Matching–Mismatching of Water Geometry and Hydrophobic Hydration

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Abstract: Based on a simple geometrical picture, the effect of a water molecule on the hydrogen bond in its adjacent pair of water molecules is related to the tetrahedral nature of water. The structural aspect of hydrophobic hydration is then treated in terms of the change in the geometry of the local environment of the solvent water due to insertion of a hydrophobic solute. It is shown that the local environment around the hydrophobic solute is favorable for the formation of hydrogen bonds between the neighboring water molecules. The density effect of liquid water is also treated in terms of the geometrical features of the local environment.

1. Introduction

Hydrophobic hydration, the solvation of an inert solute in water, is an outstanding property of aqueous solutions.[1–3] The "anomalous" nature of this hydration process is thermodynamically characterized by a negative entropy of solution, a negative enthalpy of solution, and a positive heat capacity of solution. The large negative entropy, which dominates over the negative enthalpy, is responsible for the low solubility of a hydrophobic solute in water. The negative enthalpy, which is larger in magnitude than the value extrapolated from the data for alcohol solutions, gives rise to a considerable decrease in the Ostwald coefficient with increasing temperature. The large positive heat capacity shows that the enthalpy and entropy of solution are sensitive to temperature when the solvent is water. Considerations of these thermodynamics of the solution process have led Frank and Evans to propose the "iceberg formation" model,[4] which states that the structure of the solvent water is strengthened around a hydrophobic solute. Focusing more on the solvent than on the solute, this model has bridged the thermodynamic observations (enthalpy, entropy, and heat capacity) and the molecular-level observations (structure of the solvent water).

The structural characteristic of hydrophobic hydration proposed by Frank and Evans has been examined and confirmed both experimentally and theoretically. Experimental evidence of the structure strengthening comes from a wide variety of sources: NMR relaxation,[5] dielectric relaxation,[6] etc. On the theoretical side, analyses are performed in terms of configuration (spatial and orientational distribution functions), energetics, hydrogen bonds, and dynamics (mobility) of the solvent. The spatial and orientational distribution functions are obtained from scaled-particle theory,[7,8] integral equation theory,[9–11] and computer simulations.[12–33] These studies have clarified the picture of how water molecules hydrate a hydrophobic solute and have provided such notions as the clathrate-like cage structure and the "straddling" orientation of the hydrating water. Computer simulations have made use of potential functions to study energetics. Explicit calculations of pair energies and binding energies have shown that the water molecules around a hydrophobic solute are more tightly bound to other water molecules than those in the bulk.[12–18,20–22,30,33] The study of hydrogen bonds, which is particularly useful in the analysis of water and aqueous solutions, combines the studies of configuration and energetics in the sense that the characteristics of both can be extracted. It has been revealed by the computer simulations, in accordance with the observations for configuration and energetics, that the hydrogen bonds in the solvent water are strengthened around a hydrophobic solute.[12,14,16–19,22,25,26,28,30,31,33] Moreover, the mobility of the solvent water has been shown to be slower around a hydrophobic solute, as evidenced in translational diffusion and rotational reorientation.[14,17,26,27,34]

This paper is concerned with the hydrogen bonds in the solvent water. In order to understand the whole nature of hydrophobic hydration, it is important to clarify the mechanism of the hydrogen bond strengthening around a hydrophobic solute. To achieve this goal, it is essential to understand how the hydrogen bonds among water molecules are affected by local perturbations in their neighborhood. Our focus in this paper is on the relationship between the hydrogen bond in a pair of water molecules and the neighboring environment. On the basis of this relationship, it is

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(1) Franks, F., Ed. *Water, A Comprehensive Treatise*; Plenum: New York, 1972–1982; Vols. 1–7.
(2) Ben-Naim, A. *Hydrophobic Interactions*; Plenum: New York, 1980.
(3) Pratt, L. R. *Annu. Rev. Phys. Chem.* **1985**, *36*, 433.
(4) Frank, H. S.; Evans, M. W. *J. Chem. Phys.* **1945**, *13*, 507.
(5) Goldammer, E. V.; Hertz, H. G. *J. Phys. Chem.* **1970**, *74*, 3734.
(6) Pottel, R.; Kaatze, V. *Ber. Bunsenges. Phys. Chem.* **1969**, *73*, 437.
(7) Pierotti, R. A. *J. Phys. Chem.* **1965**, *69*, 281.
(8) Stillinger, F. H. *J. Solution Chem.* **1973**, *2*, 141.
(9) Pratt, L. R.; Chandler, D. *J. Chem. Phys.* **1977**, *67*, 3683.
(10) Tani, A. *Mol. Phys.* **1983**, *48*, 1229.
(11) Yu, H.; Karplus, M. *J. Chem. Phys.* **1988**, *89*, 2366.
(12) Owicki, J. C.; Scheraga, H. A. *J. Am. Chem. Soc.* **1977**, *99*, 7413.
(13) Swaminathan, S.; Harrison, S. W.; Beveridge, D. L. *J. Am. Chem. Soc.* **1978**, *100*, 5705.
(14) Geiger, A.; Rahman, A.; Stillinger, F. H. *J. Chem. Phys.* **1979**, *70*, 263.
(15) Okazaki, S.; Nakanishi, K.; Touhara, H.; Adachi, Y. *J. Chem. Phys.* **1979**, *71*, 2421.
(16) Pangali, C.; Rao, M.; Berne, B. J. *J. Chem. Phys.* **1979**, *71*, 2982.
(17) Rossky, P. J.; Karplus, M. *J. Am. Chem. Soc.* **1979**, *101*, 1913.
(18) Alagona, G.; Tani, A. *J. Chem. Phys.* **1980**, *72*, 580.
(19) Mezei, M.; Beveridge, D. L. *J. Chem. Phys.* **1981**, *74*, 622.
(20) Bolis, G.; Clementi, E. *Chem. Phys. Lett.* **1981**, *82*, 147.
(21) Nakanishi, K.; Okazaki, S.; Ikari, K.; Touhara, H. *Chem. Phys. Lett.* **1981**, *84*, 428.
(22) Okazaki, S.; Nakanishi, K.; Touhara, H.; Watanabe, N.; Adachi, Y. *J. Chem. Phys.* **1981**, *74*, 5863.
(23) Bolis, G.; Corongiu, G.; Clementi, E. *Chem. Phys. Lett.* **1982**, *86*, 299.
(24) Alagona, G.; Tani, A. *Chem. Phys. Lett.* **1982**, *87*, 337.
(25) Jorgensen, W. L. *J. Chem. Phys.* **1982**, *77*, 5757.
(26) Rapaport, D. C.; Scheraga, H. A. *J. Phys. Chem.* **1982**, *86*, 873.
(27) Postma, J. P. M.; Berendsen, H. J. C.; Haak, J. R. *Faraday Symp. Chem. Soc.* **1982**, *17*, 55.
(28) Jorgensen, W. L.; Madura, J. D. *J. Am. Chem. Soc.* **1983**, *105*, 1407.
(29) Swope, W. C.; Andersen, H. C. *J. Phys. Chem.* **1984**, *88*, 6548.
(30) Zichi, D. A.; Rossky, P. J. *J. Chem. Phys.* **1985**, *83*, 797.
(31) Tanaka, H. *J. Chem. Phys.* **1987**, *86*, 1512.
(32) Guillot, B.; Guissani, Y.; Bratos, S. *J. Chem. Phys.* **1991**, *95*, 3643.
(33) Tanaka, H.; Nakanishi, K. *J. Chem. Phys.* **1991**, *95*, 3719.
(34) Zichi, D. A.; Rossky, P. J. *J. Chem. Phys.* **1986**, *84*, 2814.

