

Ordered-to-Disordered Transformation of Enhanced Water Structure on Hydrophobic Surfaces in Concentrated Alcohol–Water Solutions

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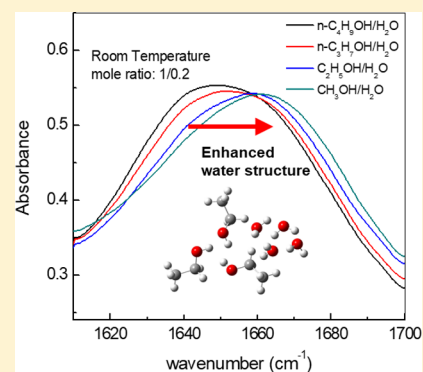
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Supporting Information

ABSTRACT: The effects of hydrophobic solutes on the structure of the surrounding water have been a topic of debate for almost 70 years. However, a consistent description of the physical insight into the causes of the anomalous thermodynamic properties of alcohol–water mixtures is lacking. Here we report experimental results that combined temperature-dependent linear and femtosecond infrared spectroscopy measurements to explore the water structural transformation in concentrated alcohol–water solutions. Experiments show that the enhancement of water structure arises around microhydrophobic interfaces at room temperature in the solutions. As temperature increases, this ordered water structure disappears and a surface topography-dependent new disordered water structure arises at concentrated solutions of large alcohols. The water structural transformation is dependent on not only the length of the alkyl chain but also the clustering of the alcohols. A more-ordered-than-water structure can transform into a less-ordered-than-water structure.



Hydrophobic hydration is widely considered to play a key role in biological processes ranging from membrane formation to protein folding and ligand binding.^{1,2} The typical model systems of hydrophobic hydration are alcohol/water mixtures. When a simple alcohol is mixed with water, the system has a negative excess entropy and a strong increase in heat capacity, compared to an ideal solution of randomly mixed molecules.^{3,4} On the basis of these findings, Frank and Evans suggested the “iceberg” model for hydrophobic hydration, in which hydrophobic solute molecules were proposed to force surrounding water molecules to create ice-like or clathrate-like structures.⁵ However, recent experimental^{6–8} and theoretical^{9–13} studies in concentrated alcohol aqueous solutions have challenged this view. Molecular level studies did not find evidence to support that the structure of water surrounding hydrophobic groups would be different from the bulk liquid water. For instance, in neutron scattering studies by Dixit et al.¹⁴ the oxygen–oxygen distances of the solvating water molecules were observed to be similar to those in bulk liquid water. Molecular dynamics (MD) simulations also pointed to preservation rather than enhancement of the water structure around the hydrophobic groups.^{15–17}

More recently, however, using Raman scattering measurements Davis et al.¹⁸ presented evidence in very dilute alcohol aqueous solutions that hydrophobic groups in molecules in fact enhance the ordering of the surrounding hydrogen-bond network of water, and the enhancement can transform with the increase of temperature. Such results seem to contradict the previous neutron scattering data.¹⁴ Recent MD simulations by Galamba¹⁹ indicated that the tetrahedral enhancement of water in the first hydration shell is not associated with the contraction of the H-bond network. This means even if the enhanced tetrahedrality of water occurs, the decrease of the O–O and O–H distances cannot be observed in the neutron diffraction experiments. However, the argument was questioned by other theorists.²⁰ The physical views suggested by the two experimental studies puzzled our understanding. Dixit et al. claimed no enhancement of the water structure surrounding methanol in concentrated (7:3 molar fraction for methanol/water)¹⁴ and dilute solutions (1:19 mole

