Increase of both Order and Disorder in the First Hydration Shell with Increasing Solute Polarity

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Monte Carlo simulations of a small model solute in an aqueous solution are used to examine the effects of solute polarity on hydration structure. A judicious definition of the orientational order parameter leads to reinterpretation of the conventional picture of hydration. As the solute varies from hydrophobic to hydrophilic the ordered first shell water simultaneously fractionates into a more highly ordered and a more disordered component. The hydrogen-bond network rearranges such that the more ordered component relaxes to configurations of optimal intermolecular angles, the other fraction being released from the network.

The manner in which water interacts with hydrophobic and hydrophilic surfaces is critical to many biological phenomena, examples being protein folding and membrane formation [1]. Hydration water is known to be significantly altered from the bulk due to specific interactions with, and the surface topography of, the solute [2] and hydration structure has been examined both experimentally (e.g., [3]) and computationally (e.g., [4]). Structural order parameters which provide a direct and quantitative insight into structure in the region of contact with the solute, and structural ordering of bulk water under different conditions, have received considerable attention in the last few years [5,6]. Several attempts to tackle generic issues of structural and dynamical properties of water at interfaces have also been reported [7,8]. However, a description of the structural order in hydration shells of simple molecular-scale solutes that reconciles cause and effect has been elusive and questions regarding the existence and the nature of water cages around molecular-scale solutes and their importance for a quantitative understanding of hydration still remain to be answered.

Here, we investigate the change of structural order within hydration shells around a small model solute interacting with water via hard sphere repulsion and a dipole field of variable intensity, with a view to the elucidation of the generic microscopic origin of differences in water packing around small hydrophobic and hydrophilic units.

We employ constant pressure Monte Carlo simulations with TIP5P water [9] and model solute in a cubic simulation box with periodic boundary conditions. We consider a system of 2668 water molecules and 1 freely moving model solute particle at $p = 1$ bar and $T = 300$ K. The hard sphere diameter of the solute is taken to be 2.8 Å (approximately the diameter of a water molecule). After an

extensive equilibration period, 1.8×10^9 simulation steps were performed.

To investigate the differences in the structure and fluctuations of water molecules around an idealized hydrophobic and increasingly polar solute, we associate a dipole moment of variable magnitude with the hard sphere. In turn, the point charges of TIP5P water interact with the field of the dipole. The potential energy of the interaction is given as $U_p = \sum_i \phi_d(R'_i)e_i$, where $\phi_d(R')$ is the electrostatic potential at point R' due to the presence of the dipole at R_d and the sum is over all point charges e_i of the TIP5P molecule. The dipole electrostatic potential expresses as $\phi_d(R') = \mu \cos(\vartheta)|R' - R_d|^{-2}$, where ϑ is the angle between the direction of dipole moment $\vec{\mu}$ and vector $R' - R_d$. Along with the hard sphere repulsion, we consider the following values of μ in units of the dipole moment of the TIP5P molecule ($\mu_{\text{TIP5P}} = 2.29$ D): 0.4, 0.8, 1.0, and 1.2.

We focus on changes in the water structure and ordering due to the presence of the model solute. The packing of water molecules at a distance r from the solute center is evaluated by means of the proximity correlation function, defined as $g(r) = \int d\Omega \langle \sum_{i=1}^N \delta(r - r_i) \rangle / [\rho_b \int d\Omega]$, where ρ_b denotes the bulk number density of water molecules, r_i is the position vector of the ith water molecule, and Ω denotes the angular integration. It follows that the average number of water molecules inside a spherical shell of thickness r is $\langle N(r) \rangle = 4\pi\rho_b \int_0^r r'^2 g(r')dr'$. $g(r)$ and $\langle N(r) \rangle$ are shown in Fig. 1.