shown that insertion of a hydrophobic solute induces a local environment which is favorable for the formation of hydrogen bonds between the neighboring water molecules.

The configuration of a pair of water molecules is largely influenced by the configuration of the water molecules surrounding it. Then it is necessary to characterize how a water molecule adjacent to the pair promotes or inhibits the hydrogen bond in the pair (the definitions of the "pair" and the "hydrogen bond" are given in section 2). For this purpose, we investigate the effect of a water molecule on the hydrogen bond in its adjacent pair by focusing on trimers in section 3. Considering the trimer geometry and the tetrahedral nature of water, we classify a water molecule as either promoting or inhibiting the hydrogen bond in its adjacent pair. In section 4, we investigate the change in the local environment around a pair of water molecules due to insertion of a hydrophobic solute. On the basis of the geometrical characterization in section 3, the change in the local environment is related to the change in the strength of the hydrogen bond in the pair.

Our approach also sheds light upon the effect of the local density fluctuations on the hydrogen bond in a pair of water molecules in the bulk. The effect of the local density fluctuations is analogous to the "anomalous" density effect of liquid water, in which the structure of water is weaker when the density increases around 1 g/cm^3. In a recent work, Sciortino *et al.* treated this effect in terms of configuration, energetics, and dynamics.[35,36] They showed that the water structure is weakened with the increase of density, and related it to the increase of the "defects" in the tetrahedral network. In section 5, we treat the density effect in terms of hydrogen bonds in the same manner as in section 4 for hydrophobic hydration. On the basis of the geometrical characterization in section 3, the local density fluctuations are related to the hydrogen bond in a pair of water molecules in the bulk.

2. Simulation Procedures and Models of the Hydrogen Bond

The water models used in this study were the ST2[37] and TIP4P[38] models truncated with the spherical cutoffs of 8.46 and 8.5 Å, respectively. Monte Carlo statistical mechanical simultions were carried out using the Metropolis sampling technique.[39] Periodic boundary conditions in the minimum image convention were employed. All the calculations were done at a temperature of 10 °C in the canonical ensemble. For pure liquid water, 216 water molecules were located in a cubic cell at a density of 1 g/cm^3. For the aqueous solution where a hydrophobic solute was dissolved, one hydrophobic solute molecule and 215 water molecules were located in a cubic cell of the same size as used for the pure water simulations. The position of the solute remained fixed at the center of the box. In this case, to enhance the statistics for the solute and its neighboring water molecules, the preferential sampling[39,40] was used. 100*K* passes for the pure water systems and 200*K* passes for the solution systems were sufficient to obtain convergent results (one pass consists of 216 attempted moves).

Xenon was used as the hydrophobic solute in the simulations. The interaction between water and the hydrophobic solute was taken to be a Lennard-Jones 12–6 interaction, and the Lennard-Jones energy and length parameters (ϵ and σ, respectively) were determined from the Lorentz–Berthelot rule, which gives

$$\epsilon_{\text{A-B}} = (\epsilon_{\text{A-A}}\epsilon_{\text{B-B}})^{1/2} \tag{2.1}$$

$$\sigma_{\text{A-B}} = (\sigma_{\text{A-A}} + \sigma_{\text{B-B}})/2 \tag{2.2}$$

In eqs 2.1 and 2.2, $\epsilon_{\text{water-water}}$ and $\sigma_{\text{water-water}}$ were taken to be $\epsilon_{\text{neon-neon}}$ and $\sigma_{\text{neon-neon}}$, respectively. The Lennard-Jones energy and length parameters of water and xenon are given in Table 1. Only the Weeks–Chandler–Andersen-type repulsive part of the Lennard-Jones potential function[42] was taken as the interaction between water and the hydrophobic solute, in order to exclude the effects of the solute–solvent attractions and to concentrate on the strengthening of the structure of the solvent water around the solute which is purely repulsive to water.[26]

Table 1. Lennard-Jones Potential Parameters for Water and the Solute

species	energy parameter (ϵ) (K)	length parameter (σ) (Å)
water–water[a]	35.60	2.749
xenon–xenon[a]	221.0	4.100
water–xenon	88.70	3.425

[a] The values are taken from ref 41.

