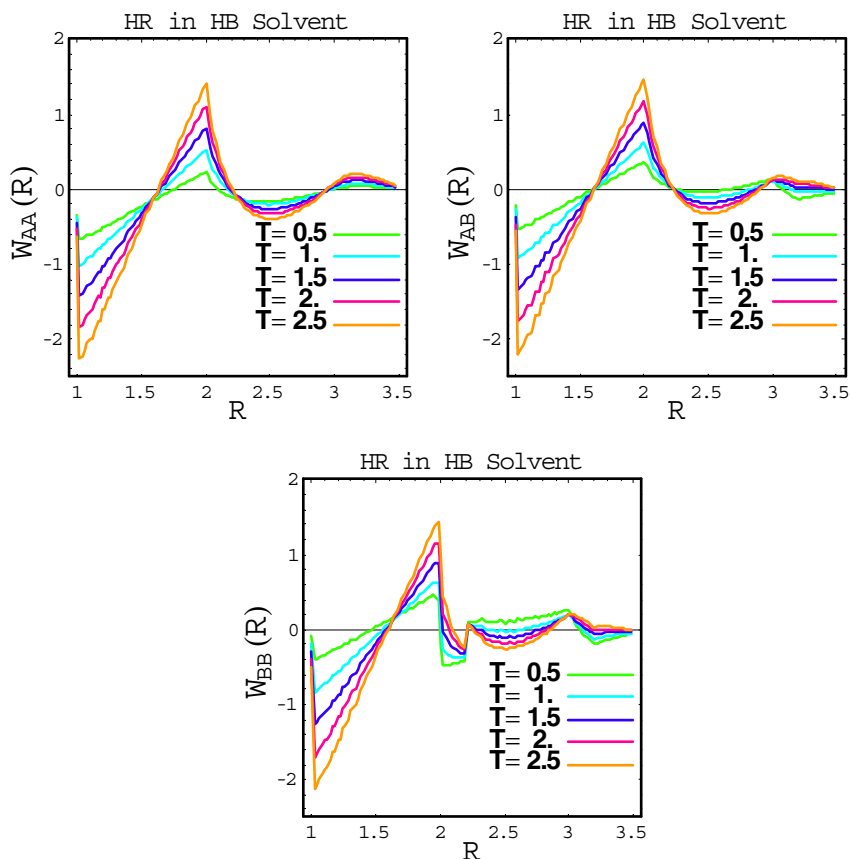


Fig. 4.38 As in Fig. 4.37 but for a solution of hard rods (a) in “hydrogen-bonding” solvent (b). Parameters are as in Eq. (4.9.3).

are relevant to the hydrophobic interaction problem. Note also that in this model the *range* of the *PMF* for the solute-solute pair almost does not change with temperature.

The reason I have doubts as to the relevance of the above results to the problem of hydrophobic interactions is the following. In Sec. 3.9, I have compared the results of solvation of a simple solute in the primitive and cluster models. We have seen that in the former we could not obtain the characteristic

temperature dependence of the solvation Gibbs energy. On the other hand, the cluster model was designed in such a way that hydrogen bonding was enhanced by the addition of a solute. Therefore, in that model we could obtain the characteristic large negative values of both the solvation enthalpy and the solvation entropy.

Unfortunately, it is not easy to calculate the solute-solute pair correlation function in the cluster model. Nevertheless, we can “predict” the results that could have been obtained in the cluster model from the following considerations. Recall that the indirect part of the potential of average force is related to the solvation Gibbs energies of two monomers and “dimer” by

$$\delta G(R) = \Delta\mu_D^* - 2\Delta\mu_M^* \quad (4.9.4)$$

In Sec. 3.9, we have calculated the solvation Gibbs energy of a simple solute as well as its temperature dependence. Therefore, repeat the same calculation as in Sec. 3.9 but now allow either one solute (M) or the “dimer” (D) to occupy a hole in the cluster. Using the same molecular parameters and assuming that a “dimer” in the hole of the cluster causes roughly the same effect on the average number of *HBs* in the solvent, we can predict that the temperature dependence of δG will be roughly similar to the temperature dependence of $-\Delta\mu_M^*$. Therefore, we expect that both δS and δH would be positive in the cluster model. Such a result would be in agreement with the experimental data on the entropy and enthalpy of *H ϕ O* interactions.

Figures 4.39 and 4.40 show the density dependence of the *PMF* in the *SW* and the *HB* solvents. Note that as the density increases the height of the first peak of $g_{AA}(R)$ increases, almost in the same manner in both solvents.⁴⁵ The depth of $W_{AA}(R)$

⁴⁵As well as in a simple liquid. See Ben-Naim (2008), where the pair correlation functions for this model are presented.

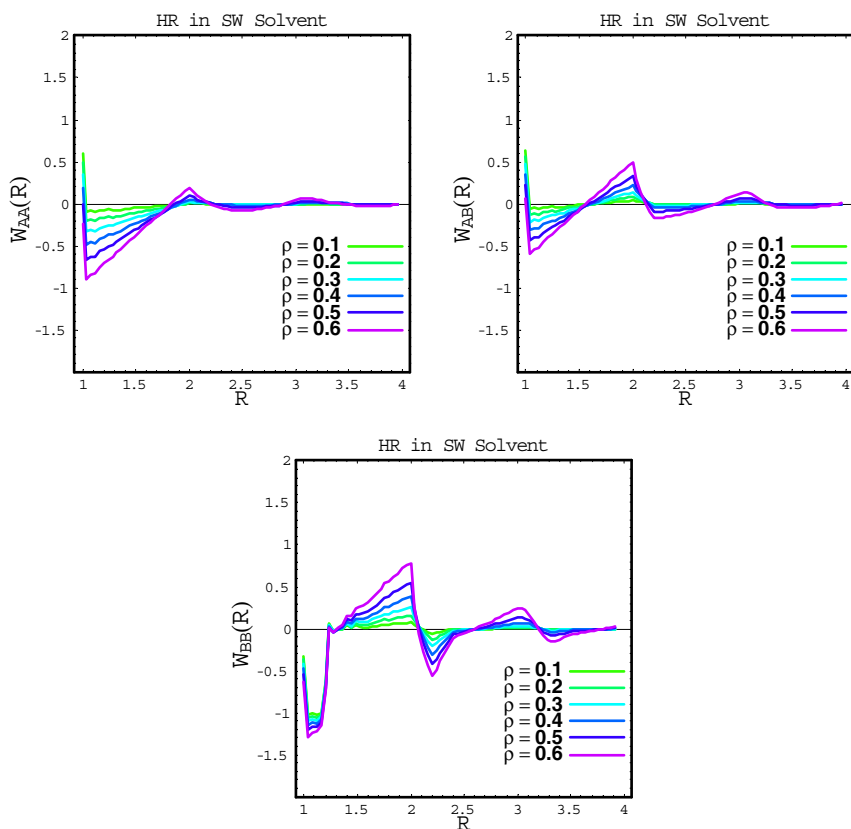


Fig. 4.39 The density dependence of the PMF for the system in Fig. 4.37 but at $T = 1$ and with varying densities.

increases in a similar manner as the density increases. These results show that the strength of the $H\phi O$ interaction, like the solvation Gibbs energy, depends on the *strength of the interactions* and not on the peculiarity of the structure of water.

4.10. Application of Two-Dimensional Models

The 2-D model described in Secs. 2.6 and 3.10 was also extended to examine the question of the $H\phi O$ interaction. We present

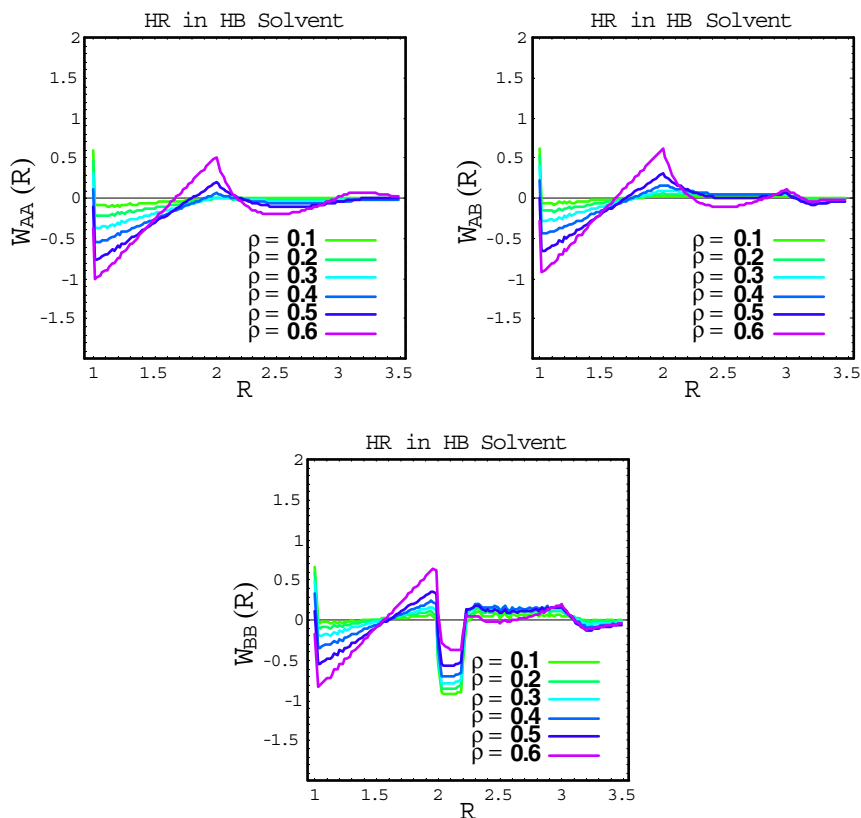


Fig. 4.40 As in Fig. 4.39 but for the *HBing* solvent.

here only a few results from the original study by Ben-Naim (1972cde).

The model is the same as described in Secs. 2.6 and 3.10. The density of the water-like particles was chosen to be $\rho_w = 0.65$ and, for the *LJ* solute, $\rho_s = 0.05$. Other parameters of the model are

$$\begin{aligned} \varepsilon_{HB}/k_B T &= -3.7, \quad R_H = 1, \quad \sigma_{ss} = 0.75, \quad \sigma_{ww} = 1.05 \\ \varepsilon_{ss}/k_B T &= \varepsilon_{sw}/k_B T = \varepsilon_{ws}/k_B T = \varepsilon_{ww}/k_B T = 0.185 \end{aligned} \quad (4.10.1)$$

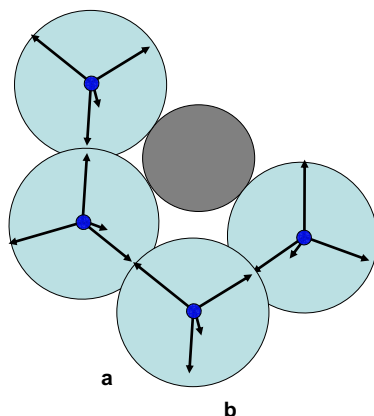


Fig. 4.41 A configuration of water-like molecules in 2-D that allow a solute to fit into the “cage” formed by *HBed* molecules (Sec. 4.10).

The reason for this particular choice of molecular parameters and the details of the computation based on the solution of the Percus–Yevick equation are discussed at great length in Ben-Naim (1972cde, 1974).

Basically, the idea was to produce local density around molecules that are fully *HBed*. The situation is schematically shown in Fig. 4.41. With the specific parameters in (4.10.1), it is clear that once a water molecule is fully *HBed*, it will not allow other water molecules to come very close to it. On the other hand, a solute molecule with a diameter of about 0.75 can come close to the fully *HBed* water molecule.

Figure 4.42 shows that when we vary the solute diameter σ_{ss} , the height of the first maximum of $g_{ss}(R)$ is largest for $\sigma_{ss}/k_B T \approx 0.75$. Other results obtained for this model with parameters as in (4.10.1) are

- (i) $g_{ss}(R_1)$ increases with the solvent density ρ_w . This has been checked for densities in the range $0.5 < \rho_w < 0.75$.
- (ii) $g_{ss}(R_1)$ increases with the *HB* energy $|\varepsilon_{HB}|$. It was found that increasing $|\varepsilon_{HB}|$ usually causes an appreciable effect on

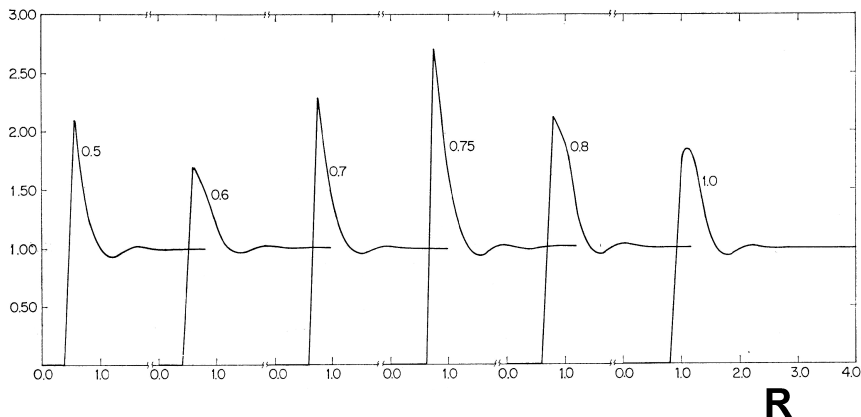
$g_{ss}(R)$ 

Fig. 4.42 Variation of the solute-solute pair correlation function with the solute diameter as indicated next to each curve (see Sec. 4.10).

both $g_{ss}(R)$ and $g_{sw}(R)$ but a smaller effect on $g_{sw}(R)$ and $g_{ws}(R)$. An example shown in Fig. 4.43 is for the parameters given in (4.10.1). Note the height of g_{ss} compared with that of g_{ww} .

- (iii) Increasing the solute density ρ_s lowers $g_{ss}(R_1)$.
- (iv) Finally, we remark on the angle dependence of the various pair correlation functions. $g_{ss}(R)$ is spherically symmetric and $g_{ww}(R, \alpha_1, \alpha_2)$ has the same angle dependence as discussed in Sec. 3.10. The function $g_{sw}(R, \alpha_2)$ depends on the orientation of the w particle. For the parameters in (4.10.1) at $R = 1.0$, it was found that

$$g_{sw}(R = 1.0) = (2.4, 1.4, 1.5, 1.4, 2.4) \quad (4.10.2)$$

which corresponds to angles of $\alpha_2 = 0^\circ, 30^\circ, 60^\circ, 90^\circ$, and 120° . Clearly, there is a large value of the pair correlation at $\alpha_2 = 0^\circ$ and $\alpha_1 = 120^\circ$. This corresponds exactly to configurations of s and w as depicted in Fig. 4.41, i.e. the orientation of the w particle toward the s particle is such

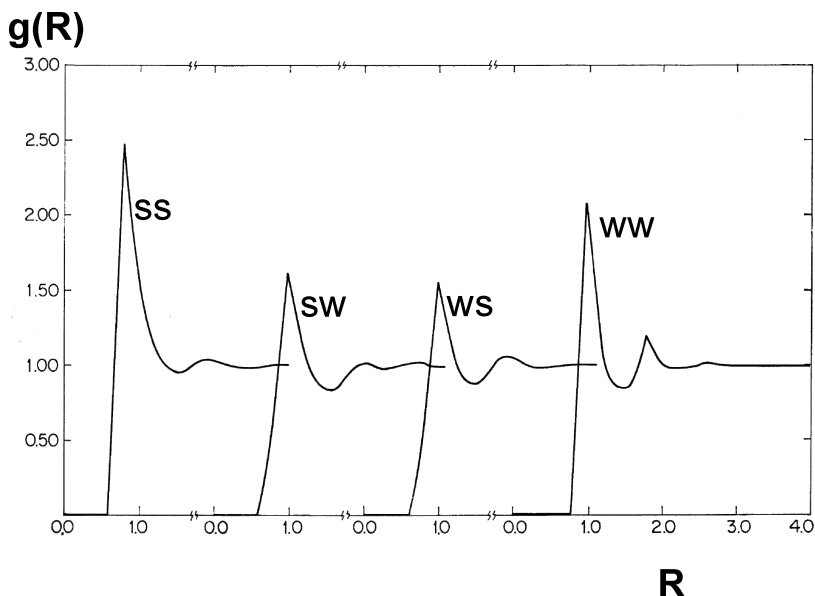


Fig. 4.43 The four pair correlation functions for aqueous solutions of a solute (s) in water-like (w) solvent in a 2-D system. Parameters as in Eq. (4.10.1).

that the bond directions are away from the line connecting the centers of the two particles. Similarly, the function $g_{sw}(R, \alpha_1)$ at $R = 1.0$ is

$$g_{sw}(R = 1.0) = (1.5, 1.6, 1.9, 1.6, 1.5) \quad (4.10.3)$$

corresponding to a maximum value of $\alpha_1 = 60^\circ$, which again is consistent with the orientation as depicted in Fig. 4.41 but viewed from the w particle.

These findings suggest that solute particles with the correct diameter have a large probability of fitting into cavities or partial cavities, where the bond directions of the w particles are not oriented toward the solute particles.

An extension of this work was carried out by Southall and Dill (2002). They used the same model as described above to

study the *PMF* between two simple *LJ* particles by Monte Carlo simulation. This work was recently reviewed by Dill *et al.* (2005), to which the reader is referred for details.

4.11. Application of Three-Dimensional Models

The first study of the *PMF* of two solutes in water-like particles by simulation methods was published by Geiger *et al.* (1979). A molecular dynamic simulation of 216 water-like particles and two “neon”-like solutes was carried out. Initially, the two solutes were placed at contact distance. During the evolution of the system, the two solute particles separated to a configuration of “two cages,” which is essentially a configuration such that the structure of water is not disrupted by the inclusion of the solute particles. The orientation of the water molecules around the solute was found to be such that no hydrogen bonding capability was lost. This is similar to the situation described in Fig. 4.41.