We first focus on translational (radial) correlation functions. In all cases under consideration the dipole field was not strong enough to induce an asymmetric distribution of the positions of water centers around the spherical solute (results not shown). In the case of the purely hydrophobic sphere the solute-water pair translational correlations
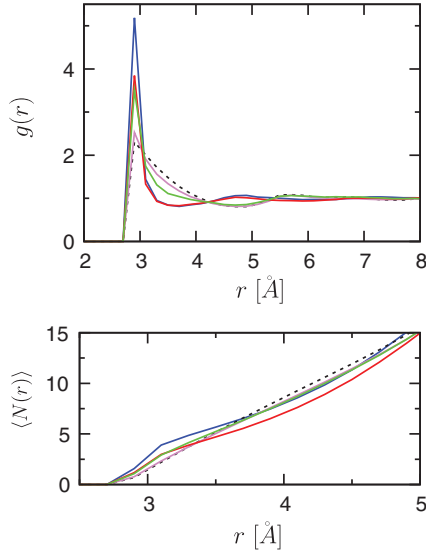
FIG. 1 (color). Proximity correlation function (upper panel) and the average number of neighbors (lower panel). Black dashed lines denote results for the hard sphere solute, pink lines correspond to a polar solute with $\mu = 0.4\mu_{\text{TIP5P}}$, green lines to $\mu = 0.8\mu_{\text{TIP5P}}$, red lines to $\mu = 1.0\mu_{\text{TIP5P}}$, and blue lines to $\mu = 1.2\mu_{\text{TIP5P}}$.

persist to about 6 Å away from the solute, and form two separate hydration shells. The thickness of the first hydration shell, determined from the minimum separating the peaks, is ~2 Å which means that the water oxygens within this shell are rather delocalized. The number of neighbors in the first hydration shell, $\langle N(r)\rangle$, is approximately 10. A dipole moment of magnitude equal to 40% of the TIP5P water dipole moment has only a minor effect on the radial function (Fig. 1), enhancing slightly the correlations in direct contact while leaving $\langle N(r)\rangle$ almost unaffected, also with no effect on the molecules in the second shell.

A further increase in polarity causes a narrowing of the width of the first hydration shell and a significant increase of the correlations in direct contact, but the total number of water molecules in the first shell remains largely unperturbed (see Fig. 1). This indicates a pronounced reordering in the first shell and suggests the formation of an apparent multiphase first shell structure. In the contact layer, comprising ~4 molecules, water molecules are radially more structured. However, the molecules in the second shell still remain unaffected. Further increasing the dipole moment to the value of TIP5P causes profound restructuring in both hydration shells (Fig. 1). The molecules in the first shell become even more localized and the second shell shifts towards the first one, such that the position of the second peak corresponds to the position of the first minimum of the case of the ideally hydrophobic solute. In the first shell ~4.5 molecules are radially more structured and this effect is even more pronounced in the case of further increased polarity, while the second peak remains unaffected. The cumulative number of molecules in both shells of the most

polar solute is approximately equal to the number of molecules in the first shell around the ideally hydrophobic solute ($N \sim 15$), suggesting that the restructuring on polarization occurs as a separation of the first shell into two.

The dipole increases the solute-water translational correlations with respect to the hard sphere solute. Since increased translational correlations imply a lowering of the translational entropy, it is instructive to also examine the density fluctuations as a function of distance from the solute center, shown in Fig. 1 of the Supplemental Material [10]. For $\mu < \mu_{\text{TIP5P}}$ the difference in density fluctuations with respect to the hard sphere is modest. For larger values of μ ($\mu = 1.0\mu_{\text{TIP5P}}$, $1.2\mu_{\text{TIP5P}}$) the density fluctuations are reduced with respect to the hard sphere solute. Both the $g(r)$ peaking and the reduced density fluctuations imply that the solute-water translational correlations are increased and correspondingly the translational entropy is expected to decrease in the presence of the dipole field. Obviously, the favorable energetic contribution and the (possibly) favorable contribution of the orientational entropy to hydration prevail over the unfavorable translational entropy.