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fraction).²¹ However, Davis et al.¹⁸ reported significant enhancement of the water structure surrounding alcohol in very dilute solutions ($\sim 1:99$ molar fraction), but this is hard to extend to the concentrated solutions because of their experimental techniques. In fact, an increasing amount of experimental and theoretical work suggested that the hydrophobic headgroups of alcohol molecules in concentrated solutions cluster together.^{22–24} It is not clear whether the different concentrations cause the disagreement between the two experiments. In this Letter, we report experimental results that combine temperature-dependent infrared spectroscopy (TD-FTIR) and ultrafast pump–probe spectroscopy measurements to explore hydrophobic hydration in concentrated alcohol/water solutions. For the FTIR, we focus on the water bending region. Although the bend vibration of water is less sensitive to molecular environment than the stretch, it nonetheless provides a useful probe of water structure. As pointed out by Skinner,²⁵ there are some advantages for detecting bending mode: First, there is only one bending mode in a molecule, which means there is essentially no intramolecular vibrational coupling. Second, the bend line shapes should not be affected too much by intermolecular vibrational coupling because of a smaller transition dipole moment. Our data, covering a number of linear alcohols, a very broad concentration range, and various temperature conditions, show clear evidence that, opposite to the conclusion from previous neutron scattering data,¹⁴ water structural transformations do occur at the hydrophobic interfaces in the concentrated alcohol solutions.

Enhanced Water Structure Revealed by Water Bending Spectra. Figure 1 displays the infrared spectra of ethanol–water

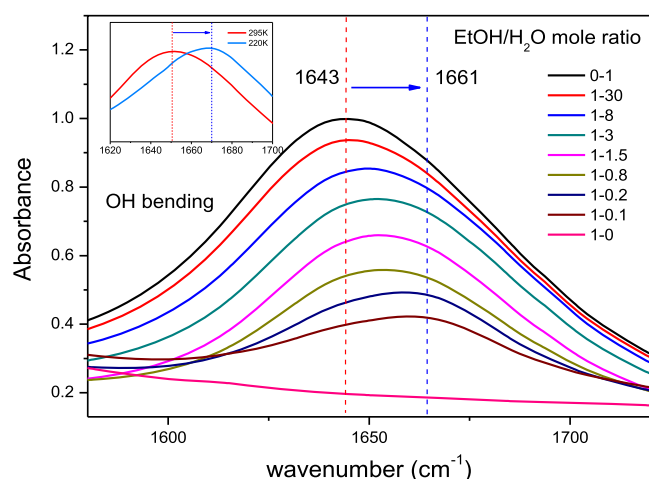


Figure 1. Infrared spectra of the water bending mode region of aqueous ethanol ($\text{C}_2\text{H}_5\text{OH}/\text{H}_2\text{O}$) solutions with different ethanol concentrations. The bending peaks show clear blue shifts from 1643 to 1661 cm^{-1} as the ethanol concentration increases. The inset is the infrared spectra of the water bending mode of ethanol aqueous solution with a mole ratio of 1:3 at temperatures of 295 and 220 K.

solutions with different concentrations in the OH bending region. The peak around 1643 cm^{-1} is purely from the water OH bending mode. There is no peak in this region in the pure ethanol liquid. In Figure 1, the water bending peak shifts to a higher frequency as the ethanol concentration increases. It shifts from 1643 cm^{-1} in the pure water to 1661 cm^{-1} in the ethanol/water solution with a molar ratio of 1/0.2. A similar

phenomenon has also been observed in aqueous methanol, *n*-propanol, and *t*-butanol solutions (see Figures S1–S3 in the Supporting Information). The blue shift of the water bending frequency could be caused by stronger hydrogen bond networks.²⁶ The inset in Figure 1 shows the temperature dependence of the water bending mode in aqueous ethanol solutions. The blue shift is also observed as temperature decreases from room temperature to 220 K, which means the stronger hydrogen-bond network at low temperature causes the water bending frequency blue shift.

In the gas phase, the vibrational frequency of water bending mode is located at $\sim 1594 \text{ cm}^{-1}$, and it shifts to a higher frequency $\sim 1643 \text{ cm}^{-1}$ in liquid and $\sim 1670 \text{ cm}^{-1}$ in ice.^{27,28} Such a blue shift of the bending mode is interpreted as being caused by a stronger hydrogen-bond network between water molecules, as confirmed by several experimental works.^{29–31} The susceptibility of the bending mode to the environment was reported more than 30 years ago.³² Recently, Kuroda et al.³³ reported the correlation between the water bending frequencies and the number of hydrogen bonds. An increase of 15 cm^{-1} in the average frequency per added hydrogen bond for the donor has been observed. The MD simulations by Skinner et al. also concluded that increased hydrogen bonding results in larger blue shift of the bending mode.²⁵ These previous experimental and theoretical studies give us confidence that the blue shift of the water bending frequency observed in Figure 1 should be caused by stronger hydrogen bond networks.