Watanabe and Andersen (1986) carried out an extensive molecular dynamics simulation of aqueous solutions of krypton. They found that there is a stable configuration of the two solutes that corresponds to the “water-separated” distance between the two solutes.

An extension of the molecular dynamics simulation to study aggregation of $H\phi O$ solutes in water was carried out by Wallqvist (1991a,b). Rappaport and Scheraga (1982) found no evidence of aggregation of non-polar solutes in water-like solvent. Recently, Paschek (2004) carried out extensive molecular dynamics simulations of aqueous solutions using various models for water-like particles.

Pangali *et al.* (1979a,b) calculated the *PMF* between two *LJ* solute particles (with $\sigma_{ss} = 4.12 \text{ \AA}$ and $\varepsilon_{ss}/k_B = 170.1 \text{ K}$) in water-like particles by Monte Carlo simulation. They found a

first minimum of the *PMF* at $R_1 \approx 4.34 \text{ \AA}$ with a depth of about $0.7k_B T$ and a second minimum at $7.13 \text{ \AA}$ and a depth of about $0.25k_B T$. The latter is consistent with the configuration of the “water-separated” distance between the two solutes (i.e. at a distance of $\sigma_{ss} + \sigma_{ww} \approx 4.12 + 3 \approx 7.13 \text{ \AA}$).

Ravishanker *et al.* (1982) extended the Monte Carlo simulation between two methane molecules in water-like particles. The results obtained by Ravishanker *et al.* are quite different from those by Pangali *et al.*, as well as those obtained by theoretical calculations by Pratt and Chandler (1977). The most striking difference is the occurrence of a second minimum at about $6 \text{ \AA}$, which corresponds to a configuration of a “water-bridge” between the two solutes rather than the “water-separated” configuration obtained by Pangali *et al.* (1979a,b) (Fig. 4.44). In my

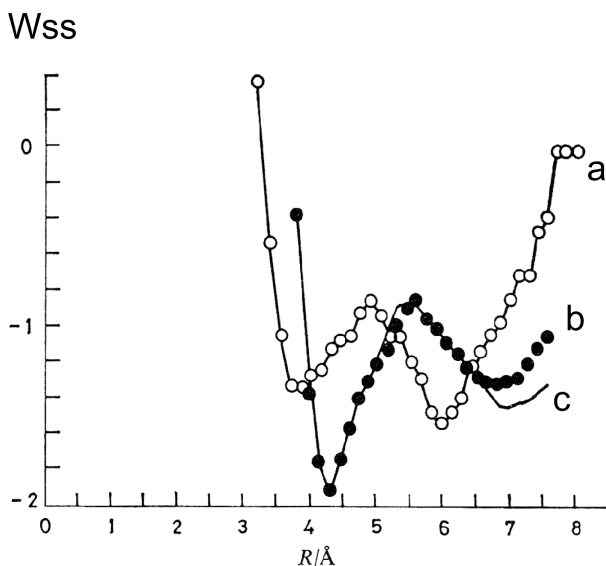


Fig. 4.44 The potential of mean force between two methane molecules in water-like particles at 25°C : (a) Monte Carlo simulation by Ravishanker *et al.* (1982), (b) by Pangali *et al.* (1979ab), and (c) theoretical calculation by Pratt and Chandler (1977).

opinion, the configuration of a “water-bridge” should be more stable than that of the “water-separated” one. The reason is simple: in the “water-separated” configuration at least one “arm” of the water molecule must be directed toward the solute. This configuration incurs a loss of Gibbs energy of about $2.2 \text{ kcal mol}^{-1}$ compared with the “water-bridge” configuration.⁴⁶

As can be seen from Fig. 4.44, there are considerable discrepancies between results obtained by different simulations and by theoretical calculations. At present, it is difficult to claim that one simulated result is better than another. This is also true for any theoretical calculations based on a specific pair potential for water. It is *a fortiori* true if the theory uses as an input the orientational averaged pair correlation function of water, as was done by Pratt and Chandler (1977). In my opinion, using such an input into the theory will inevitably fail to reproduce any property of water and aqueous solutions that is sensitive to the angular dependence of the pair potential — or, equivalently, that depends on the *principle*. For further details, see Ben-Naim (1989), Guarino and Madden (1982), and Tani (1984).

To conclude this section, I would like to add two sets of results on the pair correlation function (*PCF*) between two simple solutes in an *LJ* solvent. These results may or may not be relevant to the problem of *H ϕ O* interactions. Figure 4.45 shows the *PCF* between two hard-sphere (particles labeled *A*) solutes in an *LJ* solvent (particles labeled *B*) with varying strength of the energy parameter ϵ_{BB} . All the calculations for this and the subsequent demonstration were done by solving the Percus–Yevick integral equations⁴⁷ with the following molecular

⁴⁶More recently, Tsunekawa *et al.* (2002) found a second maximum of the methane-methane pair correlation function at about $6.5 \text{ \AA}$.

⁴⁷For details on the Percus–Yevick equation and its numerical solution, see Ben-Naim (2006).

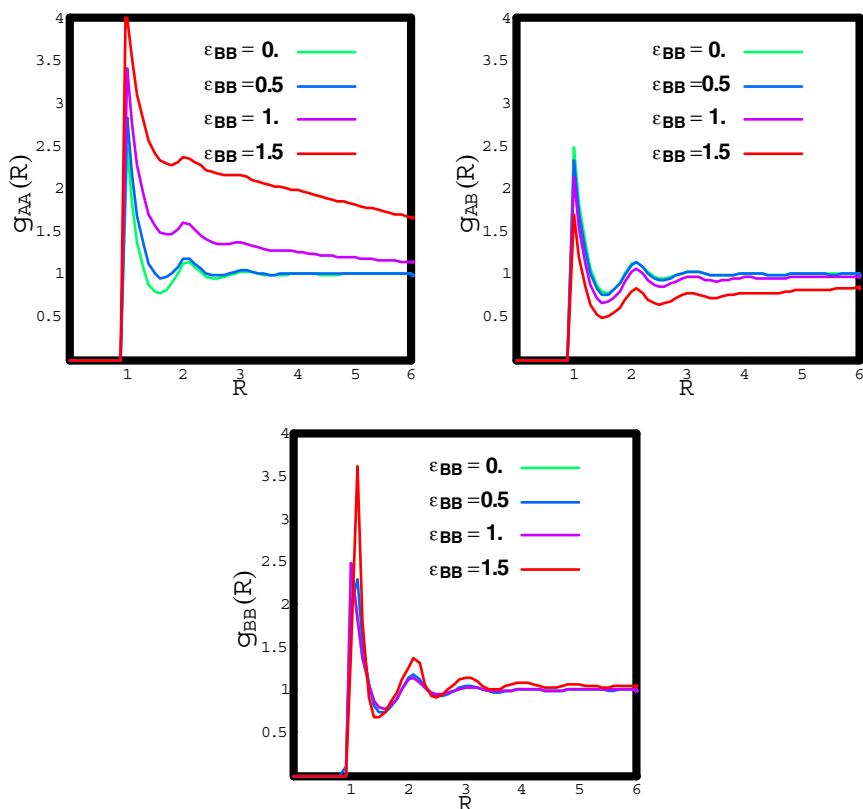


Fig. 4.45 The pair correlation function between two *HS* solutes in *LJ* solvent with different energy parameters. Parameters are as in Eq. (4.11.2).

parameters:

$$\sigma_{AA} = \sigma_{BB} = \sigma_{AB} = 1, \quad U_{AB} = U_{AA} = U_{HS} \text{ potential} \\ \text{and } \varepsilon_{BB} \text{ varies between 0 and 1.5} \quad (4.11.1)$$

$k_B = 1$, $T = 1$, the mole fraction of the solute $x_A = 0.1$ and the total volume density $\eta = 0.4$.

The most interesting observation is that the first peak of the *PCF* of the *HS solute* (A) becomes higher as we increase the strength of the *solvent-solvent* interaction (ε_{BB}) while the solvent-solvent *PCF* changes in a much more moderate way.

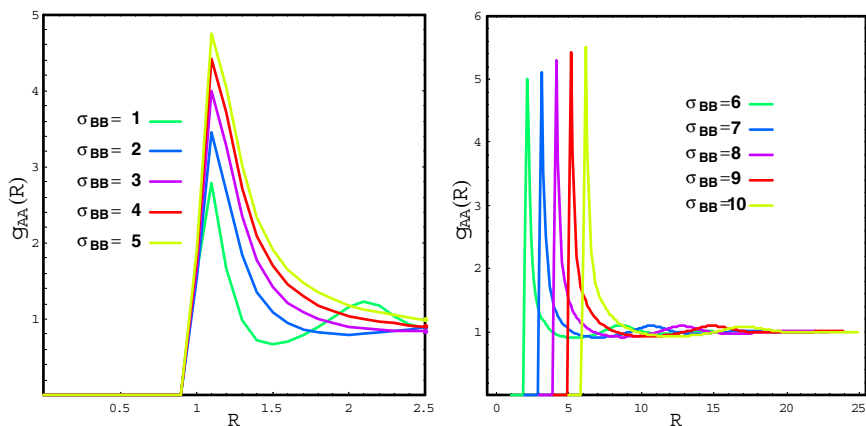


Fig. 4.46 The pair correlation function between two solutes in an *LJ* solvent with different diameters. Parameters are as in Eq. (4.11.2).

Note also the range of the solute-solute *PCF* for larger values of $|\varepsilon_{BB}|$.

In Fig. 4.46, we show the dependence of the *PCF* of an *LJ* solute on the size of the *LJ* solvent particles. The molecular parameters for these demonstrations are

$$\begin{aligned}\sigma_{AA} &= 1, \quad \sigma_{BB} \text{ varying}, \quad \sigma_{AB} = (\sigma_{BB} + \sigma_{AA})/2 \\ \varepsilon_{AA} &= \varepsilon_{AB} = \varepsilon_{BB} = 1\end{aligned}\quad (4.11.2)$$

Again, $k_B = 1$, $T = 1$, $x_A = 0.1$, and $\eta = 0.4$.

The most interesting result is that the *solute-solute PCF* increases quite dramatically with the size of the *solvent* particles while that of the solvent-solvent *PCF* is almost unchanged.

As we have seen in the 1-D model, one can obtain large values of the *PCF* between *solute* particles by varying the molecular parameters of the *solvent*. This is true also for *LJ* particles in a 3-D system.

It seems to me that the strength of the *H ϕ O* interaction as well as the range of the *H ϕ O* interaction are results of the strength of the *solvent-solvent* interaction and not of the

peculiarities of the structure of water. This is true for both the low solubility and the strength of the $H\phi O$ interactions. On the other hand, the temperature and the pressure dependence of both the solubility and the $H\phi O$ interaction are probably closely related to the peculiarities of the structure of water, i.e. to the *principle*.

4.12. Hydrophobic or Hydrophilic? That is the Question!

4.12.1. *A short history of the rise and fall of hydrophobia and hydrophilia*

In this last section of the book, I will summarize my views on the role of the hydrophobic and hydrophilic effects in biochemical processes. The views expressed here are far from being accepted by the majority of researchers in the field. I hope, however, that in the future these ideas will percolate into the minds of those who are willing to examine and hopefully accept new ideas. This section can also be viewed as a prelude to my next book where I will describe the relative importance of the $H\phi O$ and $H\phi I$ effects in actual biochemical systems.

Consider two very important biochemical processes: protein folding and protein-protein association. Both of these processes are highly *specific*: the end products of both are precise three-dimensional structures selected out of a huge number of possible structures. Both processes occur in aqueous media. It has therefore been recognized for a long time that water must play a crucial role in determining both the stability and the specificity of these end products. But how does water do it?

Direct hydrogen bonds (HBs) between functional groups (FGs), such as amines, hydroxyl, and carbonyl have long been recognized to play a major role in forming and maintaining the

3-D structures of proteins.⁴⁸ The same *FGs* that form direct *HBs* within the biomolecule can also form *HBs* to the solvent. Therefore, whenever two functional groups form a direct inter- or intramolecular *HB*, they must first get rid of the hydrogen bonding to the solvating molecule. This competition between *HBing* to the solvent and direct inter- or intra-hydrogen bonding within the biomolecule has led to the so-called “hydrogen-bond-inventory” argument,⁴⁹ as a result of which hydrophilic (*H ϕ I*) interactions were deemed to be insignificant and therefore dismissed (see Sec. 4.12.2).

Here is a typical quotation from a modern textbook⁵⁰:

“The importance of the hydrophobic effect was for a long time underestimated. Charged interactions and hydrogen bonds are not strong *intra* molecular forces because water molecules compete significantly with these effects.”

My views are diametrically opposite: the *hydrophobic* effect⁵¹ has for a long time been *overestimated* — not *underestimated*! Indeed, water molecules do compete with *intramolecular* hydrogen bonding. However, the net effect produces *strong* forces between the hydrophilic groups. Unfortunately, because of this apparent “cancellation” argument, the search for hydrophilic effects was completely abandoned.

The resulting “vacuum” was filled by Kauzmann’s conjecture of the hydrophobic (*H ϕ O*) bond, or *H ϕ O* interaction, or

⁴⁸Pauling *et al.* (1951) and Pauling and Corey (1951).

⁴⁹Fersht *et al.* (1985) and Fersht (1999).

⁵⁰Whitford (2005), page 53. Similar views are expressed by Dill (1985), Tanford (1997), and Tanford and Reynolds (2001).

⁵¹In this section, I shall use the fuzzy term “*H ϕ O* effect” to include both the *H ϕ O* solvation and *H ϕ O* interactions.

$H\phi O$ effect (see Sec. 4.12.3). Although there was no *hard evidence* for that conjecture, the hydrophobic effect was deemed to be “the most important driving force in biochemical processes.” For over half of a century, the fields of aqueous solutions, in general, and aqueous solutions of biomolecules, in particular, were dominated by $H\phi O$ effects. No other competing solvent-induced effects were recognized.

This situation radically changed when the entire question of solvent-induced effects was re-examined, including the “hydrogen-bond inventory” argument.⁵² The unexpected result of this re-examination was not only to revitalize the long dismissed $H\phi I$ interactions, but also open the door (as well as the minds of the researchers) to new arrays of $H\phi I$ effects that were previously unknown and unrecognized.

Thus, hydrogen bonding and its role in biochemical processes, which were neglected for over half of a century, have been resurrected with a rich repertoire of strong and highly specific $H\phi I$ effects. In the following three subsections, I shall try to summarize the reasons for the initial descent of the $H\phi I$ effects, followed by the ascent of the $H\phi O$ effects, and the eventual resurgence of the $H\phi I$ effects.

4.12.2. *The decline of the hydrophilic effect*

Even before the structures of proteins and nucleic acids were known, it was recognized that hydrogen bonds play a crucial role in determining the structures of proteins and DNA. However, there was a problem with these HB s when they occur in aqueous systems. In 1955, John Schellman examined the question of the energetics of HB ing in aqueous solutions. Schellman (1955) used urea as a model compound. It was known that aqueous solutions of urea do not form a dilute-ideal solution.

⁵²Ben-Naim (1991).



Fig. 4.47 (a) The stoichiometric reaction for the formation of an *HB* in vacuum. (b) The stoichiometric reaction used in the *HB*-inventory argument. (c) The stoichiometric reaction that should be used for the formation of an *HB* in solution. The colored backgrounds indicate that the molecules are solvated by water.

The deviation from ideality was ascribed to the formation of dimers. Two kinds of dimers were suggested: linear and cyclic. In the first, the two molecules form one *HB*, and in the second, two *HB*s.

Let us focus on the formation of one hydrogen bond between an amine group and a carbonyl group. In Fig. 4.47a, we show the general reaction between a molecule containing a carbonyl group and a molecule containing an amine group. In Schellman's model the two molecules are urea, but here *E* and *S* could be an enzyme and a substrate, or two groups on the same protein.

When this reaction takes place in vacuum the main contribution to its standard Gibbs energy is simply the *HB energy*. However, when the same reaction takes place in water, the stoichiometry of the reaction was modified as in Fig. 4.47b.⁵³

Without getting into the details of Schellman's arguments, the very writing of the reaction in the form of Fig. 4.47b eventually led to the so-called "*HB* inventory argument."⁵⁴ Kauzmann (1959) summarized Schellman's conclusion as follows: "Hydrogen bonds, taken by themselves, give a marginal stability to

⁵³This form of the stoichiometric reaction was probably first written by Schellman (1955).

⁵⁴See Fersht (1999).

ordered structures, which may be enhanced or disrupted by interactions of side chains.”

Schellman's conclusion was based on his finding that the standard Gibbs energy of the reaction (Fig. 4.47b) is quite small. Therefore, the contribution to the driving force⁵⁵ due to *HB*ing is probably negligible.

There were several reservations about Schellman's conclusion, some of which were discussed by Ben-Naim (1991). However, the general conclusion that *H ϕ I* interactions due to hydrogen bonding are negligible prevailed. I shall return to this argument in Sec. 4.12.4, but first let us consider the alternative “driving force” that became the major protagonist in the biochemical literature.

4.12.3. *The rise of the H ϕ O effect*

Walter Kauzmann, in his classic review “Some Factors in the Interpretation of Protein Denaturation” in 1959, discussed, among other factors, the *HB* between “peptide linkages.” Kauzmann (1959) argued that “since the non-polar side chains have low affinity for water, those polypeptide chain configurations in proteins which bring large numbers of these groups into contact with each other, and hence tend to remove them from the aqueous phase, will be more stable than other configurations, other things being equal.”

This observation led to the inception of a new era based on the *H ϕ O* bond conjecture. In Kauzmann's words⁵⁶: “This tendency of the non-polar groups of proteins to adhere to one another in aqueous environments has been referred to as *hydrophobic bonding*. The hydrophobic bond is probably one

⁵⁵Here, we use the term “driving force” as used in the biochemical literature to mean the standard free energy of the reaction. The “driving force” is obviously not a “force” in the physical sense.

