

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.

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).

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*Bonded 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).

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).

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,”

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.