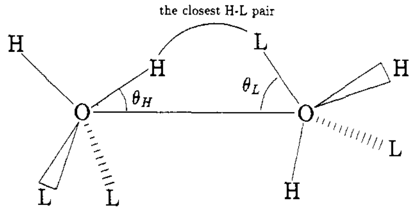

Figure 1. Definitions of the variables in a "pair". O, H, and L stand for the oxygen, hydrogen, and lone pair sites, respectively. Among eight H–L pairs, we focus on the closest H–L pair, and we define θ_{H} and θ_{L} to be respectively the H–O–O and L–O–O angles for this H–L pair.

As the main concern here is the hydrogen bond between a pair of water molecules, it is necessary to define the "pair" and the "hydrogen bond". Each water molecule has one oxygen site (O), two hydrogen sites (H), and two lone pair sites (L).[43] Two water molecules are defined to be "paired" when their O–O distance is less than the distance which corresponds to the first minimum of the oxygen–oxygen radial distribution function in the bulk. In other words, they form a "pair" when they are in the first shells of each other. Consider a pair of water molecules (see Figure 1). We take a hydrogen (H) in one water molecule and a lone pair (L) in the other water molecule. Clearly there are eight possibilities, but we focus on the closest H–L pair, and we define θ_{H} and θ_{L} to be respectively the H–O–O and L–O–O angles for this H–L pair (see Figure 1). A pair of water molecules is defined to be "hydrogen-bonded" when both of θ_{H} and θ_{L} are below a certain value. In our analyses, we examine four values, 15°, 20°, 30°, and 45°, as definitions for the hydrogen bond threshold. With these definitions, the average numbers of hydrogen bonds per water molecule in the bulk are 0.7, 1.5, 2.7, and 3.7, respectively, for the ST2 model and 0.4, 0.9, 2.0, and 3.2, respectively, for the TIP4P model. These average numbers are given with the hydrogen bond thresholds based on the pair energies of 5.3, 4.5, 3.4, and 2.0 kcal/mol, respectively, for the ST2 model and 5.4, 5.0, 4.1, and 2.8 kcal/mol, respectively, for the TIP4P model.

The qualitative features below, such as how the values in the figures and tables change and where the extrema are, do not depend on the choice of the model (ST2 or TIP4P). Therefore, the statements below are valid for both models, and we show only the results for the ST2 model.

3. Hydrogen Bond in a Pair in a Trimer

A water molecule can either promote or inhibit the hydrogen bond in its neighboring pair of water molecules depending on its geometry (orientation and distance) with respect to this pair. Then the change in the hydrogen bond strength in a pair can be related to the change in the geometry of the neighboring water molecules with respect to the pair. To evaluate how a single water molecule promotes or inhibits the hydrogen bond in its

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(35) Sciortino, F.; Geiger, A.; Stanley, H. E. *Phys. Rev. Lett.* **1990**, *65*, 3452.

(36) Sciortino, F.; Geiger, A.; Stanley, H. E. *J. Chem. Phys.* **1992**, *96*, 3857.

(37) Stillinger, F. H.; Rahman, A. *J. Chem. Phys.* **1974**, *60*, 1545.

(38) Jorgensen, W. L.; Chandrasekhar, J.; Madura, J. D.; Impey, R. W.; Klein, M. L. *J. Chem. Phys.* **1983**, *79*, 926.

(39) Allen, M. P.; Tildesley, D. J. *Computer Simulation of Liquids*; Oxford University Press: Oxford, 1987.

(40) Owicki, J. C.; Scheraga, H. A. *Chem. Phys. Lett.* **1977**, *47*, 600.

(41) Hirschfelder, J. O.; Curtiss, C. F.; Bird, R. B. *Molecular Theory of Gases and Liquids*; Wiley: New York, 1954.

(42) Weeks, J. D.; Chandler, D.; Andersen, H. C. *J. Chem. Phys.* **1971**, *54*, 5237.

(43) The locations of lone pairs are not explicit in the TIP4P model, so they are placed in such a way that the hydrogen sites are rotated 90° around the bisector of the hydrogen–oxygen–hydrogen angle, reflected through the oxygen site, and the distances from the oxygen site are shrunk to 0.7658 Å, or 0.8 times the hydrogen–oxygen distance. This procedure to place the lone pairs for the TIP4P model is similar to that for the MCY model described in ref 19.

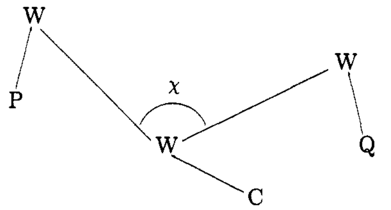

Figure 2. Configuration of a trimer, described by the O–O–O angle, χ. W stands for the O site in the water molecule. The central water molecule is labeled C, and the others are labeled P and Q.

adjacent pair of water molecules, we investigate the hydrogen bond in a pair in a trimer.

For the trimers treated in this section, the central water molecule is labeled C and the other two are labeled P and Q. To ensure that the water molecules C, P, and Q form a trimer, we require that both C–P and C–Q be paired; that is, both P and Q be in the first shell of C. The configuration of the trimer is described by the O–O–O angle, χ, as shown in Figure 2. The pair whose hydrogen bond is examined is the pair C–P, to which the water molecule Q is adjacent. Restricting our attention to the pairs which have an adjacent water molecule with the geometry described by χ, we calculate the ratio of the number of hydrogen-bonded pairs to the total number of pairs. This ratio is the probability of observing the hydrogen bond in the C–P pair in the Q–C–P trimer which has the configuration described by χ. To evaluate the effect of the adjacent water molecule Q on the hydrogen bond in the C–P pair, we also calculate the hydrogen bond probability in a bare pair. This probability is the ratio of the number of hydrogen-bonded pairs to the total number of pairs, regardless of the geometry with respect to the adjacent water molecules. This is also the hydrogen bond probability averaged over χ for a pair in a trimer.