⁵⁶Kauzmann (1959).

of the more important factors involved in stabilizing the folded configuration in many native proteins.”

Kauzmann was cautious in his statement that the $H\phi O$ bond is “*probably*” one of the *more* important factors in stabilizing the folded form of proteins. His main argument was based on the Gibbs energy of transferring non-polar solutes from water into some organic liquids. These Gibbs energies were known to be large and negative. Kauzmann’s idea was that the transfer of a non-polar group attached to the protein into the interior of the protein might be as favorable as the transfer of a non-polar solute from water into an organic liquid.

If each non-polar *group* that is initially exposed to the water, when transferred to the interior of the protein, contributes between -3 and -5 kcal mol^{-1} , as much as the Gibbs energy change for the transfer of a non-polar *solute* from water to an organic liquid, then one can expect that the combined effect of many such non-polar groups would give rise to a huge “driving force” for the process of protein folding.

Using the available data on the thermodynamics of transferring a non-polar molecule from water to a non-polar solvent, Kauzmann drew the following *tentative* conclusions:

- (i) The $H\phi O$ bonds are stabilized largely by entropy effects.
- (ii) The free energy change in the transfer from water to the non-polar environment is exergonic to the extent of about 3000 cal per mole of groups.
- (iii) Hydrophobic bonds involving aliphatic side-chains are more stable at room temperature than they are at 0°C .

Kauzmann emphasized that these conclusions are only tentative “because they are based on the behavior of small hydrocarbon molecules in which no polar groups are present.” Kauzmann’s conclusions were based on the process of transfer of non-polar *solutes* from water to organic liquid. It was

not clear at all that these conclusions also apply to the transfer of non-polar *groups* hung on a protein from being exposed to water to being exposed to the environment in the interior of the protein. In spite of the uncertainty as to the relevance of Kauzmann's model to the process of protein folding, the idea of the $H\phi O$ thrived not so much on evidence but simply due to a lack of other competing candidates.⁵⁷ It is not uncommon to find statements in textbooks in chemistry referring to the $H\phi O$ bond, or the $H\phi O$ interaction, as⁵⁸ “a major driving force in folding of macromolecules, the binding of substrate to enzymes and most other molecular interactions in biology.”

In 1980, I wrote in the preface of my book “Hydrophobic Interactions”:

“In spite of my [research] in this field over almost ten years, I cannot confirm that there is at present either theoretical or experimental evidence that unequivocally demonstrates the relative importance of the $H\phi O$ interactions over other types of interactions in aqueous solutions.”

This was in 1980. Since then I became convinced that Kauzmann's model, based on transferring a *solute* from water into an organic liquid, is inadequate for estimating the contributions of $H\phi O$ *groups* to the overall driving forces in protein folding and protein-protein association. In these processes it is

⁵⁷The “evidence” most frequently cited, aside from the facts about the Gibbs energy of solvation, is that the $H\phi O$ groups are found *inside* the protein. “Could anything be more convincing?” Tanford and Reynolds (2001) asked rhetorically. The fact that $H\phi O$ groups are found in the interior of the protein is *not* evidence that the hydrophobic effect is the driving force for protein folding. This apparently “convincing” argument is similar to the argument given in connection to mixing of two different ideal gases; we see mixing, therefore, what could be more convincing than the conclusion that the mixing is also the *driving force* for the mixing process. The fallacy of this argument is discussed in detail in Ben-Naim (2008a). Another argument was provided earlier in Ben-Naim (1992).

⁵⁸Stryer (1975).

not the Gibbs energies of *solvation* of solute that are relevant but the *conditional* solvation. Furthermore, after re-examining the entire question of solvent-induced effects on biochemical process, I became convinced that hydrophilic ($H\phi I$) rather than hydrophobic effects are probably much more important in biochemical processes. This is discussed in the next subsection.

Before embarking on a discussion of the arguments in favor of the $H\phi I$ effects, I would like to discuss another myth that has been propagating in the literature ever since Frank and Evans published their classic article in 1945. This myth concerns the “explanation” of the $H\phi O$ in terms of the pictorial idea of iceberg formation. The essence of this explanation may be summarized by the following reasoning:

- (i) ΔG_s^* of a non-polar solute in water is large and positive.
- (ii) ΔS_s^* of a non-polar solute in water is large and negative.
- (iii) ΔG_s^* is dominated by the term $T\Delta S^*$.
- (iv) ΔS_s^* is large and negative due to iceberg formation.

Assertions (i) to (iv) are correct. Therefore, one concludes that iceberg formation is responsible for the large positive ΔG_s^* , i.e. iceberg formation explains the low solubility of s . As we have seen in this and the previous chapter, this conclusion is incorrect. The roots of this erroneous conclusion are to be found in the Frank and Evans article published in 1945. This article followed two preceding articles written by Frank (Frank, 1945).

In the first part, Frank expressed the change in entropy in an isothermal process as $R \ln (V_2^f/V_1^f)$, where V_1^f and V_2^f are the so-called free volumes in the initial and in the final states. The relation between the change in volume and change in entropy for an isothermal expansion of ideal gas is

$$\Delta S = R \ln (V_2/V_1) \quad (4.12.1)$$

One can, of course, *define* the “free volumes” V_2^f and V_1^f by the relation

$$\Delta S = R \ln (V_2^f/V_1^f) \quad (4.12.2)$$

However, these “free volumes” do not have, in general, the meaning of *physical* volumes.

Nevertheless, Frank discusses in detail the entropy change in a process of association of two monomers, X and Y , to form a dimer XY . Casting the entropy change in this reaction in terms of “free volume” has an interesting interpretation in terms of *informational* change.⁵⁹ Initially, the two atoms X and Y can wander in the entire volume V . In the final state, one particle (either X or Y) can wander in the entire volume V , but the second particle is now restricted to a small spherical shell about the center of the first particle. This reduction in “free volume” is more appropriately interpreted as a reduction in *locational* missing information or in terms of conditional information [see Ben-Naim (2008a)]. It should be noted that this informational interpretation was not explicitly provided by Frank. But the general idea as expressed by Frank is interesting.

The second part of this series extends the ideas of “free volume” to liquids. It is only in the third part that Frank and Evans apply the concept of “free volume” to aqueous solutions. Examining the experimental data on aqueous solutions of non-electrolytes, they found “striking deviations from the standard behavior.” These findings led to the now famous conclusion:

“When a rare gas atom or non-polar molecule dissolves in water at room temperature, it modifies the water structure in the direction of greater “crystallinity” — the water so to speak builds a microscopic iceberg around it.”

⁵⁹See Ben-Naim (2008a).

As we have discussed in Chapter 3, the idea of iceberg formation is equivalent to interpreting the negative entropy change in terms of increase in *order* or in *structure*. Frank and Evans did not provide any *explanation* why an inert gas atom would form an iceberg or any other structure in water. Therefore, the conjecture of iceberg formation cannot be the explanation of the large negative entropy of solvation of an inert solute — unless one can provide an explanation for the iceberg formation in the first place.

Frank and Evans went a step further. Immediately after discussing the idea of iceberg formation they wrote:

“The assumption of iceberg formation gives a pictorial interpretation for the observation of Butler that the *insolubility of non-polar substances* in water is an entropy, rather an energy phenomenon.”

True, the low solubility of the inert gases in water is determined by the entropy of solvation and not by the enthalpy of solvation. However, whatever the iceberg formation contributes to the solvation entropy cannot affect the solvation Gibbs energy. Hence, the iceberg formation cannot be used to explain the low solubility. Finally, it is worthwhile mentioning that Frank and Evans were well aware of the speculative nature of their ideas about iceberg formation:

“While we have not succeeded in formulating any very satisfactory detailed picture, a rather suggestive idea is that this is an example of a sort of microscopic operation of the Le Chatelier principle.”

It is not clear to me what Frank and Evans meant by “microscopic operation of the Le Chatelier principle.” Whatever they meant, it is clear that due to the exact entropy-enthalpy

compensation, the structural changes induced by the solute can affect both ΔH_s^* and $T\Delta S_s^*$, but when forming the combination $\Delta G_s^* = \Delta H_s^* - T\Delta S_s^*$, the effect of structural change (or iceberg formation) will cancel out.

The idea that the iceberg formation *explains* the $H\phi O$ interaction seems to have been embraced by Kauzmann both in his 1959 review article and in a recent review entitled “Reminiscences from a Life in Protein Physical Chemistry.”⁶⁰ Here is a quotation from Kauzmann’s review:

“Before 1940 many people had thought about the forces that must be operating to hold proteins in their ‘native conformations.’ Mirsky and Pauling (1936) and Huggins (1937) had suggested that hydrogen bonds must be an important factor in maintaining this conformation. Others have suggested that ‘salt bridges’ between positive and negative side-chains might be of some importance.

Finally, there had been a general realization that the non-polar side-chains would tend to exist in the interior of the protein, and out of contact with water. This last ‘interaction’ was often called at the time the ‘van der Waals interaction’.

It seems to me that, in view of the fact that the driving force for the sequestering of the non-polar groups in the interior was their desire to get away from the aqueous environment, it would be more appropriate to call these bonds ‘hydrophobic bonds.’ I coined the term in a paper entitled ‘Denaturation of Proteins and Enzymes,’ given at a conference at the John Hopkins University in June 1953 and published in 1954.

In my mind at that time I had the picture that a non-polar molecule in water actually *disrupted* the water

⁶⁰Kauzmann (1993).

structure by breaking hydrogen bonds, although I did not actually say this.

It was, however, the paper of Frank and Evans (1945) that most clearly set the stage for what I believe is the *correct picture of the hydrophobic bond.*”

In these reminiscences, Kauzmann clearly states that:

- (i) The fact that non-polar side-chains are found in the interior of protein is the *driving force* for this tendency.
- (ii) That Frank and Evans’ ideas about iceberg formation, or enhancement of the structure of water, provide the correct picture of the hydrophobic bond.

It seems quite strange to me that, in spite of the fact that the exact entropy-enthalpy compensation theorem has been in the literature for over 30 years, authors still use the iceberg formation argument to explain the hydrophobic effect. I would add one more quotation to demonstrate how respected authors still invoke the iceberg formation to explain the $H\phi O$ effect, ignoring the entropy-enthalpy compensation theorem. In a very recent book, Tanford and Reynolds (2001) write (*italics are mine*):

“The next *important contribution* to the subject is in itself rather improbable as a potential influence on protein science and it came from an unlikely source, Henry Frank, a Christian missionary ...”

After a short anecdotal story about Henry Frank, they continue:

“These thermodynamic characteristics indicate that hydrogen bonds disrupted by insertion of the non-polar solute do not remain broken, but instead become rearranged in a more restricted, more ordered pattern.

Berkeley's most famous chemist, G.N. Lewis, with whom Frank discussed the work, proposed the name 'iceberg' for these ordered regions, with no implication of any detailed resemblance to the structure of an ice crystal, but simply as an illustration of the kind of organization that the thermodynamic data required.

Henry Frank knew nothing about protein chemistry, nor probably about orientation of amphiphilic solutes at surfaces — he does not even use the word 'hydrophobic' when referring to 'rare gases and other non-polar molecules.' Yet his work had a catalytic effect. It was in a sense an extension of the definition of the word 'hydrophobic,' an *illuminating clarification*. The '*pictorial interpretation*,' crude as it was, *captured the imagination* of the *protein chemists* — it provided evidence for the disproportionate strength of hydrogen bonds in water and *engendered confidence in the hydrophobic concept*. Max Perutz, for example, who had been an early research student of J.D. Bernal and could in principle have learned about hydrophobicity from him, has the following recollection (Perutz, personal communication):

'I cannot remember what Bernal said about hydrophobic groups in proteins but I do remember being very impressed by Kauzmann's review because he gave a *reason* why *hydrophobic groups would be buried* and drew my attention to the crucial paper by Frank and Evans, which otherwise I would never have seen.'

In my view, these statements by Tanford and Reynolds and by Kauzmann (1993), quoted above, are totally misleading. Though it is true that the "'pictorial interpretation,' crude as it was, captured the imagination ...," it was neither "an illuminating clarification" *nor* did it provide any interpretation of

the hydrophobic effect. To put it bluntly: Frank and Evans contributed *nothing* to the *understanding* of the hydrophobic effect. That is true if by the $H\phi O$ effect, as Tanford and Reynolds defined it, one refers to the low solubility of inert solutes in water. On the other hand, if by $H\phi O$ effect one also includes the temperature dependence of the solubility, i.e. the entropy and the enthalpy of solvation of non-polar solute, then the structural changes in the solvent can be used to explain the entropy and enthalpy of solvation only if one provides an explanation of the iceberg formation in the first place. In any case, iceberg formation or any other structural changes in the solvent, cannot be used to explain the Gibbs energy of solvation.

4.12.4. *The resurgence of the $H\phi I$ effects*

To understand the recent resurgence of the $H\phi I$ effects, one needs first to critically examine the validity of the HB -inventory argument.⁶¹ Consider the “reaction” as written in Fig. 4.47b. As Fersht explains,⁶¹ the balance of HB ing is as follows. On the left, an enzyme E makes an HB with water and substrate S makes an HB with water. On the right-hand side the enzyme and the substrate make an HB and the released water molecules also make an HB .

Without getting into the details of the strengths of the different HB s on the two sides of the equation, it seems clear that a simple *counting* of the number of HB s on the two sides of the equation leads to the conclusion that there is a balance in the energetics of this equation. This argument is fallacious for the following reasons.⁶²

⁶¹Fersht (1985,1999) and Fersht *et al.* (1985). It should be noted that Fersht discusses the energy or the enthalpy of this reaction. However, the argument presented here is valid for any thermodynamic quantity.

⁶²More details in Ben-Naim (1991). Also see Baldwin (2003).

Since we are interested in the energetics of *HBing*, we can assume that the molecules are at some fixed position and orientations. First, the “counting” of the number of *HBs* on the two sides of the equation in Fig. 4.45b counts *different* things on the two sides of the equation. On the left-hand side, the enzyme and the substrate are *solvated* by the water. Therefore, what is *lost* in this reaction is not “two *HB*” energies but two *solvation* Gibbs energies (or enthalpy or entropy) of the *HBing* group. On the right-hand side we *gain* one *HB energy*. This energy is very different from the solvation Gibbs energy. Second, whatever the molecules, released by the formation of the complex enzyme-substrate, do in the pool of water molecules does not affect the Gibbs energy of the reaction, and hence does not contribute to the “driving force” of this reaction. To estimate the driving force for the formation of the enzyme-substrate complex, one needs to consider the reaction as written in Fig. 4.47c, i.e. one needs to consider the *solvated* enzyme and the *solvated* substrate forming the *solvated* complex. The magnitude of the Gibbs energy change in this reaction depends on the number of *HBing* “arms” involved in the reaction.⁶³ For simplicity, if only one arm is involved, then the correct “count” should be: loss of the *solvation* Gibbs energy of two arms on the left-hand side and gain of one *HB energy* on the right-hand side. This count leads to a very different conclusion from the *HB* inventory argument. To give an extreme example, suppose that the reaction takes place in steam where the density of water is very low. In this case, the net driving force is mainly due to the formation of one *HB* and the reaction in Fig. 4.47c reduces to that in Fig. 4.47a. There is no “inventory argument” in this case.

Note also that in forming a complex between two molecules, there is always a negative contribution to the entropy due to loss

⁶³See Sec. 4.8.

of the translational and rotational entropy of two particles and the gain of translational and rotational entropy of the product molecule. This entropy change is the same for a reaction carried out in a gas phase or in a solution. Since we are interested here in the solvent-induced effect, we should not take that entropy change into account. That is the reason why one may assume from the outset that the molecules are localized.

In the late 1980s while I was visiting NIH, I re-examined the question of the solvent effects on the processes of protein-protein folding and protein-protein association. I asked myself the following simple question: Suppose we have a long polymer with two kinds of side-chains: $H\phi O$ groups such as methyl or ethyl, and $H\phi I$ groups such as hydroxyl or carbonyl. What can we say about the relative importance of the $H\phi O$ and the $H\phi I$ groups to the overall “driving force” for either folding or association of such a polymer? It turns out that the answer to this seemingly simple question is not simple at all. In order to answer such a question, one needs to follow the “fate” of each side-chain in the process.

For instance, a methyl group that is initially exposed to the solvent might find itself buried in the interior of the protein. It might also be on the surface of the protein but in a different environment from its initial environment. To consider all possible “fates” of each side-chain was an impossible task. To narrow down the range of possible “fates” of the side-chains I focused only on a few possibilities. One when a side-chain is completely removed from being exposed to water. The contribution of such a group to the overall “driving force” of the process would be the *conditional* solvation Gibbs energy of that group. The second possibility is when two groups that are initially exposed to the solvent, but are independently solvated, become correlated. This means that the two groups are still exposed to the solvent but

now their solvation spheres overlap. I called this process *conditional* pairwise correlation. It is similar to the pair correlation between two solutes in a solvent, except for the presence of the backbone (see Fig. 4.19c). Clearly, one can describe higher-order correlations between groups that are exposed to the solvent. However, since we have no data on these we shall stop at this stage.

At this stage, we have five different solvent-induced effects:

- (i) Loss of the conditional solvation of a $H\phi O$ group.
- (ii) Loss of the conditional solvation of a $H\phi I$ group.
- (iii) Pairwise correlation between two $H\phi O$ groups.
- (iv) Pairwise correlation between two $H\phi I$ groups.
- (v) Correlation between an $H\phi O$ and an $H\phi I$ group.

As I have explained in Sec. 4.4, the theory itself provided hints on how to devise experiments from which one could extract data on the Gibbs energies of all these ingredients.