In the concentrated alcohol aqueous solutions, water can populate around the hydrophobic group of alcohols or the hydrophilic OH group of alcohols. Even in the most concentrated solutions used, there are still some water molecules around the hydrophobic interfaces (the dangling water OH at hydrophobic interfaces has been observed, as shown below). The critical question is whether the water bending blue shift is from the hydrophobic effect or from the hydrophilic effect. For alcohols, the hydrophilic head is a hydroxyl group. H-bonded to water and H-bonded to the alcohol are very similar. Indeed, MD simulations by Laage et al.^{34,35} reported that the hydrophilic head of *n*-butanol induces a very limited frequency-shift with respect to the bulk water even in the high concentrated solutions. Dixit et al.¹⁴ also pointed out that in the 7:3 methanol–water mixture, the total number of hydrogen bonds per water molecule is about 2.9 (about 1.0 hydrogen bonds to other water molecules and 1.9 hydrogen bonds to methanol molecules), which is 20% less than in pure water. Thus, the blue shifts we observed in Figure 1 are not due to the water H-bond structures in the vicinity of the alcohol hydrophilic groups but instead are due to the hydrophobic effect. This conclusion is also confirmed by comparing results obtained from solutes with different numbers of OH head groups (there is barely a frequency shift between propanol ($\text{C}_3\text{H}_7\text{OH}$) and glycerol ($\text{C}_3\text{H}_5(\text{OH})_3$) solutions at the same concentration, as shown in Figure S4). The results mean that stronger hydrogen bond networks (more tetrahedral and fewer weak hydrogen bonds) than bulk water arise in the hydration shell with the alcohol concentration increasing. We found that such an enhancement is more pronounced with the concentration increasing.

Figure S5 shows bending spectra obtained from dilute H_2O in HOD/ D_2O ($\sim 15\%$ mole ratio). Such measurements serve to suppress intermolecular vibrational coupling. The difference between the bending band from ethanol–water (1:0.2) and that from dilute H_2O thus confirms that hydrophobic

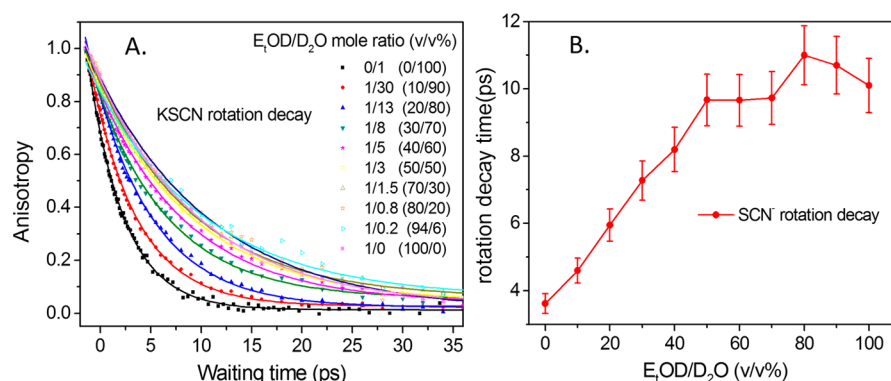


Figure 2. (A) Anisotropy decays of the SCN^- vibrational signal of KSCN in aqueous ethanol- d_1 solution with different ethanol- d_1 concentrations (the concentration of KSCN is always 0.2 M relative to D_2O , which means the mole ratio of KSCN/ D_2O is about 1/250 in the ethanol–water solutions). (B) Concentration-dependent rotational diffusion time constants of SCN^- anions of KSCN in aqueous ethanol solutions. The molecular rotation slows down as the ethanol concentration increases.