As the extent of the perturbation due to the presence of the model solute is limited to the first two hydration shells, we focus, from here on, on the ordering inside these shells. Both changes in the molecular packing as well as changes in the density fluctuations are expected to be accompanied by changes in orientational ordering. The standard order parameter describing orientational correlations in water, the tetrahedrality [5], cannot be used here in its usual form, because in the region of largest perturbation (i.e., in the vicinity of the solute), water molecules do not have four nearest neighbors. Rather, in order to capture a variable number of nearest neighbors, the tetrahedrality must be generalized. Naturally, the lowest number of neighbors allowing a physically meaningful evaluation of the degree of local tetrahedral order is 2. Thus, we can define the conditional tetrahedrality (the tetrahedrality providing the tagged water molecule has between 2 and 4 neighbors) as

$$q_i = 1 - \frac{1}{N(N-1)}\left(\frac{9}{8}\right)\sum_{j=1}^{N-1}\sum_{k=j+1}^{N}\left(\cos\psi_{jik} + \frac{1}{3}\right)^2, \quad (1)$$

with $2 \leq N \leq 4$. The normalization constant was chosen to assure $q_i = 0$ in the extreme nontetrahedral arrangement in which all "bonds" are superimposed ($\psi_{jik} = 0$). The resulting probability densities of q_i in the first hydration shells are shown in Fig. (2). Increasing the value of μ results in a higher probability of finding configurations with a very high degree of tetrahedral order (~1) in the first shell [Fig. 2(a)]. At the same time the probability of finding configurations with extremely low tetrahedral order (< 0.89) also increases. This can be seen nicely from the cumulative probability density shown in the inset of Fig. 2(a). In the second shell the tetrahedral ordering is not affected much by the dipole moment of the solute [Fig. 2(c)
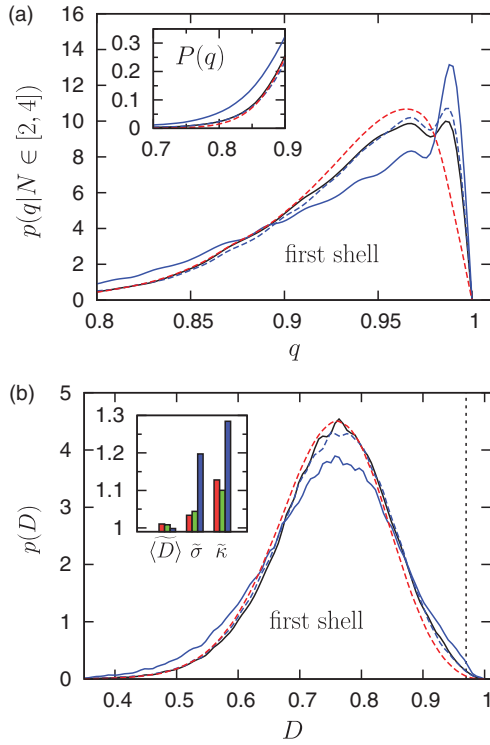
FIG. 2 (color).   Probability densities of q_i and D_i in the first hydration shell. The red dashed lines correspond to bulk water, black lines represent results for the hard sphere solute, the blue dashed lines correspond to $\mu = 0.4\mu_{\text{TIP5P}}$, and the full blue lines $\mu = 1.2\mu_{\text{TIP5P}}$. Inset in (a): Cumulative probability of q_i being less than 0.8. Inset in (b): $\langle \tilde{D} \rangle \equiv \langle D \rangle / \langle D \rangle_{bw}$, $\tilde{\sigma} \equiv \sigma / \sigma_{bw}$, and $\tilde{\kappa} \equiv \kappa / \kappa_{bw}$ of $p(D)$; red bars correspond to the hard sphere solute, green to $\mu = 0.4\mu_{\text{TIP5P}}$, and blue to $\mu = 1.2\mu_{\text{TIP5P}}$. The vertical dashed line depicts the D value of the optimal TIP5P water dimer geometry.

of the Supplemental Material [10]], although the probability of highly ordered configurations is somewhat lower.