The examination of the available data led to the following conclusions⁶⁴:

- (1) The Gibbs energy of the conditional solvation of the $H\phi O$ group strongly depends on the type of the backbone (BB). It was found that different BB s can change the conditional Gibbs energy of solvation of a methyl group by *one or two orders of magnitude*.⁶⁵ Typically, for a methyl group attached to a hydrocarbon, the conditional solvation Gibbs energy is about $+0.5k_B T$, far smaller than the solvation Gibbs energy of a methane molecule in water.

⁶⁴Ben-Naim (1990a, 1992).

⁶⁵For some numerical examples, see Ben-Naim (1990, 1992). See also Ragone and Colonna (1994) for a reassessment of the solvation and conditional solvation for the problem of protein folding.

- (2) The conditional solvation Gibbs energy of a hydrophilic group such as OH is about $-10k_{\text{B}}T$, much larger than the corresponding value for the $H\phi O$ group.
- (3) A pair of correlated $H\phi O$ groups attached to a hydrocarbon contributes about $-0.5k_{\text{B}}T$ to the overall change of the Gibbs energy of the process.
- (4) Correlation between a $H\phi O$ group and an $H\phi I$ group also contributes about $-0.5k_{\text{B}}T$.
- (5) Correlation between two $H\phi I$ groups attached to a hydrocarbon at some specific distance of about $4.5 \text{ \AA}$ and orientation such that a water molecule can “bridge” the two can contribute about $-6k_{\text{B}}T$.⁶⁶

From this limited data one can conclude that changes in the “fate” of an $H\phi I$ group in the process of protein folding contribute much more to the “driving force” for protein folding compared with the corresponding contribution of an $H\phi O$ group.

Note that the loss of the conditional solvation of an $H\phi I$ group contributes positively to the driving force. However, in most cases where $H\phi I$ groups are found in the interior of the protein, they form intramolecular HBs. The net effect of this HBing (i.e. the gain of the HB energy and the loss of the solvation of the $H\phi I$ groups) could be negative or positive depending on how many “arms” are lost in the process.

In my opinion the contribution due to various $H\phi I$ effects and in particular the $H\phi I$ interaction at a distance of about $4.5 \text{ \AA}$ should prove to be the most important factors in determining the driving forces for biochemical process, including protein solubility, protein-protein binding and protein binding to DNA. This

⁶⁶There are also some “higher-order” hydrophilic effects. These are discussed in Ben-Naim (1992).

does not mean, as some have misinterpreted my conclusion, that I deny the existence of $H\phi O$ effects.

In a recent article, Rose *et al.* (2006) came to a similar conclusion regarding the relative importance of the HB s versus the $H\phi O$ bonds. Analyzing recent experimental data led them to the conclusion that the intramolecular HB s between $H\phi I$ groups on the backbone of the protein must play a dominant role in protein folding. My views as expressed in this chapter, and will be further discussed in a future book, are somewhat more general. Instead of the proposed inversion of the “side-chain/backbone” paradigm, I propose an inversion of the $H\phi O/H\phi I$ paradigm. My proposal is more general in two senses. First, it is not restricted to intramolecular hydrogen-bonding between $H\phi I$ groups on the *backbone*. Second, it is not restricted to direct *hydrogen bonding*. The $H\phi I$ effects comprise a broader repertoire that includes both direct HB s and indirect, solvent mediated $H\phi I$ interactions.

As Tanford (1997) and Tanford and Reynolds (2001) correctly expounded on the history of the hydrophobic effect, the basic ideas of the hydrophobic phenomena were known and discussed long before Kauzmann coined the term *hydrophobic bond*. Clearly, the $H\phi O$ effects are important in processes involving either large numbers of non-polar solutes, or long chain $H\phi O$ molecules (such as the formation of micelles and membranes).

What I have tried to show in this chapter is that when the $H\phi O$ effects are applied to biochemical processes such as protein folding and protein-protein association, they are not as important as currently believed. The evidence from both experimental data, theoretical reasoning, and simulation calculations are overwhelmingly in favor of the $H\phi I$ effects.

APPENDICES

Appendix A: The Tetrahedral Geometry

The tetrahedral angle θ_T is obtained from the following simple geometric considerations (see Fig. A.1). Consider a cube with edge 1. The diagonal a is calculated using the Pythagorean theorem, i.e.

$$a^2 = 1^2 + 1^2 = 2 \quad (\text{A.1})$$

The long diagonal of the cube b is calculated from

$$b^2 = a^2 + 1^2 = 3 \quad (\text{A.2})$$

and the tetrahedral angle is obtained from the cosine theorem applied to the triangle of edges $b/2$, $b/2$, and a , i.e.

$$a^2 = \left(\frac{b}{2}\right)^2 + \left(\frac{b}{2}\right)^2 - \left(\frac{b}{2}\right)^2 \cos \theta_T \quad (\text{A.3})$$

Hence

$$\cos \theta_T = -\frac{1}{3} \quad (\text{A.4})$$

or equivalently

$$\theta_T = \arccos\left(-\frac{1}{3}\right) = 109.471^\circ \quad (\text{A.5})$$

If the distance between the center and one of the vertices of the cube ($b/2$ in Fig. A.1) is taken as the nearest-neighbor distance between two oxygen atoms in ordinary ice ($2.76 \text{ \AA}$), then the

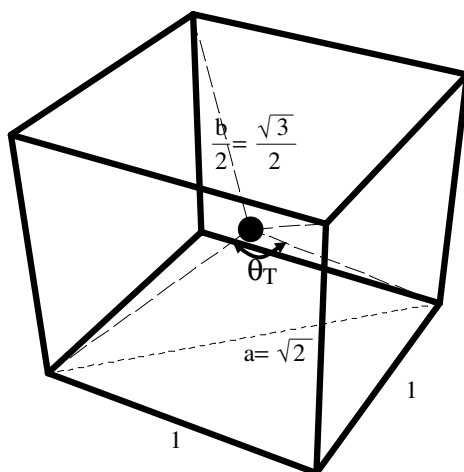


Fig. A.1

second nearest-neighbor distance is

$$2 \times 2.76 \times \sin\left(\frac{\theta_T}{2}\right) = 4.507 \text{ \AA} \quad (\text{A.6})$$

Appendix B: Calculation of the Residual Entropy of Water

This appendix is largely taken from Rushbrooke (1949).

There are two methods of calculating the entropy of a pure substance. One is referred to as the experimental method (sometimes referred to as the calorimetric method), and the other is referred to as the theoretical, or the spectroscopic, method.

The calorimetric entropy is calculated from the thermodynamic equation

$$\left(\frac{\partial S}{\partial T}\right)_P = \frac{C_P}{T} \quad (\text{B.1})$$

Hence

$$\Delta S = S(T) - S(0) = \int_0^T \frac{C_P(T')}{T'} dT' + \sum_i \frac{\Delta H_i}{T_i} \quad (\text{B.2})$$

Table B.1 The Various Contributions to the Experimental Entropy of Water [Eq. (B.2)]

	Entropy (in cal mol ⁻¹ K ⁻¹)
Debye extrapolation between 0 and 10 K	0.022
Integration [Eq. (B.2)] between 10 and 273 K for ice	9.081
Solid-liquid phase transition at 273 K	5.257
Integration [Eq. (B.2)] between 273 and 298 K	1.580
Liquid-gas phase transition at 298 K	35.220
Compression to 1 atm	-6.886
Correction to non-ideality of the gas	0.002
Total	44.28

where $C_P(T)$ is the heat capacity at constant pressure as a function of T , and ΔH_i is the enthalpy change for the phase transition at temperature T_i . Since one cannot measure the heat capacity down to absolute zero, one assumes from the Debye theory that the heat capacity is proportional to T^3 at very low temperatures.

Table B.1 summarizes the various contributions to the entropy ΔS as in (B.2). This is referred to as the experimental entropy. The result is

$$S_{\text{exp}} = \Delta S = 44.28 \text{ cal mol}^{-1} \text{ K}^{-1} \quad (\text{B.3})$$

The theoretical entropy is calculated from the partition function of an ideal gas

$$Q(T, V, N) = \frac{V^N Q_{\text{rot}} Q_{\text{vib}}}{N! \Lambda^{3N}} = Q_{\text{tr}} Q_{\text{rot}} Q_{\text{vib}} \quad (\text{B.4})$$

where the three factors on the right-hand side of (B.4) correspond to the translational, rotational, and vibrational partition functions, respectively. Note that Q_{tr} includes the volume V for each particle, the momentum partition function, and $N!$. Q_{vib} and Q_{rot} are calculated from the vibrational frequencies and the moments of inertia of the water molecule. Note that Q_{vib} and

Q_{rot} are respectively the vibrational and rotational *PF* of all the particles in the system.

The theoretical entropy is a sum of the three contributions

$$\begin{aligned} S_{\text{theor}} &= S_{\text{tr}} + S_{\text{rot}} + S_{\text{vib}} = 34.61 + 10.48 + 0.00 \\ &= 45.09 \text{ cal mol}^{-1} \text{ K}^{-1} \end{aligned} \quad (\text{B.5})$$

Note that the major part of the theoretical entropy comes from the translational entropy (calculated from the Sackur-Tetrode equation). The vibrational contribution is almost zero due to the fact that at 298 K most of the water molecules are in the vibrational ground state.

The difference between the theoretical and the experimental results is obtained from (B.2), (B.3), and (B.5):

$$\Delta S = S_{\text{theor}} - S(0) = S_{\text{exp}} \quad (\text{B.6})$$

or

$$\begin{aligned} S(0) &= S_{\text{theor}} - S_{\text{exp}} = 45.09 - 44.28 \\ &= 0.81 \text{ cal mol}^{-1} \text{ K}^{-1} \end{aligned} \quad (\text{B.7})$$

The difference between the two calculated entropies in (B.7) is referred to as the *residual* entropy and is interpreted in terms of the number of states the system attains at absolute zero, i.e.

$$S(0) = k_B \ln \Omega(0) = 0.81 \text{ cal mol}^{-1} \text{ K}^{-1} \quad (\text{B.8})$$

This value should be compared with the theoretical value calculated by Pauling, in Sec. 1.3.2.

Table B.2 shows some values of S_{exp} , S_{theor} , and the difference ΔS between the two, for various substances.

Table B.2 Values of S_{exp} , S_{theor} , and the Difference ΔS between them (in $\text{cal mol}^{-1} \text{K}^{-1}$)

Substance	S_{theor}	S_{exp}	$\Delta S = k \ln \Omega$
Ar	37.0	36.4	0.6
HCl	44.6	44.5	0.1
NH ₃	44.1	44.1	0.0
O ₂	49.0	49.0	0.0
CO ₂	47.5	47.5	0.0
CO	47.3	46.2	1.1
NNO	48.5	47.4	1.1
CH ₃ D	39.5	36.7	2.8
CH ₄	36.61	36.53	0.07
CH ₃ Br	57.99	57.86	0.13
H ₂ O	45.09	44.28	0.81

Exercise B.1: Calculate the residual entropy for CO and NNO, assuming that in the solid state there are two configurations for each molecule with equal probabilities. Calculate the residual entropy for CH₃D, assuming that in the solid state there are four configurations for each molecule with equal probabilities.

Appendix C: The Kirkwood–Buff Integrals for an Ideal Gas

We start with a hypothetical ideal gas of strictly non-interacting particles. For a system of such particles, it is known that the pair correlation functions in the open and the closed systems are¹

$$g_{\text{O}}(R) = 1 \quad (\text{C.1})$$

and

$$g_{\text{C}}(R) = 1 - \frac{1}{N} \quad (\text{C.2})$$

¹Hill (1956), Munster (1969), and Ben-Naim (2006).

The Kirkwood–Buff integral (KBI) is defined as

$$G_O = \int_V [g_O(R) - 1] d\mathbf{R} = 0 \quad (\text{C.3})$$

The analog of the KBI in a closed system is

$$G_C = \int_V [g_C(R) - 1] d\mathbf{R} = -\frac{1}{N} \int d\mathbf{R} = -\frac{1}{\rho} \quad (\text{C.4})$$

where the integration is performed over the entire volume V of the system. Clearly, the two quantities G_O and G_C are very different. While G_O is identically zero, the quantity G_C is finite and diverges to G_O when $\rho \rightarrow 0$.

Next, we examine ideal gas systems of “real particles,” i.e. interacting particles but at very low densities $\rho \rightarrow 0$. For the open and closed systems we have

$$g_O(R) \cong \exp[-\beta U(R)] \quad (\text{C.5})$$

and

$$g_C(R) \cong \exp[-\beta U(R)] \left(1 - \frac{1}{N}\right) \quad (\text{C.6})$$

We define the functions $G(R_M)$ for spherical systems of radius R_M (and volume $V(R_M)$) as

$$\begin{aligned} G_O(R_M) &= \int_{V(R_M)} [g_O(R) - 1] d\mathbf{R} \\ &= \int_0^{R_M} \exp[-\beta U(R) - 1] 4\pi R^2 dR \end{aligned} \quad (\text{C.7})$$

and

$$\begin{aligned} G_C(R_M) &= \int_{V(R_M)} [g_C(R) - 1] d\mathbf{R} \\ &= G_O(R_M) - \int_0^{R_M} \frac{\exp[-\beta U(R)]}{N} 4\pi R^2 dR \end{aligned} \quad (\text{C.8})$$

Clearly, while $G_O(R_M)$ converges to the *KBI* at the limit of large R_M , the corresponding function in the closed system diverges for $R_M \rightarrow \infty$.

For instance, for hard spheres of diameter σ we have

$$G_O(R_M) = \int_0^\sigma -4\pi R^2 dR = \frac{-4\pi\sigma^3}{3} \quad (\text{C.9})$$

and

$$\begin{aligned} G_C(R_M) &= \frac{-4\pi\sigma^3}{3} - \int_0^{R_M} \frac{4\pi R^2}{N} dR \\ &= \frac{-4\pi\sigma^3}{3} - \frac{4\pi R_M^3}{3N} \xrightarrow{R_M \rightarrow \infty} -\infty \end{aligned} \quad (\text{C.10})$$

Thus, to obtain the correct *KBI*, we can either use the pair correlation function $g_O(R)$ in an open system and take the macroscopic limit of the integral $G_O(R_M)$, or we can *first* take the macroscopic limit of $g_C(R)$ (i.e. we let $N \rightarrow \infty$, and $V \rightarrow \infty$, but N/V constant) and *then* perform the integration, i.e.

$$\lim_{R_M \rightarrow \infty} \int_0^{R_M} \lim_{N \rightarrow \infty} [g_C(R) - 1] 4\pi R^2 dR \rightarrow G_O \quad (\text{C.11})$$

However, if one first takes the integral $G_C(R_M)$ as in (C.8) and then takes the limit $R_M \rightarrow \infty$, the result diverges.

Appendix D: The Equivalence Between the One-Component and the Mixture-Model Views of the Same System

In this appendix, we demonstrate the equivalence between the one-component and the mixture-model (*MM*) views of the same system. We choose an ideal gas system consisting of N molecules at some temperature T and volume V . The canonical partition

function (PF) is

$$Q(T, V, N) = \frac{q^N V^N}{N! \Lambda^{3N}} \quad (D.1)$$

where Λ^3 is the momentum PF and q is the internal PF of a single molecule. We write

$$q = \sum_i \exp[-\beta \varepsilon_i] \quad (D.2)$$

where ε_i are the *energy levels* of the molecule and the sum is over all the *states* of the molecule.

We now split the sum in (D.2) into two sums:

$$q = \sum_{i \in A} \exp[-\beta \varepsilon_i] + \sum_{i \in B} \exp[-\beta \varepsilon_i] = q_A + q_B \quad (D.3)$$

The split of q into a sum of $q_A + q_B$ may be motivated either by our knowledge that the molecule has two isomers (or conformers) or may be completely arbitrary. We may refer to q_A as the internal PF of a molecule of type A , and similarly to q_B as the internal PF of a molecule of type B . The two “types” of molecules do not necessarily exist as pure components. These molecules are *defined* by their internal energy levels in (D.3).

We now define

$$Y_A = \frac{q_A V}{\Lambda^3}, \quad Y_B = \frac{q_B V}{\Lambda^3} \quad (D.4)$$

where Λ^3 is the same for the two species. We also define

$$Y = Y_A + Y_B \quad (D.5)$$

and rewrite the PF (D.1) as

$$\begin{aligned} Q(T, V, N) &= \frac{Y^N}{N!} = \frac{(Y_A + Y_B)^N}{N!} \\ &= \frac{1}{N!} \sum_{N_A=0}^N \frac{N!}{N_A! N_B!} Y_A^{N_A} Y_B^{N_B} \end{aligned} \quad (D.6)$$

where we used the binomial expansion. The summation is over all possible values of N_A (where N_B is defined by $N_B = N - N_A$).

We now define the quantity

$$Q(T, V, N_A, N_B) = \frac{Y_A^{N_A} Y_B^{N_B}}{N_A! N_B!} \quad (\text{D.7})$$

and rewrite (D.6) as

$$Q(T, V, N) = \sum_{N_A=0} Q(T, V, N_A, N_B) \quad (\text{D.8})$$

with $N_B = N - N_A$.

We identify $Q(T, V, N_A, N_B)$ in (D.7) as the *PF* of a *two-component mixture* of *A* and *B* in an ideal gas. How did we get a two-component system from a one-component system? We did not! We did not *get* a two-component system. We simply *chose* to view a one-component system as being composed of two components. The partition function of our system is (D.8), not (D.7). Equation (D.7) is the *PF* of a two-component system having any arbitrary but fixed values of N_A and N_B . In our case, the summation over N_A makes the sum (D.8) independent of N_A so that the resulting sum on the right-hand side of (D.8) is a function of N only. However, there exists a particular value of N_A (and N_B) for which $Q(T, V, N)$ may be approximated by $Q(T, V, N_A, N_B)$.