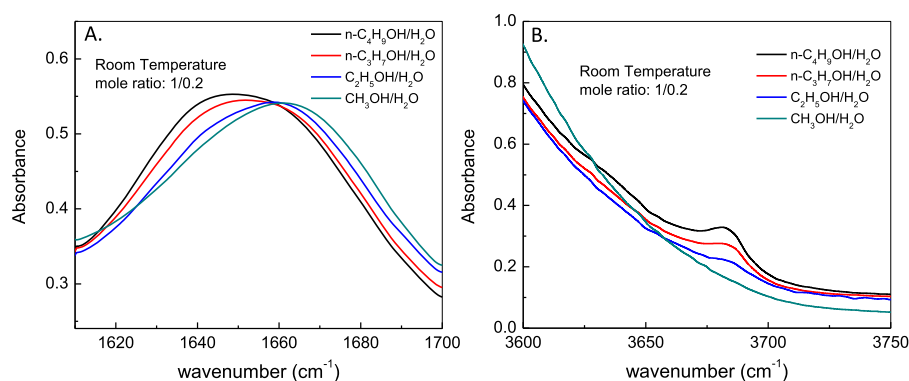


Figure 3. Effect of alcohol linear chain length on water structural transformation. Infrared spectra (bend mode region (A) and OH stretch region (B)) of aqueous alcohol solutions at room temperature with the alcohol/water molar ratio of 1/0.2.

hydration leads to an increase of the strongest hydrogen bond (highest bending frequency) population. We obtain the fraction of water molecules whose bending vibrations are perturbed by the hydrophobic interface, and hence differ from bulk water, by fitting the bending spectra (see Tables S1 and S2 in the Supporting Information). The results show the fraction increase of high-frequency components as the ethanol concentration increases (Figure S6).

To further explore the water structure enhancement observed in Figure 1, molecular rotational dynamics were measured. In previous studies, the dynamics of water molecules surrounding hydrophobic groups were observed to be different from those of bulk liquid water. From nuclear magnetic resonance (NMR),^{36,37} dielectric relaxation,^{38,39} and femto-second mid-infrared spectroscopy measurements,^{40–42} it was observed that solvating water molecules show slower reorientation dynamics than the molecules in bulk liquid water. However, because of the complicated water dynamics, like energy transfer, chemical exchange, and jump reorientation, a consistent picture of the effect of hydrophobic groups on the structural dynamics of water is yet to be agreed upon by these experiments. In this work, we chose the KSCN molecule as a probe. Molecular KSCN is weakly hydrated and has a long lifetime (~ 20 ps) in D_2O solutions. When a small amount of KSCN is dissolved in ethanol- $\text{d}_1/\text{D}_2\text{O}$ solutions (the mole ratio of KSCN/ D_2O is always about 1/250), the rotation of SCN^- ion can be affected only by the surrounding environment, i.e., water structures. Figure 2 shows anisotropy decays

of the SCN^- vibration of KSCN in aqueous ethanol- d_1 solution with different ethanol- d_1 concentrations. Because of the huge difference of KSCN solubility in water and ethanol (the solubility of KSCN in water is several tens of times larger than that in ethanol), most of the KSCN is dissolved in water even in a solution with the ethanol/water mole ratio of 1/0.8 (80/20 volume ratio). The SCN^- ion rotation clearly slows down from 3.6 ps in pure water to ~ 10 ps in concentrated ethanol solutions as the ethanol concentration increases. In these liquids, the viscosity change is moderate (1.0 for pure water, and 1.95 for the solution with an ethanol/water mole ratio of 1/0.8). This means the water structure solvating SCN^- must change as the concentration of ethanol increases. It becomes more rigid and less mobile, compared to that of the pure water. The same phenomenon has also been observed in *n*-propanol and *n*-butanol water solutions (see Figure S7). The results are consistent with the conclusion from the bending spectra in Figure 1 that the water structure becomes more ordered (more tetrahedral hydrogen bonds) and less mobile with the increase of ethanol concentration.

Figure 3A displays a comparison of the water bending spectra in solutions with alcohols of different hydrophobic linear chain length at room temperature. The solutions have the same concentration of 1/0.2 (alcohol/water) molar ratio. Opposite to the intuition that with the linear hydrophobic chain length increasing the hydrophobic effect should increase and the enhancement of water structure should be more pronounced and the frequency shift of the bending mode

should be larger, the experimental results are surprising. In fact, the frequency shift is larger with a smaller alcohol, i.e., methanol > ethanol > *n*-propanol > *n*-butanol. The fitting results also show the fraction of high-frequency components decreases as the chain length increases (Figure S6). This observation is consistent with the fact that hydrophobic groups can aggregate to “hide” from water in concentrated solutions, which means a larger cluster due to aggregation has a smaller total hydrophobic surface area and fewer water molecules can populate around the hydrophobic surface to enhance the water structure (for example, in concentrated solutions alcohols presumably form micelle-like structure^{43,44} and hydrophobic groups hide from the water phase). Such aggregations are more severe in aqueous solutions with larger alcohols.^{45,46} Actually, solvation of small molecules is dominated by excluded volume, and thus entropic, while solvation of large molecules or near extended interfaces is dominated by deformation of those interfaces and thus enthalpic.⁶ Thus, for short chain alcohols, aggregation is minimal and longer alcohol aggregation does occur.