If hydrogen bonding is the primary (leading-order) interaction in bulk water and is reduced at higher local densities, one might expect that the leading-order interaction at higher densities would be dipole-dipole interactions. Furthermore, at very high densities (i.e., approaching close packing) one can speculate that the interactions will be dominated by van der Waals forces. Therefore, it is highly desirable to have an order parameter which is able to capture simultaneously different interacting regimes. One way to obtain this is to start from the dipole-dipole interaction energy written in the form $U_{d_id_j} = -\alpha_{ij}|\boldsymbol{p}_i||\boldsymbol{p}_j|/r_{ij}^3$, with $\alpha_{ij} = 3(\boldsymbol{n}_{ij} \cdot \boldsymbol{\pi}_i)(\boldsymbol{n}_{ij} \cdot \boldsymbol{\pi}_j) - \boldsymbol{\pi}_i \cdot \boldsymbol{\pi}_j$, where we have defined the intermolecular unit vector $\boldsymbol{n}_{ij} = \boldsymbol{r}_{ij}/|\boldsymbol{r}_{ij}|$ and $\boldsymbol{\pi}_{ij} = \boldsymbol{p}_{ij}/|\boldsymbol{p}_{ij}|$. α_{ij} reflects the relative dipolar ordering and varies between -2 and 2, in the case of extremely repulsive or extremely attractive dipole-dipole orientations, respectively. To examine the mutual ordering in a cluster of nearest water molecules it is useful to define an order parameter D_i by

$$D_i = \frac{1}{N} \sum_{j=1}^{N} \left(\frac{\alpha_{ij} - \alpha_{ij}^{\min}}{\alpha_{ij}^{\max} - \alpha_{ij}^{\min}} \right), \tag{2}$$

where $i \neq j$ and the sum is taken over the N neighbors in the first coordination shell of the ith water molecule and $\alpha_{ij}^{\max} = \sqrt{1 + 3(\boldsymbol{n}_{ij} \cdot \boldsymbol{\pi}_i)^2}$ and $\alpha_{ij}^{\min} = -\alpha_{ij}^{\max}$ correspond to maximal and minimal dipole-dipole attractions given fixed $\boldsymbol{n}_{ij}$ and $\boldsymbol{\pi}_{ij}$. In this way, D_i takes values between 0 (maximal repulsion) and 1 (maximal attraction). The optimal geometry of TIP5P water dimer, given by the flap angle $\tau = 51°$ [9] corresponds to $D_i = 0.975$. The probability densities of D_i in the first hydration shell are shown in Fig. 2(b).

The probability densities $p(D)$ are much smoother and well behaved than $p(q)$, while also conveniently representing the changes of the probability of finding highly tetrahedral configurations. Furthermore, $p(D)$ is not influenced by the probability of a tagged molecule having between 2 and 4 nearest neighbors. Thus, it is clear, especially if considering the large dispersion of q, that the order parameter D is very well suited for the description of the orientational ordering of water molecules (or any anisotropic molecules for that matter). Moreover, due to the large dispersion, the average tetrahedrality does in fact not have a well-defined physical meaning.

Since the distributions $p(D)$ resemble, in essence, a Gaussian, it is instructive to compute the average, $\langle D \rangle$, standard deviation, $\sigma = \sqrt{\langle D^2 \rangle - \langle D \rangle^2}$ and skewness, $\kappa = (\langle D^3 \rangle - 3\langle D \rangle \sigma^2 + 2\langle D \rangle^3)/\sigma^3$ of $p(D)$. In particular, σ can be used to quantify the orientational fluctuations while κ is a measure of the asymmetry of the distribution, and more specifically of the deviations from the mean in both directions. $\kappa = 0$ for a symmetric distribution, $\kappa < 0$ for a left-skewed distribution and $\kappa > 0$ for a right-skewed distribution. The parameters are expressed as relative values with respect to their values in bulk water, which is denoted by the subscript bw. Inspection of these parameters reveals clearly that large solute dipoles increase orientational fluctuations in the first hydration shell while having a negligible effect on the mean orientational ordering [see inset of Fig. 2(b)]. In all cases $p(D)$ is left skewed. In agreement with the tetrahedrality values we also find an increased fraction of highly ordered configurations with respect to the hard sphere case. At the same time there is also an increase of the relative fraction of orientationally disordered configurations (having D around 0.5) with respect to highly ordered ones. In the second shell the increasing polarity apparently affects only the skewness, which decreases upon increasing μ (see Fig. 2 of the Supplemental Material [10]).