According to the general rule of statistical thermodynamics, each term in the *PF* is proportional to the probability of the event characterized by that term. Here, $Q(T, V, N_A, N_B)$ is proportional to the probability of finding our (one-component) system in a state such that precisely N_A molecules are in the state *A* and the rest, N_B molecules, are in the state *B*. Thus

$$\text{Pr}(N_A) = \frac{Q(T, V, N_A, N_B)}{Q(T, V, N)} \quad (\text{D.9})$$

With the help of this distribution function we can easily calculate three specific values of N_A :

- (i) the most probable value of N_A , denoted by N_A^* ,
- (ii) the average value of N_A , denoted $\langle N_A \rangle$, and
- (iii) the equilibrium value of N_A , denoted N_A^e .

These are three conceptually different quantities. As we shall soon see, their numerical values are, from the macroscopic point of view, identical.

The most probable value of N_A is defined as the value of N_A for which

$$\frac{\partial \Pr(N_A)}{\partial N_A} = 0 \quad (\text{D.10})$$

It is easy to see that $\Pr(N_A)$ has one extremum, which is a maximum. From (D.7) and (D.10) we obtain, using the Stirling approximation,

$$\frac{\partial \ln \Pr(N_A)}{\partial N_A} = \ln Y_A - \ln Y_B - \ln N_A + \ln(N - N_A) = 0 \quad (\text{D.11})$$

Solving (D.11) for N_A , we obtain

$$N_A^* = N \frac{Y_A}{Y_A + Y_B} \quad (\text{D.12})$$

For $N_A = N_A^*$, we also have

$$\frac{\partial^2 \ln \Pr(N_A)}{\partial N_A^2} = - \left[\frac{1}{N_A} + \frac{1}{N - N_A} \right]_{N_A=N_A^*} < 0 \quad (\text{D.13})$$

which means that $\ln \Pr(N_A)$, as well as $\Pr(N_A)$ has a maximum at $N_A = N_A^*$.

The average value of N_A is defined by

$$\langle N_A \rangle = \sum_{N_A=0}^N N_A \Pr(N_A) = \frac{1}{Q(T, V, N)} \sum_{N_A} N_A \frac{Y_A^{N_A} Y_B^{N_B}}{N_A! N_B!} \quad (\text{D.14})$$

To evaluate the sum on the right-hand side of (D.14), we note the identity

$$Y_A \frac{\partial}{\partial Y_A} \left[\sum_{N_A} \frac{Y_A^{N_A} Y_B^{N_B}}{N_A! N_B!} \right] = \sum_{N_A} N_A \frac{Y_A^{N_A} Y_B^{N_B}}{N_A! N_B!} \quad (\text{D.15})$$

Hence, using (D.6), (D.14) and (D.15), we obtain

$$\begin{aligned} \langle N_A \rangle &= \frac{Y_A}{Q} \frac{\partial}{\partial Y_A} \left[\sum_{N_A} \frac{Y_A^{N_A} Y_B^{N_B}}{N_A! N_B!} \right] = \frac{Y_A}{Q} \frac{\partial}{\partial Y_A} \left[\frac{(Y_A + Y_B)^N}{N!} \right] \\ &= \frac{Y_A N}{Q} \left[\frac{(Y_A + Y_B)^{N-1}}{N!} \right] = N \frac{Y_A}{Y_A + Y_B} \end{aligned} \quad (\text{D.16})$$

We find that the value of $\langle N_A \rangle$ in (D.16) is equal to the value of N_A^* in (D.12).

The third quantity is the equilibrium value of N_A . This is defined as the solution of the equation

$$\mu_A(N_A^e) = \mu_B(N_B^e) \quad (\text{D.17})$$

where μ_A and μ_B are the chemical potentials of A and B, respectively.

It is easy to show that N_A^e defined in (D.17) is also equal to

$$N_A^e = N \frac{Y_A}{Y_A + Y_B} \quad (\text{D.18})$$

which again has the same value as N_A^* and $\langle N_A \rangle$. Note that from (D.18) we have the equilibrium condition $N_A^e/N_B^e = Y_A/Y_B$.

We now show that the sum on the right-hand side of (D.8) may be replaced by a single term. This is the term for which we substitute $N_A = N_A^e$ and $N_B = N_B^e$, i.e. we can write

$$Q(T, V, N) = \sum_{N_A=0}^N Q(T, V, N_A, N_B) \approx Q(T, V, N_A^e, N_B^e) \quad (\text{D.19})$$

where N_A^e fulfills condition (D.18). This is quite a remarkable result. The sum on the left-hand side is over a great number of terms (N is of the order of 10^{23}) including the term on the right-hand side of (D.19). We shall now see in what sense we may claim that (D.19) is an equality. To do that, we start from the right-hand side of (D.19) and proceed to obtain the left-hand side:

$$\begin{aligned} Q(T, V, N_A^e, N_B^e) &= \frac{Y_A^{N_A} Y_B^{N_B}}{N_A! N_B!} \cong \left[\frac{Y_A e}{N_A^e} \right]^{N_A^e} \left[\frac{Y_B e}{N_B^e} \right]^{N_B^e} \\ &= e^N \left[\frac{Y_A}{N_A^e} \right]^{N_A^e} \left[\frac{Y_B}{N_B^e} \right]^{N_B^e} \\ &= e^N \left[\frac{Y_A}{N_A^e} \right]^{N_A^e} \left[\frac{Y_A}{N_A^e} \right]^{N_A^e} \\ &= e^N \left[\frac{Y_A}{N_A^e} \right]^N = e^N \left[\frac{Y_A + Y_B}{N_A^e + N_B^e} \right]^N \\ &= e^N \frac{(Y_A + Y_B)^N}{N^N} \cong \frac{Y^N}{N!} = Q(T, V, N) \end{aligned} \quad (\text{D.20})$$

where we have used the Stirling approximation in the form

$$\ln N! = N \ln N - N \quad (\text{D.21})$$

for N_A, N_B , and N , as well as the identity

$$\frac{Y_A}{N_A^e} = \frac{Y_B}{N_B^e} = \frac{Y_A + Y_B}{N_A^e + N_B^e} \quad (\text{D.22})$$

We see that within the Stirling approximation, (D.19) turns into an equality. In thermodynamic terms this conclusion is equivalent to the statement that introducing or removing a catalyst does not result in any measurable change in the Helmholtz energy. The same holds true when introducing an inhibitor after a chemical equilibrium has been reached.

Thus, we can conclude that, in the limit of large systems, a one-component system is equivalent (thermodynamically speaking) to a *mixture* of two components A and B , provided we choose the composition of the two components as (N_A^e, N_B^e) .

Appendix E: The Generalized Euler Theorem

In this appendix, we present the generalized Euler theorem for homogeneous functions of order one. We first write the Euler theorem for a discrete quasi-component distribution function (*QCDF*) and then generalize by analogy for a continuous *QCDF*. A more detailed proof is available.²

Let E be any extensive thermodynamic quantity expressed as a function of the variables T, P , and N (where N is the total number of molecules in the system). Viewing the system as a mixture of quasi-components, we can express E as a function of the new set of variables T, P , and N . For concreteness, consider the *QCDF* based on the concept of CN . The two possible functions mentioned above are then

$$E(T, P, \mathbf{N}) = E(T, P, N_{CN}(0), N_{CN}(1), \dots) \quad (\text{E.1})$$

For the sake of simplicity, we henceforth use $N(K)$ in place of $N_{CN}(K)$ so that the treatment will be valid for any discrete

²Ben-Naim (1972b).

QCDF. Since E is an extensive quantity, it has the property

$$E(T, P, \alpha N(0), \alpha N(1), \dots) = \alpha E(T, P, N(0), N(1), \dots) \quad (\text{E.2})$$

for any real $\alpha \geq 0$, i.e. E is a homogeneous function of order one with respect to the variables $N(0), N(1), \dots$, keeping T, P constant. For such a function, the Euler theorem states that

$$E(T, P, \mathbf{N}) = \sum_{i=0}^{\infty} \bar{E}_i(T, P, \mathbf{N}) N(i) \quad (\text{E.3})$$

where $\bar{E}(T, P, \mathbf{N})$ is the partial molar (or molecular) quantity defined by

$$\bar{E}(T, P, \mathbf{N}) = \left[\frac{\partial E}{\partial N(i)} \right]_{T, P, N(j), j \neq i} \quad (\text{E.4})$$

In (E.3) and (E.4) we have stressed the fact that the partial molar quantities depend on the whole vector $\mathbf{N}$.

At this point, we digress to discuss the meaning of the partial derivatives introduced in (E.4). We recall that the variables $N(i)$ are not independent; therefore, it is impossible to take the derivatives of (E.4) experimentally. One cannot, in general, add $dN(i)$ of the i -species while keeping all the $N(j), j \neq i$ constant, a process which can certainly be achieved in a mixture of independent components. However, if we assume that, in principle, E can be expressed in terms of the variables T, P and $\mathbf{N}$, then $\bar{E}_i$ is the component of the gradient of E along the i th axis. Here, we must assume that in the neighborhood of the equilibrium vector $\mathbf{N}$ there is a sufficiently dense set of vectors (which describe various frozen-in systems) so that the gradient of E exists along each axis.

The generalization of (E.3) and (E.4) to the case of a continuous *QCDF* requires the application of the technique of functional differentiation. We introduce the generalized Euler theorem by way of analogy with (E.3).

The generalization can be easily visualized if we rewrite (E.3) in the form

$$E(T, P, \mathbf{N}) = \sum_{i=0}^{\infty} \bar{E}(T, P, \mathbf{N}; i) N(i) \quad (\text{E.5})$$

where we have introduced the (discrete) variable i as one of the arguments of the function $\bar{E}$. If $\mathbf{N}$ is a vector derived from a *QCDF* based on a continuous variable, say ν , then the generalization of (E.5) is simply

$$E(T, P, \mathbf{N}) = \int_{-\infty}^{\infty} \bar{E}(T, P, \mathbf{N}; \nu) N(\nu) d\nu \quad (\text{E.6})$$

where $\bar{E}(T, P, \mathbf{N}; \nu)$ is the functional derivative of $E(T, P, \mathbf{N})$ with respect to $N(\nu)$, written as

$$\bar{E}(T, P, \mathbf{N}; \nu) = \frac{\delta E(T, P, \mathbf{N})}{\delta N(\nu)} \quad (\text{E.7})$$

By analogy with the discrete case we may assign to $\bar{E}(T, P, \mathbf{N}; \nu)$ the meaning of a partial molar quantity of the ν -species. The functional derivative in (E.7) is viewed here as a limiting case of (E.4) when the index i refers to a continuous variable.

As an example of (E.6), the volume of the system is written as (see Sec. 2.3)

$$V(T, P, \mathbf{N}_{\psi}) = \int_0^{\infty} \phi N_{\psi}(\phi) d\phi \quad (\text{E.8})$$

Note that this relation is based on the fact that the volumes of the Voronoi polyhedra of all particles add up to build the total volume of the system. Here, we have an example of an explicit dependence between V and N_{ψ} that could have been guessed. Therefore, the partial molar volume of the ϕ -species can be obtained by taking the functional derivative of V with

respect to $N_\psi(\phi)$:

$$\bar{V}(T, P, \mathbf{N}_\psi; \phi') = \frac{\delta V(T, P, \mathbf{N}_\psi)}{\delta N_\psi(\phi')} = \phi' \quad (\text{E.9})$$

This result states that the partial molar volume of the ϕ -species is exactly equal to the volume of its VP . We note that, in general, the partial molar volume of a species is not related in a simple manner to the actual volume which it contributes to the total volume of the system.

A second example is the average internal energy E , which in the T, P, N ensemble is given by (see Sec. 2.3)

$$E(T, P, N_{BE}) = N\varepsilon^K + \frac{1}{2} \int_{-\infty}^{\infty} v N_{BE}(v) dv \quad (\text{E.10})$$

Note that in (E.10), E stands for the energy, whereas in previous expressions in this appendix we have used E for any extensive thermodynamic quantity.

Since the normalization condition for N_{BE} is

$$\int_{-\infty}^{\infty} N_{BE}(v) dv = N \quad (\text{E.11})$$

we can rewrite (E.10) as

$$E(T, P, N_{BE}) = \int_{-\infty}^{\infty} \left(\varepsilon^K + \frac{1}{2} v \right) N_{BE}(v) dv \quad (\text{E.12})$$

This again is an explicit relation between the energy and the $QCDF$, N_{BE} . By direct functional differentiation, we obtain

$$\bar{E}(T, P, N_{BE}; v') = \frac{\delta E(T, P, N_{BE})}{\delta N_{BE}(v')} = \varepsilon^K + \frac{1}{2} v' \quad (\text{E.13})$$

Thus, the partial molar energy of the v' -species is equal to its average kinetic energy and half of its BE .

Appendix F: Some Identities in the Mixture-Model Approach

We start with a system of N_w water molecules (w) and N_s solute molecules (s) at some temperature T and pressure P . Suppose we choose to view the water molecule as a two-component mixture of A and B , at equilibrium, such that $N_w = N_A + N_B$ and the condition of equilibrium is

$$\Delta\mu = \mu_B - \mu_A = 0 \quad (\text{F.1})$$

We assume that we have made an exact classification of all water molecules into two species A and B .

The total differential of $\Delta\mu$, viewed as a function of T, P, N_A, N_B, N_s , is

$$\begin{aligned} d\Delta\mu = & \left(\frac{\partial\Delta\mu}{\partial T} \right)_{P, N_A, N_B, N_s} dT + \left(\frac{\partial\Delta\mu}{\partial P} \right)_{T, N_A, N_B, N_s} dP \\ & + \left(\frac{\partial\Delta\mu}{\partial N_A} \right)_{T, P, N_B, N_s} dN_A + \left(\frac{\partial\Delta\mu}{\partial N_B} \right)_{T, P, N_A, N_s} dN_B \\ & + \left(\frac{\partial\Delta\mu}{\partial N_s} \right)_{T, V, N_A, N_B} dN_s \end{aligned} \quad (\text{F.2})$$

Taking the derivative of $\Delta\mu$ with respect to temperature along the equilibrium line, we have

$$\begin{aligned} 0 = & \left(\frac{\partial\Delta\mu}{\partial T} \right)_{T, P, N_w, N_s} = \left(\frac{\partial\Delta\mu}{\partial T} \right)_{P, N_A, N_B, N_s} \\ & + \left(\frac{\partial\Delta\mu}{\partial N_A} - \frac{\partial\Delta\mu}{\partial N_B} \right) \left(\frac{\partial N_A}{\partial T} \right)_{P, N_s, N_w} \end{aligned} \quad (\text{F.3})$$

Along the equilibrium line we have

$$\Delta\mu = \Delta\bar{H} - T\Delta\bar{S} = 0 \quad (\text{F.4})$$

Therefore

$$\left(\frac{\partial \Delta \mu}{\partial T}\right)_{P, N_A, N_B, N_s} = -\Delta \bar{S} = \frac{\Delta \bar{H}}{T} \quad (\text{F.5})$$

Hence, we can rewrite (F.3) as

$$\left(\frac{\partial N_A}{\partial T}\right)_{P, N_w, N_s} = (\mu_{AA} - 2\mu_{AB} + \mu_{BB})^{-1} \frac{\Delta \bar{H}}{T} \quad (\text{F.6})$$

where

$$\begin{aligned} \mu_{AB} &= \left\{ \frac{\partial}{\partial N_A} \left[\left(\frac{\partial G}{\partial N_B} \right)_{T, P, N_A, N_s} \right] \right\}_{T, P, N_B, N_s} \\ &= \left\{ \frac{\partial}{\partial N_B} \left[\left(\frac{\partial G}{\partial N_A} \right)_{T, P, N_B, N_s} \right] \right\}_{T, P, N_A, N_s} = \mu_{BA} \end{aligned} \quad (\text{F.7})$$

Similarly, for the derivative with respect to pressure along the equilibrium line, we get from (F.3)

$$\left(\frac{\partial N_A}{\partial P}\right)_{T, N_w, N_s} = -(\mu_{AA} - 2\mu_{AB} + \mu_{BB})^{-1} \Delta \bar{V} \quad (\text{F.8})$$

And for the derivative with respect to N_s we have

$$\left(\frac{\partial N_A}{\partial N_s}\right)_{T, P, N_w} = -(\mu_{AA} - 2\mu_{AB} + \mu_{BB})^{-1} \left(\frac{\partial \Delta \mu}{\partial N_s}\right)_{T, P, N_A, N_B} \quad (\text{F.9})$$

It is important to note the different types of the derivatives on the two sides of equations (F.6), (F.8), and (F.9). On the left-hand side, we have a derivative along the equilibrium line (this is indicated by constant N_w). On the other hand, on the right-hand side of these equations, we have derivatives in a “frozen-in” system, i.e. we view the system as a mixture of three components N_A, N_B, N_s , and we “freeze in” the equilibrium between

A and B . In other words, we treat N_A and N_B as being *independent* variables.