In Figure 3, the hydrogen bond probability in the C–P pair in the Q–C–P trimer is shown as a function of $\cos(\chi)$ for the various threshold values defining the hydrogen bond. As a reference, the hydrogen bond probability in a bare pair is shown by the straight line independent of $\cos(\chi)$. The hydrogen bond probability in the C–P pair in the Q–C–P trimer has a maximum around the tetrahedral angle ($\cos(\chi) = -^1/_3$), and it gets smaller as χ departs from the tetrahedral angle. Compared with the bare pair, when the water molecule adjacent to the C–P pair, Q, has a trimer geometry of $-0.65 \lesssim \cos(\chi) \lesssim 0.05$ ($85° \lesssim \chi \lesssim 130°$), the hydrogen bond in the C–P pair is promoted, while for a trimer geometry of $0.05 \lesssim \cos(\chi)$ ($\chi \lesssim 85°$) or $\cos(\chi) \lesssim -0.65$ ($130° \lesssim \chi$), the hydrogen bond in the C–P pair is inhibited. In other words, when the trimer geometry "matches" the tetrahedral nature of the central water molecule C, the hydrogen bond in the C–P pair is promoted, and when the trimer geometry "mismatches" the tetrahedrality, the hydrogen bond in the C–P pair is inhibited. We thus call the geometries for which $-0.65 \leq \cos(\chi) \leq 0.05$ the "matching" region of the trimer geometry, and we call those for which $0.05 \leq \cos(\chi)$ or $\cos(\chi) \leq -0.65$ the "mismatching" region of the trimer geometry. We can also define the "matching" and "mismatching" regions of the C–P pair as follows. Take a space point, X, in the first shell of the water molecule C. If the X–C–P angle, θ, is such that $-0.65 \leq \cos(\theta) \leq 0.05$, then X is in the "matching" region. If θ is such that $0.05 \leq \cos(\theta)$ or $\cos(\theta) \leq -0.65$, then X is in the "mismatching" region.[44,45]

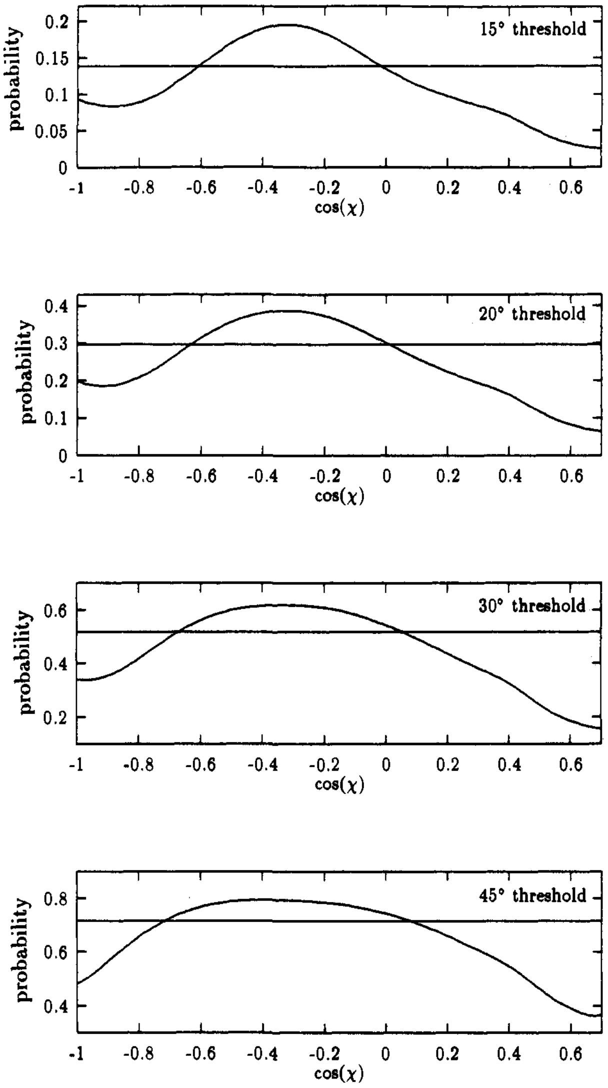

Figure 3. Probability of observing the hydrogen bond in a pair. The curves peaked around $\cos(\chi) = -^1/_3$ are for a pair in a trimer. The straight lines are for a bare pair. The vertical axis shows the probability, and the horizontal axis shows $\cos(\chi)$. The threshold angles defining the hydrogen bond in the pair are 15°, 20°, 30°, and 45° from top to bottom.

The more the trimer geometry "matches"/"mismatches" the tetrahedral nature of the water molecule, the more promoted/inhibited the hydrogen bond in the pair. On the basis of this geometrical relationship, we relate the hydrogen bond in a pair to the tetrahedrality of the distribution of the water molecules adjacent to the pair. A water molecule adjacent to the pair forms a trimer with the pair. When the geometry of the trimer that this water molecule forms with the pair "matches" the tetrahedrality more, this water molecule contributes more to making the distribution tetrahedral. When the geometry of the trimer "mismatches" the tetrahedrality more, this water molecule contributes more to making the distribution nontetrahedral. Thus, the pair is more likely to be hydrogen-bonded when the distribution of the water molecules adjacent to the pair is more tetrahedral.

To illustrate the relation between the hydrogen bond in a pair and the tetrahedrality of the distribution of the water molecules adjacent to the pair, we define a measure of the tetrahedrality of the distribution, MT, as follows. Suppose a water molecule has NN water molecules in its first shell. One of the NN water molecules is viewed as forming a pair with the central water molecule, and each of the other (NN – 1) water molecules in the first shell forms a trimer with the pair. Let χ_i be the O–O–O angle in the ith (i = 1, ..., (NN – 1)) trimer. MT is then defined

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(44) Actually, the boundaries of the "matching" and "mismatching" regions are not sharp. We define them sharply for convenience in the rest of the paper.