In Fig. 3 distributions of the average number of close contacts and hydrogen bonds (HBs) formed by individual water molecules in the first shell are shown. Two molecules are assumed to be in close contact if their oxygen atoms are
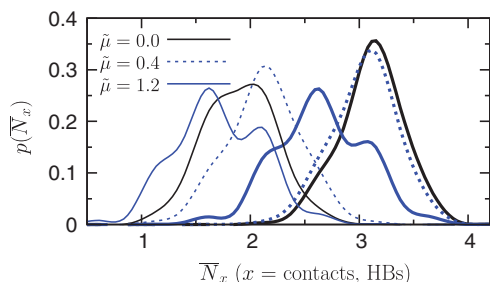
FIG. 3 (color). Distributions of the number of contacts at cut-off radius 3 Å per water molecule in the first hydration shell (thick curves) and of the hydrogen bonds (thin curves).

less than 3 Å apart and are said to form a hydrogen bond if furthermore the angle O-H$\cdots$O is larger than $150°$ [11]. A clear tendency of water to organize so as to form fewer contacts and HBs when solvating a strong hydrophilic solute relative to the hydrophobic solute is revealed.

The above results lead to the following scenario for hydration changes accompanying the transition from hydrophobic to hydrophilic solvation. In the case of an ideal hydrophobic solute the hydrogen-bond network is apparently enhanced relative to the bulk but without achieving the optimal packing, which follows from the fact that highly ordered (tetrahedral) configurations are present but do not dominate. Also, a slight increase of solute polarity leads to more efficient water-water hydrogen bonding in the first shell as revealed by the right shift of the HB distribution in Fig. 3. The first shell is thus subjected to high density fluctuations (Fig. 1 in the Supplemental Material [10]). The fraction of orientationally disordered configurations (low values of q and D) is small and very similar to that of the bulk water. These observations can be explained in terms of the tendency of water molecules to compensate for the lack of favorable interactions with the solute.

Upon increasing solute polarity both the fractions of highly ordered and highly disordered configurations increase. This suggests that the hydrogen-bond network rearranges such that one part of the network relaxes to configurations of optimal intermolecular angles, and hence optimized energy, while the other part is released from the network. The formation of the two types of texture around strong polar solute, orientationally ordered and disordered, suggests a symmetry breaking of the tetrahedral liquid in the first hydration shell. However, the existence of such a bimodal state of water does not persist and propagates into the second shell, remaining localized in the first hydration shell. In contrast, in the case of solvated ions water beyond the first hydration shell has been reported to be affected [12] due most likely to stronger electric fields. We have shown that the weaker perturbations generated by the dipole field, although strong enough to break the symmetry of hydrogen bonding in the first hydration shell, are not sufficient to enable the propagation of structural

heterogeneity on nm length scales, such as those postulated for pure water in Ref. [13]. Our findings are, however, in accord with the view of classifying hydration water at ambient conditions as a tetrahedral liquid [14] perturbed by the solute.

From the structural rearrangement of the hydration layer and from the increased variations σ of the order parameter D [inset of Fig. 2(b)], one expects increased rotational instability of water around hydrophilic relative to the hydrophobic solute. Indeed, it has been found experimentally by Halle and co-workers, [15], as well as in simulations [8,16], that rotational water dynamics is faster in a more polar relative to a nonpolar environment.

The present results suggest that the picture of water being more tetrahedrally ordered around hydrophobic than around hydrophilic solutes [17] is not correct. Rather, the hydrogen-bond network around an ideally hydrophobic solute is less orientationally flexible, and on average involves a significantly larger fraction of water molecules in the first hydration shell, relative to a hydrophilic solute. The hydrogen-bond network around an increasingly polar solute becomes more fragile such that it more rapidly breaks and rebuilds, leading on average to the portions of either significantly more tetrahedrally ordered or less ordered waters introducing rotational instability of water around the solute. The relaxation of structural frustrations in the hydrogen-bond network when passing from the hydrophobic to the hydrophilic regime appears to be a many body effect which simultaneously includes both intra- and intercluster molecular reorganization and cannot be explained by melting of microscopic "icebergs."

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[10] See Supplemental Material at http://link.aps.org/supplemental/10.1103/PhysRevLett.107.267801 for results of local density fluctuations, order parameters in the second hydration shell, and correlations between order parameters.

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