The quantity $\mu_{AA} - 2\mu_{AB} + \mu_{BB}$ appearing in (F.6), (F.7), and (F.9) is always positive. This follows from the condition of stability of the system. At equilibrium, at constant T, P, N_s, N_w , the Gibbs energy has a minimum with respect to variation in N_A and N_B . Therefore, for any variation in N_A away from equilibrium, the corresponding change in the Gibbs energy must be positive. Hence, expanding G to second order in dN_A , we get

$$\begin{aligned} 0 \leq dG &= G(N_A + dN_A, N_B + dN_B) - G(N_A, N_B) \\ &= \frac{\partial G}{\partial N_A} dN_A + \frac{\partial G}{\partial N_B} dN_B + \frac{1}{2} \left[\frac{\partial^2 G}{\partial N_A^2} dN_A^2 + 2 \frac{\partial^2 G}{\partial N_A \partial N_B} \right. \\ &\quad \left. \times dN_A dN_B + \frac{\partial^2 G}{\partial N_B^2} dN_B^2 \right] + \dots \end{aligned} \quad (\text{F.10})$$

At equilibrium, the condition of chemical equilibrium (F.1) leads to

$$\frac{\partial G}{\partial N_A} dN_A - \frac{\partial G}{\partial N_B} dN_A = (\mu_A - \mu_B) dN_A = 0 \quad (\text{F.11})$$

Therefore, in the limit of small dN_A , we must have

$$\frac{1}{2} [\mu_{AA} - 2\mu_{AB} + \mu_{BB}] dN_A^2 \geq 0 \quad (\text{F.12})$$

or equivalently

$$\mu_{AA} - 2\mu_{AB} + \mu_{BB} \geq 0 \quad (\text{F.13})$$

Finally, we derive some general relations between the spatial pair correlation functions of the various quasi-components. We begin with the simplest case of a two-structure model. We denote by $g_{\alpha\beta}(R)$ the pair correlation function for the pair of species α and β . Then, $\rho_\alpha g_{\alpha\beta}(R)$ is the local density of an α molecule at a

distance R from a β molecule. Conservation of the total number of w molecules around an A molecule gives

$$\rho_A g_{AA}(R) + \rho_B g_{BA}(R) = \rho_w g_{wA}(R) \quad (\text{F.14})$$

where we denote by $g_{wA}(R)$ the pair correlation function between an A molecule and *any* water molecule. Similarly, considering the total density of molecules around a B molecule, we get the equality

$$\rho_B g_{BB}(R) + \rho_A g_{AB}(R) = \rho_w g_{wB}(R) \quad (\text{F.15})$$

Multiplying (F.14) by ρ_A and (F.15) by ρ_B and summing the two equations, we get

$$\begin{aligned} \rho_A^2 g_{AA}(R) + 2\rho_A \rho_B g_{BA}(R) + \rho_B^2 g_{BB}(R) \\ = \rho_w [\rho_A g_{wA}(R) + \rho_B g_{wB}(R)] \\ = \rho_w^2 g_{ww}(R) \end{aligned} \quad (\text{F.16})$$

where $g_{ww}(R)$ is the ordinary pair correlation function for water molecules. Dividing through by ρ_w^2 , we get

$$x_A^2 g_{AA}(R) + 2x_A x_B g_{AB}(R) + x_B^2 g_{BB}(R) = g_{ww}(R) \quad (\text{F.17})$$

Relations similar to (F.17) can be generalized to any number of components. In the case of a discrete *QCDF*, we get the relation

$$\sum_{K'=0}^{\infty} \sum_{K=0}^{\infty} x(K) x(K') g(K, K', R) = g(R) \quad (\text{F.18})$$

where $g(R)$ is the ordinary pair correlation function of the system and $g(K, K', R)$ is the pair correlation function between the quasi-components K and K' . Similarly, for a continuous *QCDF*, we get

$$\int dv \int dv' x(v) x(v') g(v, v', R) = g(R) \quad (\text{F.19})$$

Appendix G: The Statistical Mechanical Expression for the Solvation Gibbs Energy of Hard Spheres and the Work of Cavity Formation

In this appendix, we briefly show that the expression for $\Delta\mu_s^*$ for any solute in any solvent is

$$\Delta\mu_s^* = -k_B T \ln \langle \exp[-\beta B_s] \rangle_0 \quad (\text{G.1})$$

and that this expression follows directly from the definition of the solvation process. For more details, see Ben-Naim (2006).

Let $\Delta(T, P, \mathbf{N})$ be the $T, P, \mathbf{N}$ partition function (PF) of a system with composition $\mathbf{N} = \{N_1, \dots, N_c\}$ and the total number of molecules $N = \sum N_i$. Let $\Delta(T, P, \mathbf{N}; \mathbf{R}_s)$ be the partition function of the same system, but with an additional s molecule placed at a fixed position $\mathbf{R}_s$. The molecule s could be the same as one of the other N molecules, or a different one. The pseudo-chemical potential is defined by

$$\begin{aligned} \exp[-\beta\mu_s^{*l}] &= \frac{\Delta(T, P, \mathbf{N}; \mathbf{R}_s)}{\Delta(T, P, \mathbf{N})} \\ &= q_s \int dV d\mathbf{X}^N P(V, \mathbf{X}^N) \exp[-\beta B_s] \\ &= q_s \langle \exp[-\beta B_s] \rangle_0 \end{aligned} \quad (\text{G.2})$$

where $P(V, \mathbf{X}^N)$ is the probability density of finding the volume V and the configuration $\mathbf{X}^N$ in the $T, P, \mathbf{N}$ ensemble, and B_s is the *binding energy* of s defined by

$$B_s = U(\mathbf{R}_s, \mathbf{X}_1, \dots, \mathbf{X}_N) - U(\mathbf{X}_1, \dots, \mathbf{X}_N) \quad (\text{G.3})$$

Note that the average in (G.2) is taken with the distribution $P(V, \mathbf{X}^N)$ of the “pure” solvent, i.e. the system of N molecules *before* the insertion of s at $\mathbf{R}_s$. q_s is the internal partition function of s , which is assumed to be separable from the configurational PF .

Assuming that q_s is the same in the liquid and in an ideal gas phase, the pseudo-chemical potential of s in an ideal gas phase is simply

$$\exp[-\beta\mu_s^{*ig}] = q_s \quad (\text{G.4})$$

Hence, from (G.2) and (G.4) we have

$$\Delta\mu_s^* = -k_B T \ln \langle \exp[-\beta B_s] \rangle_0 \quad (\text{G.5})$$

A special case of (G.5) is for a hard-sphere (*HS*) solute. In this case, the interaction between s and any other molecule is either zero or infinity according to whether the molecule is away from or within the excluded region produced by s . The function $\exp[-\beta B_{HS}]$ is accordingly either zero or one. Therefore, the average in (G.5) may be written as

$$\begin{aligned} \int dV d\mathbf{X}^N P(V, \mathbf{X}^N) \exp[-\beta B_s] &= \int_{V-V^{EX}(\mathbf{R}_s)} dV d\mathbf{X}^N P(V, \mathbf{X}^N) \\ &= P(V^{EX}, \mathbf{R}_s) \end{aligned} \quad (\text{G.6})$$

where $V - V^{EX}(\mathbf{R}_s)$ is the region for which $\exp[-\beta B_s]$ is unity. Since $P(V, \mathbf{X}^N)$ is a probability density, the integral on the right-hand side of (G.6) is the probability of finding all particles in $V - V^{EX}(\mathbf{R}_s)$ or, equivalently, the probability that no solvent particle will occupy the region $V^{EX}(\mathbf{R}_s)$. This is the same as the probability of finding a cavity of volume V^{EX} at $\mathbf{R}_s$, which we denote as $P(V^{EX}, \mathbf{R}_s)$. Thus, for the *HS* solute we have

$$\Delta\mu_{HS}^* = -k_B T \ln P(V^{EX}, \mathbf{R}_s) \quad (\text{G.7})$$

It should be noted that this relation is valid for any choice of the location $\mathbf{R}_s$. However, $\mathbf{R}_s$ is included in the notation on the right-hand side of (G.7) to stress that cavity must be at some *fixed* position in the liquid.

A special case of (G.7) is for a point HS , defined as an HS of radius zero. For a one-component solvent with an effective diameter σ , the size of the excluded volume formed by the point HS is simply $\frac{4\pi\sigma^3}{3}$ (see Fig. 3.20).

The sphere of volume $4\pi\sigma^3/3$ at the fixed position $\mathbf{R}_s$ can accommodate at most one solvent particle at any given time. Therefore, the probability of finding the volume $4\pi\sigma^3/3$ at $\mathbf{R}_s$ empty is

$$P_0\left(V^{EX} = \frac{4\pi\sigma^3}{3}, \mathbf{R}_s\right) = 1 - \rho \frac{4\pi\sigma^3}{3} \quad (\text{G.8})$$

and the corresponding solvation Gibbs energy is

$$\Delta\mu_{\bullet}^* = -k_B T \ln \left(1 - \rho \frac{4\pi\sigma^3}{3} \right) \quad (\text{G.9})$$

Appendix H: The Solubility of a Simple Solute in Water and Structural Changes Induced in the Solvent

In this appendix, we use a very simple two-structure model to describe the effect of structural changes induced by a solute or by a co-solvent on the solubility of the solute.

The chemical potential of a solute s is defined by

$$\mu_s = \left(\frac{\partial G}{\partial N_s} \right)_{T, P, N_w} \quad (\text{H.1})$$

We view the solvent water as a mixture of two components, L and H . Let N_L and N_H be the average number of L and H at the given temperature T and pressure P , for a system of composition N_w, N_s . The quantities N_L and N_H are determined

by the condition of chemical equilibrium:

$$\mu_L(T, P, N_L, N_H, N_s) = \mu_H(T, P, N_L, N_H, N_s) \quad (\text{H.2})$$

with the condition $N_L + N_H = N_w$, N_w being the total number of water molecules. Viewing G as a function of the independent variables T, P, N_L, N_H , we can write the chemical potential as (T and P are always constants and will be omitted from the notation),

$$\begin{aligned} \mu_s &= \left(\frac{\partial G}{\partial N_s} \right)_{N_w} = \left(\frac{\partial G}{\partial N_s} \right)_{N_L, N_H} + \left(\frac{\partial G}{\partial N_L} \right)_{N_s, N_H} \left(\frac{\partial N_L}{\partial N_s} \right)_{N_w} \\ &\quad + \left(\frac{\partial G}{\partial N_H} \right)_{N_s, N_L} \left(\frac{\partial N_H}{\partial N_s} \right)_{N_w} \\ &= \mu_s^{fr} + (\mu_L - \mu_H) \left(\frac{\partial N_L}{\partial N_s} \right)_{N_w} = \mu_s^{fr} \quad (\text{H.3}) \end{aligned}$$

The last form of the equality (H.3) follows from the condition of chemical equilibrium (H.2).

The conclusion derived from (H.3) may be stated as follows: The chemical potential of s in the system is not affected by the structural changes induced by the solute s . Note that any other partial molar quantity might be affected by the structural changes induced by the solute s . It should be noted that the above conclusion is valid for any initial state (T, P, N_w, N_s) , when the “frozen-in” of the equilibrium $L \rightleftharpoons H$ is imposed at this state.

Next, we explore a different situation. Suppose we start with pure water at (T, P, N_w) or equivalently at (T, P, N_L^0, N_H^0) , where N_L^0 and N_H^0 are determined by the condition of chemical equilibrium (H.2) but with $N_s = 0$. We now “freeze in” the equilibrium $L \rightleftharpoons H$, adding a *finite* quantity of s , N_s . The chemical potential at this “frozen-in” state is $\mu_s(T, P, N_L^0, N_H^0, N_s)$.

Next, we release the constraint on fixed N_L^0, N_H^0 and ask: In which direction will the chemical potential of s change?

To first order in $\Delta N_L = N_L - N_L^0$, we write the expansion of the chemical potential

$$\begin{aligned}\mu_s(T, P, N_L, N_H, N_s) &= \mu_s^{fr}(T, P, N_L^0, N_H^0, N_s) \\ &\quad + \left(\frac{\partial \mu_s}{\partial N_L} - \frac{\partial \mu_s}{\partial N_H} \right) \Delta N_L \\ &= \mu_s^{fr} + \frac{\partial(\mu_L - \mu_H)}{\partial N_s} \Delta N_L\end{aligned}\quad (\text{H.4})$$

Note that ΔN_L is a result of the addition of the *finite* quantity of the solute s . The derivative $\partial(\mu_L - \mu_H)/\partial N_s$ is related to the structural changes in the solvent by the identity (see Appendix F)

$$\left(\frac{\partial(\mu_L - \mu_H)}{\partial N_s} \right)_{N_L^0 N_H^0} = -(\mu_{LL} - 2\mu_{LH} + \mu_{HH}) \left(\frac{\partial N_L}{\partial N_s} \right)_{N_w} \quad (\text{H.5})$$

where $\mu_{ij} = \partial^2 G / \partial N_i \partial N_j$ and $\mu_{LL} - 2\mu_{LH} + \mu_{HH} > 0$.

Thus, we can rewrite (H.4) as

$$\begin{aligned}\mu_s(T, P, N_L, N_H, N_s) &= \mu_s^{fr} - (\mu_{LL} - 2\mu_{LH} + \mu_{HH}) \\ &\quad \times \left(\frac{\partial N_L}{\partial N_s} \right) \Delta N_L\end{aligned}\quad (\text{H.6})$$

Note that $(\partial N_L / \partial N_s)_{N_w}$ is the effect of s on N_L at the point (T, P, N_L^0, N_H^0) , i.e. the initial effect of an *infinitesimal* addition of dN_s to pure water. ΔN_L is the result of the addition of the *finite* quantity N_s .

We now assume that s stabilizes the component L , i.e. N_L increases from the initial state $(T, P, N_L^0, N_H^0, N_s)$ to the final state (T, P, N_L, N_H, N_s) . Therefore, the second term on the right-hand side of (H.6) will be negative. Thus, upon relaxing the

constraint on L and H , the chemical potential of s will decrease, which means that the structural changes induced by s will tend to *increase* the solubility.³

The next situation is relevant to the solubility of s in a mixture of solvents, water w and a co-solvent v . We start with an initial state (T, P, N_w, N_s, N_v) , add dN_v , and examine the change in the chemical potential of s . Again, we view water as a mixture of L and H and expand μ_s to first order in dN_v :

$$\begin{aligned} \mu_s(T, P, N_L + dN_L, N_H - dN_L, N_s, N_v + dN_v) \\ = \mu_s(T, P, N_L, N_H, N_s, N_v) \\ + \left(\frac{\partial \mu_s}{\partial N_v} \right)_{N_s, N_L, N_H} + \left(\frac{\partial \mu_s}{\partial N_L} - \frac{\partial \mu_s}{\partial N_H} \right) dN_L \end{aligned} \quad (\text{H.7})$$

or equivalently

$$\begin{aligned} \left(\frac{\partial \mu_s}{\partial N_v} \right)_{N_s, N_w} &= \left(\frac{\partial \mu_s}{\partial N_v} \right)_{N_s, N_L, N_H} \\ &+ \left(\frac{\partial (\mu_L - \mu_H)}{\partial N_s} \right)_{N_L, N_H, N_v} \left(\frac{\partial N_L}{\partial N_v} \right)_{N_s, N_w} \\ &= \left(\frac{\partial \mu_s}{\partial N_v} \right)_{N_s, N_L, N_H} - (\mu_{LL} - 2\mu_{LH} + \mu_{HH}) \\ &\times \left(\frac{\partial N_L}{\partial N_s} \right)_{N_w, N_v} \left(\frac{\partial N_L}{\partial N_v} \right)_{N_w, N_s} \end{aligned} \quad (\text{H.8})$$

Note that in this case, we start from a state $(T, P, N_L, N_H, N_s, N_v)$, “freeze in” the equilibrium $L \rightleftharpoons H$ at N_L, N_H (not at pure water), and add dN_v . The effect of this addition on

³Ben-Naim (1966).

the chemical potential of s is

$$\Delta\mu_s = \left(\frac{\partial\mu_s}{\partial N_v} \right)_{N_s N_L N_H} dN_v - [\mu_{LL} - 2\mu_{LH} + \mu_{HH}] \left(\frac{\partial N_L}{\partial N_s} \right)_{N_w N_v} \left(\frac{\partial N_L}{\partial N_v} \right)_{N_w N_s} dN_v \quad (\text{H.9})$$

There are three possible cases:

- (i) If both the solute s and the co-solvent v stabilize the structure of water, then the product of $\partial N_L / \partial N_s$ and $\partial N_L / \partial N_v$ is positive, and we get a negative contribution to the right-hand side of (H.9).
- (ii) If only one of the two co-solvents, either s or v , stabilizes L , then we get a positive contribution to (H.9).
- (iii) When both s and v destabilize L , we get again a negative contribution to the right-hand side of (H.9).

Although it is not possible to make any quantitative statements, I believe that these three cases correspond to the three slopes of the solubility (or the solvation Gibbs energy) of s in the mixtures of water and ethanol (see Fig. 3.5). Probably, initially, when we add a small amount of alcohol to pure water, both s and v stabilize the structure of water. The negative contribution to $\Delta\mu_s$ in (H.9) means that the solubility of s will initially increase. At larger concentrations of alcohol, the solute s still stabilizes L , but the co-solvent v does not. This is probably the reason for the decrease in the solubility of s . At higher concentrations of v , the water is very diluted in v , there is not much of the L component left, and both s and v do not stabilize the L component.

It should be noted that the first term on the right-hand side of (H.9) is always negative. What we have examined above is

the possible additional effects on $\Delta\mu_s$ due to structural changes induced by s and ν .

Appendix I: An Estimate of the Strength of Hydrophilic Interaction at $R = 4.5 \text{ \AA}$

Let 1 and 2 be either two water molecules or two functional groups attached to a backbone (BB).

We start with the expression for $\delta G_{HB/LJ}$ in (4.8.13):

$$\delta G_{HB/LJ} = -k_B T \frac{\langle \exp[-\beta B_{1,2}^{HB}(4.5)] \rangle_{BB}}{\langle \exp[-\beta B_1^{HB}(4.5)] \rangle_{BB}^2} \quad (\text{I.1})$$

B_1^{HB} is the HB part of the binding energy of water molecule 1 to the rest of the system. $B_{1,2}^{HB}(4.5)$ is the HB part of the binding energy of the two water molecules designated 1 and 2 when they are at a distance $4.5 \text{ \AA}$ and oriented in such a way that a third water molecule can form a hydrogen-bond bridge between 1 and 2 (see Fig. 4.33). The average $\langle \cdot \rangle_{BB}$ is a conditional average given the BB . Here, the BB includes the LJ part of the interaction energy as well as an additional BB attached to the functional groups 1 and 2.