(45) The results in Figure 3 are consistent with the observation in refs 35 and 36 that the local minimum for a "bifurcated bond" has a higher energy than that for a "linear bond". But Figure 3 does not provide explicit information about local minima on the potential energy surface. Our focus is on a correlation between one structural property at a given temperature and another structural or geometrical property at that temperature, rather than on local minima and the dynamics among them addressed in the inherent structure theory employed in refs 35, 36, and 46.

(46) Stillinger, F. H.; Weber, T. A. *Science* **1984**, *225*, 983.

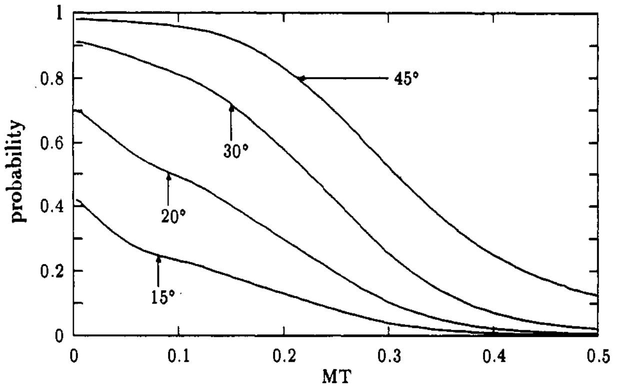

Figure 4. Probability of observing the hydrogen bond in a pair as a function of MT defined by eq 3.1 in the text. The horizontal axis shows the value of MT, and the vertical axis shows the probability. The threshold angles defining the hydrogen bond in the pair are 45°, 30°, 20°, and 15° from top to bottom.

as

$$\mathrm{MT} = \frac{1}{\mathrm{NN}-1}\sum_{i=1}^{\mathrm{NN}-1}[\cos(\chi_i) - (-{}^1/_3)]^2 \qquad (3.1)$$

For the distribution of the O–O–O angles of the (NN – 1) trimers, MT is the mean square deviation of $\cos(\chi_i)$ from the tetrahedral value ($\cos(\chi) = -{}^1/_3$) and is thus one of the measures of the deviation from the tetrahedrality of the distribution of the water molecules adjacent to the pair. When MT increases, the "tetrahedrality" decreases, and when MT decreases, the "tetrahedrality" increases.

We show in Figure 4 the probability of observing the hydrogen bond in the pair as a function of MT for the various threshold values of the hydrogen bond. The probability decreases monotonically as MT increases (the "tetrahedrality" decreases). Thus, Figure 4 shows that the hydrogen bond probability in the pair increases with the tetrahedrality of the distribution of the water molecules adjacent to the pair.

4. Effect of a Hydrophobic Solute on the Hydrogen Bond

In this section, we focus on the hydrogen bond in a pair of water molecules near a hydrophobic solute, A. The water molecules in this pair are labeled C and P. To ensure that the C–P pair is near the solute, we require that the water molecule C be in the first hydration shell of the solute A (a water molecule is in the first hydration shell when the A–O distance is less than the distance corresponding to the first minimum of the A–O radial distribution function). Depending on whether the water molecule P lies inside or outside the first hydration shell of the solute, there are two types of pairs near the solute. When P lies inside the first hydration shell, we call the C–P pair a pair inside the shell. When P lies outside the first hydration shell, we call the C–P pair a pair across the boundary. These two types of pairs are treated separately in the following analyses.

4.1. A Pair inside the First Hydration Shell. For the C–P pair, let φ be the A–O–O angle in the A–C–P triplet, as shown in Figure 5. The distribution of the solute A with respect to the C–P pair can then be expressed as a function of $\cos(\varphi)$. We show the probability distribution of $\cos(\varphi)$, $P(\varphi)$, in Figure 6. As shown in Figure 6, $P(\varphi)$ has a peak around 65°, and φ is mainly in the "mismatching" region defined in section 3. In other words, the solute is mainly found in the "mismatching" region of a pair of water molecules inside the shell. This reflects the fact that the size of the hydrophobic solute is comparable to that of the water molecule and that any two molecules in the solute–water–water triplet are close to each other; to be more precise, the O–O distance is between 2.3 and 3.4 Å (two water molecules are paired) and the A–O distance is between 2.9 and 5.3 Å (the water molecule is in the first hydration shell of the solute).

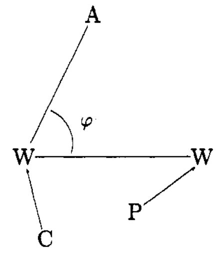

Figure 5. Configuration of a solute–water–water triplet, described by the A–O–O angle, φ. W stands for the O site in the water molecule. A stands for the hydrophobic solute. The central water molecule in the triplet is labeled C, and the other water molecule is labeled P.

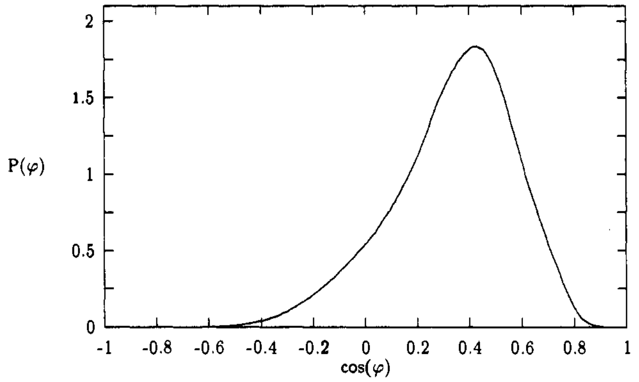

Figure 6. Probability distribution, $P(\varphi)$, of the A–O–O angle, φ. The area of the curve is normalized to 1. The horizontal axis shows $\cos(\varphi)$, and the vertical axis shows $P(\varphi)$. Both of the water molecules are in the first hydration shell of the hydrophobic solute.