The average in the denominator of Eq. (I.1) was already estimated in Sec. 2.7.6. We need to estimate the average in the numerator of (I.1). Before we carry out the calculation we recall two features of the hydrogen bonding that make this estimate feasible. First, the saturation effect: an *arm* of a $H\phi I$ group can form at most one hydrogen bond with a water molecule. Second, a water molecule forming an HB with the arm of another water molecule (or a functional group, such as OH , C=O , NH) can do so only from a very small region (location and

orientation). This was symbolically indicated by the squares in Fig. 4.22.

To estimate the average in the numerator of Eq. (I.1), we repeat essentially the same steps as in Sec. 2.7.6 except that here we have two arms in the configuration denoted $(R_2, \Omega_{HB}^{(2)})$ in Sec. 4.8. Thus, we write

$$\langle \exp[-\beta B_{1,2}^{HB}(4.5)] \rangle_{BB} = \int d\mathbf{X}^N P(\mathbf{X}^N / BB) \exp[-\beta B_{1,2}^{HB}(4.5)] \quad (\text{I.2})$$

where the integration is over all N solvent molecules ($i = 3, 4, \dots, N + 2$) not including groups 1 and 2. We further split the integral on the left-hand side of (I.2) as in Sec. 2.7.6:

$$\begin{aligned} & \int d\mathbf{X}^N P(\mathbf{X}^N / BB) \exp[-\beta B_{1,2}^{HB}(4.5)] \\ &= \int_{\substack{\text{one } w \\ \text{HBed to } (1, 2)}} + \int_{\substack{\text{no } w \\ \text{HBed to } (1, 2)}} \\ &= \sum_{j=3}^{N+2} \left\{ \int_{\substack{j\text{th } w \\ \text{HBed to 1} \\ \text{only}}} + \int_{\substack{j\text{th } w \\ \text{HBed to 2} \\ \text{only}}} + \int_{\substack{j\text{th } w \\ \text{HBed to} \\ 1 \text{ and } 2}} + \int_{\substack{\text{no } w \\ \text{HBed} \\ \text{to } (1, 2)}} \right\} \end{aligned} \quad (\text{I.3})$$

In Eq. (I.3), we split the integral over all configurations of the solvent water molecules (i.e. $i = 2, 3, \dots, N + 2$) into two regions. One region includes all configurations of the water molecules such that one water molecule forms *HBs* with the “unit” denoted $(1, 2)$. The second includes all configurations of the N water molecules such that no water molecule forms *HBs* to the unit $(1, 2)$.

The first integral is further split into three regions: one from which a specific water molecule forms *HBs* only to group 1,

the second from which a specific molecule forms *HBs* only to group 2, and the third from which a specific water molecule forms *HBs* with both 1 and 2. These three regions together are equal to the entire region from which a specific water molecule, say j , forms an *HB* with the unit (1, 2). Since all the water molecules are equivalent, we can choose one specific water molecule and sum over all j to obtain N integrals, i.e.

$$\sum_{j=1}^{N+2} \int_{\substack{j\text{th } w \\ \text{HBed to 1} \\ \text{only}}} = N \int_{\substack{\text{water 3} \\ \text{HBed to 1} \\ \text{only}}} \quad (\text{I.4})$$

and similar equalities for the three integrals on the right-hand side of (I.3). The fourth integral on the right-hand side of (I.3) is over the region of all configurations from which no water molecule forms *HBs* with the unit (1, 2). Since in this region the binding energy $B_{1,2}^{HB}$ (4.5) is zero, the fourth integral on the right-hand side of (I.3) is a probability. This is the probability that no water molecule forms an *HB* with the unit. As a probability it can be written as

$$\begin{aligned} & \text{Pr}\{\text{no water molecule forms } HB \text{ with } (1, 2)\} \\ &= 1 - \text{Pr}\{\text{at least one water molecule form } HB \text{ to } (1, 2)\} \\ &= 1 - N \text{Pr}\{\text{water 3 forms } HB \text{ with } (1, 2)\} \end{aligned} \quad (\text{I.5})$$

This can be combined with (I.3) and (I.4) to obtain

$$\begin{aligned} & \langle \exp[-\beta B_{1,2}^{HB}(4.5)] \rangle_{BB} \\ &= 1 + \int d\mathbf{X}_w \{ \exp[-\beta U^{HB}(1, \mathbf{X}_w)] - 1 \} \rho^{(1)}(\mathbf{X}_w / BB) \\ & \quad + \int d\mathbf{X}_w \{ \exp[-\beta U^{HB}(2, \mathbf{X}_w)] - 1 \} \rho^{(1)}(\mathbf{X}_w / BB) \end{aligned}$$

$$\begin{aligned}
& + \int d\mathbf{X}_w \{ \exp[-\beta U^{HB}(1, \mathbf{X}_w) \\
& - \beta U^{HB}(2, \mathbf{X}_w) - 1] \rho^{(1)}(\mathbf{X}_w / BB) \}
\end{aligned} \tag{I.6}$$

In (I.6), we have also integrated over all water molecules except the one which is hydrogen bonded, denoted now by w [instead of “3” in Eq. (I.4)], to obtain the conditional density of water molecules at $\mathbf{X}_w$ given the BB . There is a slight difference in the condition “ BB ” between the first two integrals and the third. We ignore this difference here.⁴

As in Sec. 2.7.6, we also recognize that the regions of integrations for which the integrands are non-zero are very small. Also, assuming the pair potential as defined in Sec. 2.7.2 is discrete, i.e. an HB is formed or not, we can rewrite (I.6) as

$$\begin{aligned}
& \langle \exp[-\beta B_{1,2}^{HB}(4.5)] \rangle_{BB} \\
& \approx 1 + 2\{\exp[-\beta \varepsilon_{HB}] - 1\} 2\rho_w \left(\frac{\Delta \mathbf{X} - \Delta \mathbf{X}'}{8\pi^2} \right) g(R_2) \\
& + \{\exp[-\beta \varepsilon_{HB}] - 1\} 2\rho_w \frac{\Delta \mathbf{X}'}{8\pi^2} g'(R_2)
\end{aligned} \tag{I.7}$$

The first two integrals on the right-hand side of (I.6) are equal, and they are approximated by the product of the value of the integrand and the size of the region. Here, $\Delta \mathbf{X}$ is the same as in Sec. 2.7.6, the region from which a water molecule forms an HB with an arm of another water molecule or a functional group. This was estimated in Sec. 2.7.3 to be

$$\frac{\Delta X}{8\pi^2} \approx 5.1 \times 10^{-3} \text{ cm}^3 \text{ mol}^{-1} \tag{I.8}$$

choosing ($\varepsilon_{HB} = -6.5 \text{ kcal mol}^{-1}$).

⁴For details, see Ben-Naim (1989).

The region $\Delta X'$ is the region from which a water molecule can form two *HBs* with both groups 1 and 2. Clearly, this region is much smaller than the region ΔX .

While the quantity ΔX was estimated from the second virial coefficient, we do not have an estimate of $\Delta X'$. Both depend on how we define the pair potential. We therefore arbitrarily assume that

$$\Delta X' = \frac{20}{360} \Delta X \quad (\text{I.9})$$

In Eq. (I.7), we also wrote the conditional density of water molecules around 1 and around the pair (1, 2) as a product of the density of water at 298 K, $\rho_w = 0.0555 \text{ mol cm}^{-3}$, and assumed the correlation functions $g(R_2)$ and $g'(R_2)$ at the distance from 1 and 2 of about $2.76 \text{ \AA}$ is of the order of 2. Note also that the first factor 2 in the second term on the right-hand side of (I.7) is for two integrals on the right-hand side of (I.6). The second factor of 2 in the second and the third terms in (I.7) are due to the two possibilities of a water molecule to form *HBs* with either 1 or with the pair (1, 2).

Combining all these estimates and using the estimated value of the denominator in (I.1) from Sec. 2.7, we arrive at

$$\begin{aligned} \delta G_{HB/LJ} &= -k_B T \ln \langle \exp [-\beta B_{1,2}^{HB}(4.5)] \rangle_{BB} \\ &\quad + 2k_B T \ln \langle \exp [-\beta B_1^{HB}] \rangle_{BB} \\ &\approx -7.27 + 2 \times 2.25 \approx -2.8 \text{ kcal mol}^{-1} \end{aligned} \quad (\text{I.10})$$

Clearly, this is a very crude estimate involving many assumptions. However, the order of magnitude seems to be correct and in agreement with estimates based on the model compounds discussed in Sec. 2.8.

Appendix J: Calculated Data on $H\phi I$ Interactions

The solvation Gibbs energies of dihydroxybenzene were calculated by Censky *et al.* (2007) based on the assumption of group additivity. This assumption is not supported by theory, but it seems to work quite well.

From the data of Censky *et al.*, we calculated the indirect Gibbs energies of transfer of a hydroxyl group (Fig. J.1). All values are at 298 K and 1 atm [taken from Table 12 of Censky *et al.* (2007)]:

$$\begin{aligned} \text{(a)} \quad \delta G((1,4) \rightarrow (1,3)) &= \Delta G_{1,3}^* - \Delta G_{1,4}^* \approx -13.3 \text{ kJ mol}^{-1} \\ &= -3.18 \text{ kcal mol}^{-1} \end{aligned} \quad (\text{J.1})$$

$$\begin{aligned} \text{(b)} \quad \delta G((1,4) \rightarrow (1,2)) &= \Delta G_{1,2}^* - \Delta G_{1,4}^* \approx 7.1 \text{ kJ mol}^{-1} \\ &= -1.69 \text{ kcal mol}^{-1} \end{aligned} \quad (\text{J.2})$$

These values are in qualitative agreement with those reported in Sec. 4.8.⁵

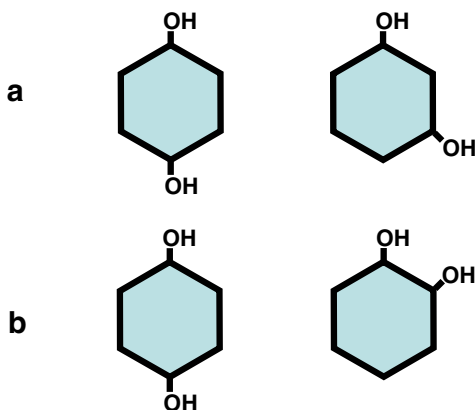


Fig. J.1

⁵Note, however, that in Table 12 of Censky *et al.* (2007), there are also values of the solvation Gibbs energies of diaminobenzene. All three isomers have the same values. This is an indication of the failure of the group additivity assumption for these cases.

Table J.1 Partial Molar Volumes of the Various Dihydroxybenzene^a

T (K)	P (MPa)	$\bar{V}_{1,2}^0$ (cm ³ mol ⁻¹)	$\bar{V}_{1,3}^0$ (cm ³ mol ⁻¹)	$\bar{V}_{1,4}^0$ (cm ³ mol ⁻¹)
298.15	0.1	86.883	88.803	88.703
338.15	0.1	90.800	92.383	92.100
298.15	30	86.956	88.392	88.138

a) From Jedelsky *et al.* (1999).

Table J.2 Volume Change Corresponding to the Transfer of a Hydroxyl Group

T (K)	P (MPa)	$\delta V(1, 4 \rightarrow 1, 2)$ (cm ³ mol ⁻¹)	$\delta V(1, 4 \rightarrow 1, 3)$ (cm ³ mol ⁻¹)
298.15	0.1	-1.82	0.1
298.15	30	-1.182	0.253
338.15	0.1	-1.3	0.283

For the same compounds, we can also calculate the volume change corresponding to the $H\phi I$ process. Table J.1 shows the partial molar volume of these compounds at infinite dilution at two temperatures and two pressures. The corresponding values of δV are shown in Table J.2.

The volume changes for the hydrophilic process in bringing a hydroxyl group from (1, 4) to (1, 2) are relatively large and negative, while the corresponding quantities to transfer from (1, 4) to (1, 3) are relatively small and positive. These results may be interpreted as follows. At position (1, 3), the two hydroxyl groups can form an *HB*-bridge with a water molecule. This structure fits very well into the ice-like structure of the water itself; therefore, only a small change in the volume of the system is expected. As for the sign of δV in this case, the positive result indicate that the (1, 3) isomer slightly enhances the open structure of water relative to the (1, 4) isomer.

On the other hand, in the (1, 2) isomer, because of the proximity of the two hydroxyl groups, hydrogen bonding of the

Table J.3 Values of δG for the Two Processes as in (J.1) and (J.2)

Process	Dihydroxybenzene (kcal mol ⁻¹)	Diaminobenzene (kcal mol ⁻¹)
$\delta G((1, 4) \rightarrow (1, 3))$	-3.1	-0.74
$\delta G((1, 4) \rightarrow (1, 2))$	-0.52	-3.5

water molecule to one hydroxyl group interferes with the capacity of the second hydroxyl group to form an *HB*. This causes a disruption of the structure of water near the two hydroxyl groups, and hence a large negative value of δV .

In Table J.3, we report some values of δG for the transfer of a hydroxyl group as in Fig. J.1 and also the corresponding values for transferring an amine group in diaminobenzene. These calculations were made by Thomas Allison using the program Gaussian 03, Revision D.01.⁶ As can be seen, the values calculated for the dihydroxybenzene in Table J.3 are similar to the results in (J.1) and (J.2).

Appendix K: Experimental Evidence for the Entropy-Enthalpy Compensation

In Sec. 3.5, we discussed an exact result which may be referred to as the exact entropy-enthalpy compensation (*EEC*). Lumry and Rajender (1970) compiled an impressive body of experimental examples which they referred to as *EEC*. They found that for many processes carried out in aqueous solutions the standard enthalpy of the process is a linear function of the standard entropy of the process. The slope T_C was referred to as the compensation temperature. Two sets of experimental data showed the *EEC*. One was obtained by varying the chemical

⁶Frisch *et al.* (2004). The solvation free energies and optimized geometries were obtained at the $HF/6-311++g^{**}$ level of theory within the IEFPCM continuum solvation model.

compounds involved in the process, the second involving variation in the solvent composition. Lumry and Rajender concluded:

“It is tentatively concluded that the pattern is real, very common and a consequence of the properties of liquid water as a solvent regardless of the solutes and the solute processes studied.”

“It is proposed that the linear enthalpy-entropy relationship be used as a diagnostic test for participation of water in protein processes.”

I fully agree with the first statement quoted above but the latter needs a slight modification for the following reasons. As I discussed earlier (Ben-Naim, 1992), for any process carried out in any solvent, one may write the standard entropy and enthalpy of the processes as

$$\Delta S^\circ = \Delta S^f + \Delta S^r \quad (\text{K.1})$$

$$\Delta H^\circ = \Delta H^f + \Delta H^r \quad (\text{K.2})$$

Furthermore, there exists the *exact EEC*:

$$\Delta H^r = T \Delta S^r \quad (\text{K.3})$$

which is valid in any solvent. From these equations we can write the following exact relationship between ΔS_i° and ΔH_i° for any specific process depending on the parameter i :

$$\Delta H_i^\circ - \Delta H_i^f = T[\Delta S_i^\circ - \Delta S_i^f] \quad (\text{K.4})$$

Clearly, whenever the relaxation terms ΔS^r and ΔH^r dominate the values of ΔS° and ΔH° in (K.1) and (K.2), one can neglect the variation of ΔH_i^f and ΔS_i^f with the parameter i . If this condition is met, then one may obtain an approximate *EEC* equation from (K.4), namely

$$\Delta H_i^\circ \approx \Delta G^\circ + T \Delta S_i^\circ \quad (\text{K.5})$$

In other words, if ΔG° is relatively small, then the exact *EEC* in (K.3) will produce an approximate *EEC* in (K.5). In this regard, the modification in Lumry and Rajender's conclusion reads: "... the *EEC* relationship can be used as a diagnostic test for processes involving *relatively large structural changes* in the solvent." For reasons provided in Chapter 3, large structural changes in the solvent are expected to occur in aqueous solutions. But there is no guarantee that every process carried out in aqueous solutions will produce large structural changes in the solvent.

Appendix L: Solutions to Selected Exercises

Solution to E.3.9

Note that the temperature dependence of ΔG_s^* depends on the "degree of structure" of water, but it is not necessarily a monotonic dependence. We have seen that ΔS_s^* depends on the structural *changes* induced by the solute, and the extent of the structural changes depends, in an ideal mixture model for water, on product $x_i x_p$. This means that in some regions, an increase in x_i can either increase or decrease the product $x_i(1 - x_i)$. In a non-ideal mixture-model approach, the dependence of the structural changes induced by the solute is not so simple as $x_i(1 - x_i)$, but the general conclusion that ΔS_s^* is non-linear or even monotonic in x_i is still valid.

Solution to Exercise E.3.10

This is a very simple binding system. With the assumptions listed in Exercise E.3.10 (Sec. 3.7), we can write down the canonical *PF* immediately:

$$Q(T, M, N_s) = \frac{M! q_s \exp[-\beta N_s U_s]}{N_s! (M - N_s)!} \quad (\text{L.1})$$

Note that besides the internal degrees of freedom of s included in q_s , there is only one energy level $N_s U_s$ with

degeneracy $\binom{M}{N_s}$, i.e. there are $\binom{M}{N_s}$ distinguishable configurations with the same total binding energy $N_s U_s$.