Next we compare the water trimer in the bulk with that containing a pair inside the shell. As the hydrophobic solute is mainly found in the region of $45° \lesssim \varphi \lesssim 90°$, it is expected that the possibility of the geometry with the O–O–O angle, χ, of $45° \lesssim \chi \lesssim 90°$ is substantially smaller for the trimer containing a pair inside the shell because the hydrophobic solute excludes water molecules.

We then investigate the distribution of the water molecules adjacent to the C–P pair. Let NP be the average number of water molecules in the first shell of the water molecule C. The water molecule P is then one of the NP water molecules, and the other (NP – 1) is adjacent to the C–P pair. Each of these (NP – 1) water molecules forms a trimer containing the C–P pair, and the geometry of the trimer is represented by the O–O–O angle, χ, as in section 3. The distribution of these (NP – 1) water molecules adjacent to the C–P pair can then be expressed as a function of $\cos(\chi)$. In Figure 7, we show the distribution of $\cos(\chi)$, $D(\chi)$, for the C–P pair inside the shell and that for the C–P pair in the bulk. Each curve in Figure 7 is normalized to (NP – 1). (NP – 1) is the average number of trimers containing the C–P pair; that is, the average number of water molecules adjacent to the C–P pair in the first shell of the central water molecule C.

According to Figure 7, the distribution reduces substantially in the region of $45° \lesssim \chi \lesssim 90°$ for the C–P pair inside the shell, as was expected above. This region mostly corresponds to the "mismatching" region, while in the "matching" region, the change in the distribution is relatively small. Thus, the distribution is more tetrahedral for a pair inside the shell than for a pair in the bulk. Because the hydrophobic solute does not have a direct orientational influence on water molecules, the hydrogen bond in a pair near the hydrophobic solute is related only to the distribution of the water molecules surrounding the pair. Thus, the probability of observing the hydrogen bond in a pair increases inside the first hydration shell of the hydrophobic solute, as shown in Table 2.

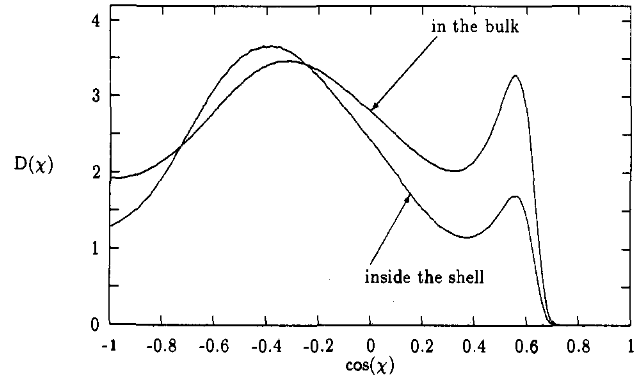

Figure 7. Distributions, $D(\chi)$, of the water molecules adjacent to the C–P pair expressed as a function of the O–O–O angle in the trimer, χ. The area of each curve is normalized to (NP − 1), where NP is the average number of water molecules in the first shell of the central water molecule C. The horizontal axis shows $\cos(\chi)$, and the vertical axis shows $D(\chi)$.

Table 2. Probability of Observing the Hydrogen Bond in a Pair

threshold angle	in the bulk	inside the shell	across the boundary
15°	0.14 ± 0.01	0.18 ± 0.02	0.14 ± 0.02
20°	0.30 ± 0.01	0.39 ± 0.03	0.31 ± 0.03
30°	0.52 ± 0.01	0.66 ± 0.03	0.53 ± 0.03
45°	0.72 ± 0.01	0.85 ± 0.02	0.72 ± 0.02

Table 3. Probabilities of Finding the Solute A and of Observing the Hydrogen Bond in a Pair of Water Molecules across the Shell Boundary

	A–C–P geometry (φ)		
threshold angle	"mismatching" ($\cos(\varphi) \le -0.65$)	"matching" ($-0.65 \le \cos(\varphi) \le 0.05$)	"mismatching" ($0.05 \le \cos(\varphi)$)
	Probability of Finding the Solute A		
	0.47 ± 0.03	0.49 ± 0.03	0.04 ± 0.03
	Hydrogen Bond Probability in the C–P Pair		
15°	0.17 ± 0.02	0.12 ± 0.02	0.15 ± 0.02
20°	0.35 ± 0.03	0.26 ± 0.02	0.33 ± 0.05
30°	0.60 ± 0.03	0.46 ± 0.03	0.56 ± 0.06
45°	0.78 ± 0.02	0.66 ± 0.02	0.76 ± 0.05

The above considerations lead to the following statement: because the hydrophobic solute blocks the "mismatching" region of a pair of water molecules inside the first hydration shell, it enhances the tetrahedrality of the distribution of the water molecules adjacent to this pair and strengthens the hydrogen bond.

4.2. A Pair across the Shell Boundary. The configuration of the A–C–P triplet is described by the A–O–O angle, φ, as shown in Figure 5. Depending on the value of φ, the solute A is either in the "matching" region or in the "mismatching" region of the C–P pair across the boundary. In Table 3, we show the probability of finding the solute A in each of these regions. As shown in Table 3, the hydrophobic solute is found in the "matching" region as well as in the "mismatching" region.