From the PF , one gets the Helmholtz energy

$$A = -k_B T \ln Q \quad (\text{L.2})$$

and from A the chemical potential of s in the system

$$\mu_s = \left(\frac{\partial A}{\partial N_s} \right)_{T,M} = -k_B T \ln q_s + U_s + k_B T \ln \left[\frac{\theta}{1 - \theta} \right] \quad (\text{L.3})$$

where $\theta = N_s/M$. For a very “dilute” system, i.e. $\theta \ll 1$, we get

$$\mu_s = -k_B T \ln q_s + U_s + k_B T \ln \theta \quad (\text{L.4})$$

The analog of the pseudo-chemical potential in this system is

$$\mu_s^* = -k_B T \ln q_s + U_s \quad (\text{L.5})$$

It is instructive to calculate the canonical partition function as above, but where a solute s is first placed at a specific site in the system. The pseudo-chemical potential is given by

$$\exp[-\beta \mu_s^*] = \frac{Q(T, M, N_s = 1; \text{ at specific site})}{Q(T, M)} \quad (\text{L.6})$$

The pseudo-chemical potential of s in an ideal gas phase is simply

$$\mu_s^{*ig} = -k_B T \ln q_s \quad (\text{L.7})$$

The Helmholtz energy of solvation is thus

$$\Delta A_s^* = \mu_s^* - \mu_s^{*ig} = U_s$$

The entropy and energy of solvation are

$$\begin{aligned} \Delta S_s^* &= \frac{-\partial \Delta A_s^*}{\partial T} = 0 \\ \Delta E_s^* &= \Delta A_s^* + T \Delta S_s^* = U_s \end{aligned} \quad (\text{L.8})$$

In this simple example, the solvation Helmholtz energy is equal to the solvation energy and to the energy of the interaction of s with the site. The entropy of solvation is zero.

Solution to Exercise E.3.11

The canonical partition function for a system of N_s solute molecules on $M_L + M_H$ sites is

$$\mathcal{Q}(T, M_L, M_H, N_s) = \sum_{N_L + N_H = N_s} \binom{M_L}{N_L} \binom{M_H}{N_H} q_L^{N_L} q_H^{N_H} q_s^{N_s} \quad (\text{L.9})$$

where N_L and $N_H = N_s - N_L$ are the number of solutes adsorbed on L and H sites, respectively. The sum is over all possible values of N_L such that $N_L + N_H = N_s$. In (L.9), we denoted by $q_s = \exp[-\beta U_s]$, $q_L = \exp[-\beta U_{sL}]$, and $q_H = \exp[-\beta U_{sH}]$.

It is easier and more elegant to transform from the canonical to the grand PF . The result is⁷

$$\Xi(T, M_L, M_H, \lambda_s) = \xi_L^{M_L} \xi_H^{M_H} \quad (\text{L.10})$$

where the absolute activity of s is related to the chemical potential of s by $\mu_s = k_B T \ln \lambda_s$, and where we define

$$\xi_L = 1 + q_s q_L \lambda_s \quad (\text{L.11})$$

$$\xi_H = 1 + q_s q_H \lambda_s \quad (\text{L.12})$$

The factorization of Ξ into a product of the grand PF of each site is a result of the independence between sites. The two terms on the right-hand side of (L.11) and (L.12) correspond to the two states of each type of site: empty and occupied.

⁷The reader is urged to do this example as a prelude to Exercise E.3.12. For more details, see Ben-Naim (1992, 2001).

The average number of s molecules in the entire system is

$$N_s = \lambda_s \frac{\partial \ln \Xi}{\partial \lambda_s} = M_L \frac{q_s q_L \lambda_s}{1 + q_s q_L \lambda_s} + M_H \frac{q_s q_H \lambda_s}{1 + q_s q_H \lambda_s} \quad (\text{L.13})$$

From this equation, we can solve for λ_s as a function of the mole fraction $x_s = N_s/M$, where $M = M_L + M_H$, taking the limit $N_s/M \rightarrow 0$. There are two solutions to this equation. We choose the physically accepted solution, the result of which is

$$\lambda_s = \frac{x_s}{x_L q_s q_L + x_H q_s q_H} \quad (\text{L.14})$$

where $x_L = M_L/M$ and $x_H = M_H/M$.

The chemical potential of the solute is

$$\mu_s = k_B T \ln x_s - k_B T \ln (x_L q_L + x_H q_H) - k_B T \ln q_s \quad (\text{L.15})$$

and the pseudo-chemical potential is

$$\mu_s^* = -k_B T \ln (x_L q_L + x_H q_H) - k_B T \ln q_s \quad (\text{L.16})$$

The solvation quantities in this system are

$$\begin{aligned} \Delta A_s^* &= \mu_s^* - \mu_s^{*ig} = -k_B T \ln (x_L q_L + x_H q_H) \\ &= -k_B T \ln \langle \exp[-\beta B_s] \rangle_0 \end{aligned} \quad (\text{L.17})$$

$$\Delta S_s^* = k_B \ln \langle \exp[-\beta B_s] \rangle_0 + \frac{1}{T} \langle B_s \rangle_s \quad (\text{L.18})$$

$$\Delta E_s^* = \langle B_s \rangle_s \quad (\text{L.19})$$

Note that $\langle \cdot \rangle_0$ is an average with the distribution of (x_L, x_H) . On the other hand, $\langle B_s \rangle_s$ is an average with the mole fractions

$$y_L = \frac{x_L q_L}{x_L q_L + x_H q_H}, \quad y_H = \frac{x_L q_H}{x_L q_L + x_H q_H} \quad (\text{L.20})$$

It is important to distinguish between the two averages in (L.17) and (L.18). The first depends only on the mole fractions

of the two types of sites. These probabilities do not depend on the binding energies of s to L or to H . On the other hand, the distribution (y_L, y_H) depends both on the mole fractions of the sites and on the relative binding energies. Another way of interpreting the two distributions is as follows. Before s is adsorbed on the site, x_L is the probability of finding a site of type L . On the other hand, y_L is the conditional probability that the site is L given that it is occupied by s .

It is clear that ΔA_s^* and ΔE_s^* are determined by different kinds of averages. The solvation Helmholtz energy depends on the quantities $\exp[-\beta U_{sL}]$ and $\exp[-\beta U_{sH}]$, and the average of these two is determined only by the mole fractions of the two sites before the adsorption of s took place. On the other hand, ΔE_s^* depends on the strength of the binding energies U_{sL} and U_{sH} , and the average is taken with a distribution that depends on both the mole fractions of the two sites as well as the relative binding energies on the two kinds of sites.

Solution to Exercise E.3.12

We solve this problem in three steps. First, we discuss the equilibrium condition for the empty system of L and H . Then we examine the system with a ligand (or a solute) s . And finally we calculate the solvation quantities.

(i) *The empty system*: The canonical PF of the system of M empty sites at temperature T is

$$\begin{aligned} Q(T, M) &= (Q_L + Q_H)^M = \sum_{M_L=0}^M \frac{M!}{M_L! M_H!} Q_L^{M_L} Q_H^{M_H} \\ &= \sum_{M_L} Q^*(T, M_L, M_H) \end{aligned} \quad (\text{L.21})$$

where Q_L and Q_H are defined by

$$Q_L = \exp[-\beta E_L], \quad Q_H = \exp[-\beta E_H]$$

and E_L and E_H are the “energy levels” of L and H , respectively.

The equilibrium (or average) values of M_L and M_H are obtained from

$$\frac{\partial \ln Q^*}{\partial M_L} = 0 \quad (\text{L.22})$$

which leads to the equilibrium condition

$$\frac{\bar{M}_H}{\bar{M}_L} = \frac{Q_H}{Q_L} \quad (\text{L.23})$$

We define the equilibrium constant

$$K = \frac{Q_H}{Q_L} = \exp[-\beta(E_H - E_L)] \quad (\text{L.24})$$

The mole fractions of empty sites in the two states are

$$x_L^0 = \frac{\bar{M}_L}{M} = \frac{Q_L}{Q_L + Q_H} = \frac{1}{1 + K} \quad (\text{L.25})$$

$$x_H^0 = \frac{\bar{M}_H}{M} = \frac{Q_H}{Q_L + Q_H} = \frac{K}{1 + K} \quad (\text{L.26})$$

These are also the probabilities of finding a specific site in the L or H state for the empty system.

(ii) *The system with solute s:* We now turn to the case where we also have N_s adsorbed molecules distributed over the sites. The canonical partition function for such a system is

$$\begin{aligned} Q(T, M, N_s) \\ = \sum_{\substack{M_L + M_H = M \\ N_L + N_H = N_s}} \binom{M}{M_L} \binom{M_L}{N_L} \binom{M_H}{N_H} Q_L^{M_L} Q_H^{M_H} q_L^{N_L} q_H^{N_H} \end{aligned} \quad (\text{L.27})$$

where q_L and q_H have the same meaning as in Exercise E.3.11. In (L.27), N_L and N_H are the number of molecules adsorbed on

L and H sites, respectively. The summation in (L.27) extends over all possible values of M_L, M_H, N_L, N_H with the conditions

$$\begin{aligned} M_L + M_H &= M, & N_L + N_H &= N_s, \\ N_L &\leq M_L, & N_H &\leq M_H \end{aligned} \quad (\text{L.28})$$

Note that for simplicity, we assume that the internal PF of s is unity, i.e. $q_s = 1$.

Clearly, the auxiliary parameters N_L, N_H, M_L, M_H serve as intermediate quantities which determine the energy levels of the system, namely

$$\begin{aligned} E(N_L, N_H, M_L, M_H) \\ = M_L E_L + M_H E_H + N_L U_{sL} + N_H U_{sH} \end{aligned} \quad (\text{L.29})$$

The degeneracy of these energy levels is given by the product of three combinatorial factors in (L.27).

The summation in (L.27) cannot be carried out to obtain a closed form of the partition function. This is easily achieved, however, by transforming to an open system with respect to the solute molecules, i.e. we define the grand partition function by

$$\begin{aligned} \Xi(T, M, \lambda_s) &= \sum_{N_s=0}^M \lambda_s^{N_s} Q(T, M, N_s) \\ &= \sum_{M_L=0}^M \sum_{N_L=0}^{M_L} \sum_{N_H=0}^{M_H} \lambda_s^{N_L} \lambda_s^{N_H} \binom{M}{M_L} \binom{M_L}{N_L} \\ &\quad \times \binom{M_H}{N_H} Q_L^{M_L} Q_H^{M_H} q_L^{N_L} q_H^{N_H} \\ &= \sum_{M_L=0}^M \binom{M}{M_L} Q_L^{M_L} (1 + \lambda_s q_L)^{M_L} \\ &\quad \times Q_H^{(M-M_L)} (1 + \lambda_s q_H)^{(M-M_L)} \end{aligned}$$

$$\begin{aligned}
 &= (Q_L + Q_H + \lambda_s q_L Q_L + \lambda_s q_H Q_H)^M \\
 &= \xi^M
 \end{aligned} \tag{L.30}$$

where $\lambda_s = \exp(\beta\mu_s)$ is the absolute activity of the solute and μ_s is its chemical potential.

The last form of the *PF* is typical of a system of independent sites: ξ defined in (L.30) may be viewed as the grand *PF* of a single site.⁸ The four terms in ξ correspond to the four possible states of each site, i.e. empty *L*, empty *H*, occupied *L*, and occupied *H*.

The terms in (L.30) correspond to the probabilities of finding a specific site in each of its four states, namely

$$\begin{aligned}
 \Pr(L, 0) &= Q_L/\xi, & \Pr(H, 0) &= Q_H/\xi \\
 \Pr(L, s) &= \lambda q_L Q_L/\xi, & \Pr(H, s) &= \lambda q_H Q_H/\xi
 \end{aligned} \tag{L.31}$$

The probabilities of finding a site empty $\Pr(0)$ or occupied $\Pr(s)$, independently of its state, are

$$\Pr(0) = \Pr(L, 0) + \Pr(H, 0) = \frac{Q_L + Q_H}{\xi} \tag{L.32}$$

$$\Pr(s) = \Pr(L, s) + \Pr(H, s) = \frac{\lambda_s q_L Q_L + \lambda_s q_H Q_H}{\xi} \tag{L.33}$$

The conditional probability $\Pr(L/s)$ of finding a site in state *L* when it is known to be occupied is

$$\begin{aligned}
 \Pr(L/s) &= \frac{\Pr(L, s)}{\Pr(s)} \\
 &= \frac{\lambda_s q_L Q_L/\xi}{(\lambda_s q_L Q_L + \lambda_s q_H Q_H)/\xi} \\
 &= \frac{q_L Q_L}{q_L Q_L + q_H Q_H}
 \end{aligned} \tag{L.34}$$

⁸For more details, see Ben-Naim (2001).

Similarly, the conditional probability of finding a site in state H given that it is occupied is

$$\Pr(H/s) = \frac{q_H Q_H}{q_L Q_L + q_H Q_H} \quad (\text{L.35})$$

The average number of solute molecules in the system is given by

$$\bar{N}_s = \lambda_s \frac{\partial \ln \Xi}{\partial \lambda_s} = \frac{\lambda_s M}{\xi} (q_L Q_L + q_H Q_H) \quad (\text{L.36})$$

Let θ be the average fraction of sites occupied. This is also equal to the probability of finding a specific site being occupied. From (L.31) and (L.36), we obtain

$$x = \Pr(L, s) + \Pr(H, s) = \Pr(s) \quad (\text{L.37})$$

Elimination of λ_s from (L.36), we get the absolute activity of s :

$$\lambda_s = \left(\frac{\theta}{1 - \theta} \right) \frac{Q_L + Q_H}{q_L Q_L + q_H Q_H} \quad (\text{L.38})$$

where $\theta = \bar{N}_s/M$.

The chemical potential of the solute s is thus

$$\mu_s = k_B T \ln \left(\frac{\theta}{1 - \theta} \right) - k_B T \ln \left(\frac{q_L Q_L + q_H Q_H}{Q_L + Q_H} \right) \quad (\text{L.39})$$

Using the distribution of two states in the empty system given in (L.25) and (L.26), we may rewrite (L.39) as

$$\begin{aligned} \mu_s &= k_B T \ln \left(\frac{\theta}{1 - \theta} \right) - k_B T \ln (q_L x_L^0 + q_H x_H^0) \\ &= k_B T \ln \left(\frac{\theta}{1 - \theta} \right) - k_B T \ln \langle \exp(-\beta B_s) \rangle_0 \end{aligned} \quad (\text{L.40})$$

where we have introduced the quantity B_s , which will be referred to as the *binding energy* of s to the site. More specifically, B_s is a function of the state $\alpha = L, H$ and is defined as

$$B_s(\alpha) = \begin{cases} U_{sL} & \text{if } \alpha = L \\ U_{sH} & \text{if } \alpha = H \end{cases} \quad (\text{L.41})$$

In (L.40), we denoted by $\langle \cdot \rangle_0$ an average of the function $\exp[-\beta B_s(\alpha)]$. The average is taken over all states of the sites, here L and H , with the probability distribution x_L^0 and x_H^0 as given in (L.25) and (L.26), i.e. of the empty system.

The partial molar (or molecular) entropy of the solute s is obtained from (L.40) by differentiation with respect to the temperature:

$$\begin{aligned} \bar{S}_s &= - \left(\frac{\partial \mu_s}{\partial T} \right)_{M, N_s} \\ &= -k_B T \ln \left(\frac{\theta}{1 - \theta} \right) + k_B T \ln \langle \exp(-\beta B_s) \rangle_0 \\ &\quad + \frac{1}{T} \left[\frac{q_L Q_L (E_L + U_{sL}) + q_H Q_H (E_H + U_{sH})}{q_L Q_L + q_H Q_H} \right. \\ &\quad \left. - \frac{Q_L E_L + Q_H E_H}{Q_L + Q_H} \right] \end{aligned} \quad (\text{L.42})$$

Using the conditional probabilities of (L.34) and (L.36), relation (L.42) may be written as

$$\begin{aligned} \bar{S}_s &= -k_B \ln \left(\frac{\theta}{1 - \theta} \right) + k_B \ln \langle \exp(-\beta B_s) \rangle_0 \\ &\quad + \frac{1}{T} [\langle E + B_s \rangle_s - \langle E \rangle_0] \end{aligned} \quad (\text{L.43})$$

where E is the energy of the site defined as

$$E(\alpha) = \begin{cases} E_L & \text{for } \alpha = L \\ E_H & \text{for } \alpha = H \end{cases} \quad (\text{L.44})$$

The symbol $\langle \cdot \rangle_s$ signifies a conditional average taken with the conditional distribution given in (L.34) and (L.35).

The partial molar (or molecular) energy of the solute s is given by

$$\begin{aligned}\bar{E}_s &= \mu_s + T\bar{S}_s = \langle E + B_s \rangle_s - \langle E \rangle_0 \\ &= \langle B_s \rangle_s + (\langle E \rangle_s - \langle E \rangle_0)\end{aligned}\quad (\text{L.45})$$

(iii) *The solvation thermodynamic quantities:* As in Exercise E.3.11, we define the adsorption process as the process of transferring s from a fixed position in vacuum into a *fixed empty* site. The corresponding thermodynamic quantities are

$$\Delta A_s^* = -k_B T \ln \langle \exp(-\beta B_s) \rangle_0 \quad (\text{L.46})$$

$$\begin{aligned}\Delta S_s^* &= k_B \ln \langle \exp(-\beta B_s) \rangle_0 + \frac{1}{T} (\langle B_s \rangle_s \\ &\quad + \langle E \rangle_s - \langle E \rangle_0)\end{aligned}\quad (\text{L.47})$$

$$\Delta E_s^* = \langle B_s \rangle_s + \langle E \rangle_s - \langle E \rangle_0 \quad (\text{L.48})$$

Compare these equations to the analogous ones in Exercise E.3.11. Here, in contrast to the previous case, we have a relaxation term, i.e. the change in the distribution of states L and H upon the addition of s .

The Helmholtz energy is the same as in Exercise E.3.11 except that the average is taken with respect to the distribution of the *empty* sites (x_L^0, x_H^0) . Similarly, the entropy and the enthalpy of solvation have the terms $k_B \ln \langle \exp[-\beta B_s] \rangle_0$ and $\langle B_s \rangle_s$ bearing the same significance as in Exercise E.3.11. The new terms in (L.47) and (L.48) represent the shift in the *average energy of the sites* caused by the adsorption of a solute s . These terms can also be cast as relaxation terms. For details, the reader is referred to Ben-Naim (1992).

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