Next, for each region of the A–C–P geometry in Table 3, we restrict our attention to the C–P pairs across the boundary which have the solute A in that region and calculate the ratio of the number of hydrogen-bonded pairs to the total number of pairs. This ratio is the hydrogen bond probability in the C–P pair in the A–C–P triplet with the geometry in that region. We show this probability in Table 3. We then compare the hydrogen bond probability in the bulk displayed in Table 2 with that displayed in Table 3. The comparison shows that when the hydrophobic solute blocks the "matching" region, the hydrogen bond in the C–P pair is inhibited, and that when the hydrophobic solute blocks the "mismatching" region, the hydrogen bond in the C–P pair is promoted.[47]

Because the hydrophobic solute is found in the "matching" region as well as in the "mismatching" region, its effects of strengthening and weakening the hydrogen bond in a pair across the boundary cancel each other out. Thus, we do not observe a significant change in the hydrogen bond probability in this pair, as shown in Table 2.[48]

4.3. Remarks. By performing the simulation in which a hard sphere is used as the hydrophobic solute, we observe that the results in this section are also valid for the case of the hard sphere solute. This is quite natural because the structural aspects of the hydration described in subsections 4.1 and 4.2 are based only on the effect that the hydrophobic solute excludes water molecules.

When the solute–solvent interaction contains an orientational part, which may be attractive or repulsive, the solute has a direct orientational influence on water molecules. In such a case, the effect of the solute in the "matching" or "mismatching" region on the hydrogen bond in the solvent water is different from that of a hydrophobic solute. If the main part of the solute–solvent interaction is short-range, the approach in this section may be applied to treat the hydration of such a solute by taking into account the direct effect of the solute on the solvent around it. However, this approach has to be modified in order to account for the hydration of a solute with a long-range interaction with solvent, such as ionic hydration. The details of ionic hydration will be addressed in a future work.

5. Local Density and the Hydrogen Bond

The number of water molecules in the first shell (the coordination number) of a water molecule is variable and can be used to define the "local density" of the water molecule. It is of interest to consider how the hydrogen bonds formed by the water molecule are related to the fluctuations in the local density, since the effect of the local density is analogous to the "anomalous" density effect of water. In this section, we focus on the hydrogen bond as a function of the local density on the basis of the geometrical relationship investigated in section 3.

Suppose a water molecule, C, has NN water molecules in its first shell. One of the NN water molecules, P, is viewed as forming a pair with the central water molecule C, and the other (NN − 1) is adjacent to the C–P pair. Each of these (NN − 1) water molecules forms a trimer containing the C–P pair, and the geometry of the trimer is represented by the O–O–O angle, χ, as in section 3. The distribution of these (NN − 1) water molecule adjacent to the C–P pair can then be expressed as a function of $\cos(\chi)$. We show the distributions of $\cos(\chi)$, $D(\chi)$, in Figure 8a for various values of NN. Each curve in Figure 8a is normalized to (NN − 1). (NN − 1) is the number of trimers containing the C–P pair; that is, the number of water molecules adjacent to the C–P pair in the first shell of the central water molecule C. With an increase of NN by 1, one water molecule joins the first shell of the central water molecule C. Since the curves in Figure 8a are normalized to (NN − 1), the comparison of the two curves

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(47) In this section, the change in the distribution of the water molecules in the first shell of the water molecule C is considered. But a water molecule adjacent to the C–P pair may be in the first shell of C or in that of P. Thus, the distribution of the water molecules adjacent to the C–P pair consists of the water molecules in the first shell of C and those in the first shell of P. For the C–P pair inside the shell treated in the last subsection, as both C and P are in the first hydration shell, the distribution of the water molecules in the first shell of C is the same as that of P. Therefore, it is enough to consider the change in the distribution around C (or P). For the C–P pair across the boundary treated in this subsection, the distribution around C is different from that around P. As C lies inside the shell and P lies outside the shell, the hydrophobic solute mainly affects the distribution around C. Therefore, the water molecule C is treated as the "central" water molecule, around which the change in the distribution is considered, and the water molecule P is viewed as one of the water molecules in the first shell of C.

(48) The results in Table 2 are consistent with those for the pair energy reported in refs 12, 16, and 30.

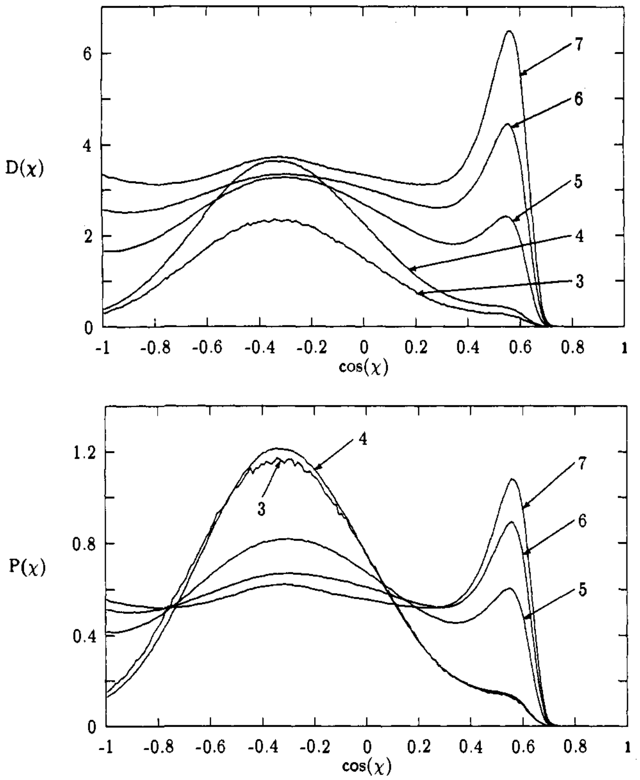

Figure 8. (a, top) Distributions, $D(\chi)$, of the water molecules adjacent to the C–P pair expressed as a function of the O–O–O angle in the trimer, χ, for various values of NN. The area of each curve is normalized to (NN − 1), where NN is the number of water molecules in the first shell of the central water molecule C. The horizontal axis shows $\cos(\chi)$, and the vertical axis shows $D(\chi)$. (b, bottom) Probability distributions of $\cos(\chi)$, $P(\chi)$, for various values of NN. The area of each curve is normalized to 1. The horizontal axis shows $\cos(\chi)$, and the vertical axis shows $P(\chi)$.

whose values of NN differ by 1 shows which type, "matching" or "mismatching", of water molecule increases with the introduction of a water molecule into the first shell. Figure 8b shows the probability distributions of $\cos(\chi)$, $P(\chi)$, for various values of NN. Each curve in Figure 8b is normalized to 1, and Figure 8b shows the tetrahedrality of the distributions of the water molecules around the central water molecule C for various values of NN.

According to Figure 8a, for NN ≥ 4, the changes in the distributions with the change in NN are relatively small around the tetrahedral angle ($\cos(\chi) \approx -{}^1/_3$), and the distributions increase more rapidly with NN when χ is farther from the tetrahedral angle. In other words, the introduction of a water molecule into the first shell mainly increases the "mismatching" type of water molecule, while the "matching" region is crowded for NN ≥ 4. The distribution of the water molecules around the central water molecule is then less tetrahedral for larger NN, as shown in Figure 8b.

For NN < 4, as shown in Figure 8a, the "matching" region is not crowded yet, and a water molecule joining the first shell of the central water molecule enters the "matching" region as well as the "mismatching" region. Figure 8b shows that the probability distribution of $\cos(\chi)$ hardly changes and that the distributions of the water molecules around the central water molecule are almost equally tetrahedral for NN = 3 and 4.

Thus, the tetrahedrality of the distribution of the water molecules around the central water molecule hardly changes for NN ≤ 4, while the distribution gets less tetrahedral with the saturation of the "matching" region as NN increases above 4.

We next determine the hydrogen bond probability in the C–P pair as a function of NN. This probability is also the ratio of the number of hydrogen-bonded water molecules in the first shell to the total number of water molecules in the first shell. We show this probability as a function of NN in Figure 9. Figure 9 shows that the probability does not change significantly for NN = 3 and 4 and that it decreases monotonically with NN for NN ≥ 4. The behavior for NN = 3 and 4 corresponds to the uniform change in the distribution of $\cos(\chi)$ shown in Figures 8a and 8b, and that for NN ≥ 4 corresponds to the increase of the "mismatching" water molecules with the increase of NN shown in Figure 8a. Thus, the change in the hydrogen bond probability as a function of the local density accords with the changes in the numbers of "matching" and "mismatching" water molecules. In other words, the variation of the hydrogen bond probability with the local density parallels the change in the tetrahedrality of the distribution of the water molecules around the central water molecule.

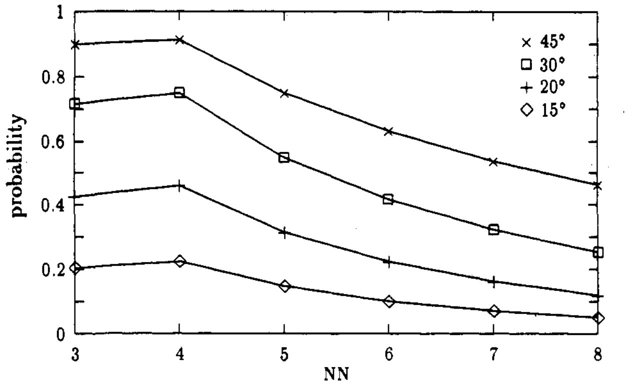

Figure 9. Probability of observing the hydrogen bond with one of the neighboring water molecules as a function of NN, the number of water molecules in the first shell. The vertical axis shows the probability, and the horizontal axis shows NN. The threshold angles defining the hydrogen bond in the pair are 45°, 30°, 20°, and 15° from top to bottom. The errors in the probabilities are less than 0.005.

In a study on the density dependence, Sciortino *et al.* showed that the water structure is weakened with the increase of density when the coordination number is 4 or more, and related it to the increase of the "defects" in the tetrahedral network.[35,36] Indeed, as shown in Figures 8a and 8b, the tetrahedrality decreases with NN when NN ≥ 4, and the presence of the "mismatching" water molecules causes the "defects" in the tetrahedral network. These authors also stated that the structure strengthening of water around a hydrophobic solute can be understood as a consequence of the lower local density around it.[36] This agrees with our results in the sense that decreasing the local density leads to the decrease of the number of "mismatching" water molecules, to which the hydrogen bond strengthening around a hydrophobic solute is related.

6. Conclusions

The effect of a water molecule on the hydrogen bond in its adjacent pair of water molecules is related to the geometry of the trimer consisting of the water molecule and this adjacent pair. When the trimer geometry "matches"/"mismatches" the tetrahedral nature of water, the hydrogen bond in the pair is promoted/inhibited. In the solution of a hydrophobic solute in water, as the hydrophobic solute blocks the formation of the "mismatching" trimers containing a pair of water molecules inside the first hydration shell, it promotes the hydrogen bond in this pair. On the other hand, as the hydrophobic solute blocks the formation of both the "matching" and the "mismatching" trimers containing a pair across the shell boundary, its effects of strengthening and weakening the hydrogen bond in this pair cancel each other out. For a water molecule in the bulk, when the coordination number is 4 or more, only the number of "mismatching" trimers increases, and the hydrogen bonds formed by this water molecule are weakened as the coordination number increases. When the coordination number is 3 or 4, there is hardly a change in the tetrahedrality of the distribution of the neighboring water molecules, and the hydrogen bonds formed by this water molecule do not change significantly.

In this paper, it has been shown that the "anomalous" structural properties of water, observed in such phenomena as hydrophobic hydration and the density effect, are related to the tetrahedral geometry of water in a natural way. As our approach is based on a simple picture of the geometry of molecules and is insensitive to the details of the underlying potential functions, it will hopefully be useful for addressing problems on more complex solutes or on other solvents with directional forces such as alcohols, amines, hydrogen fluoride, etc.

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