Temperature-Dependent Water Structural Transformation. The enhanced water structure around hydrophobic groups should dissociate as the temperature increases. Figure 4 shows the water bending spectra in alcohol aqueous solutions as the solution temperature increases toward 100 °C. The solutions have the same concentration of 1/0.2 (alcohol/water). The water bending peak clearly red shifts from $\sim 1660\text{ cm}^{-1}$ to

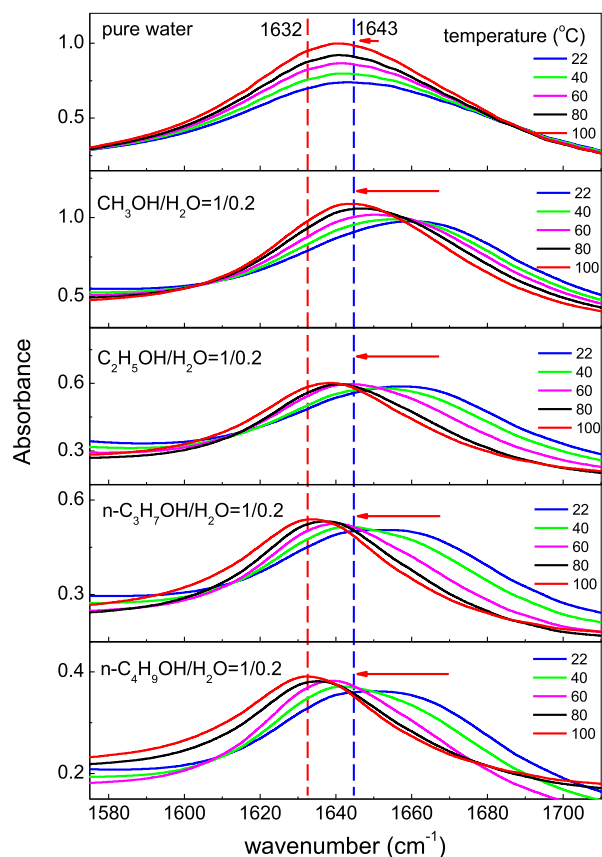


Figure 4. Temperature-dependent infrared spectra of aqueous alcohol solutions and pure water. The mole ratio of alcohol/water is 1/0.2. The spectra reveal clear red shifts when the temperature increases, which can be regarded as the ordered water structures surrounding hydrophobic groups “melting” upon an increase in temperature.

$\sim 1640\text{ cm}^{-1}$ or below in the alcohol aqueous solutions from room temperature to 100 °C. Such a red shift is much larger than the disorder induced by temperature increase in pure water (only 4 cm^{-1} red shift). This reveals the water structural transformation from ordered structure (more tetrahedral hydrogen bonds) to disordered structure (less tetrahedral hydrogen bonds) around hydrophobic groups, similar to the melting process. It is interesting that in the methanol–water solution, the peak is still a little higher than that in pure water at 100 °C, which means the water in the hydrophobic shell does not melt thoroughly in the methanol–water solution. The peak in the ethanol–water solution is similar to that in the pure water at 100 °C. However, for larger alcohols, like *n*-propanol, *n*-butanol, and *n*-pentanol, the peaks red shift to $\sim 1630\text{ cm}^{-1}$ at 100 °C, more than 10 cm^{-1} on the red side of the pure water peak. The results indicate that a more disordered structure with weaker hydrogen bonds than bulk water (at the same temperature) emerges.

A comparison of the water bending spectra at 100 °C of the concentrated alcohol solutions (molar ratio 1/0.2) with different chain lengths is displayed in Figure 5. A sudden

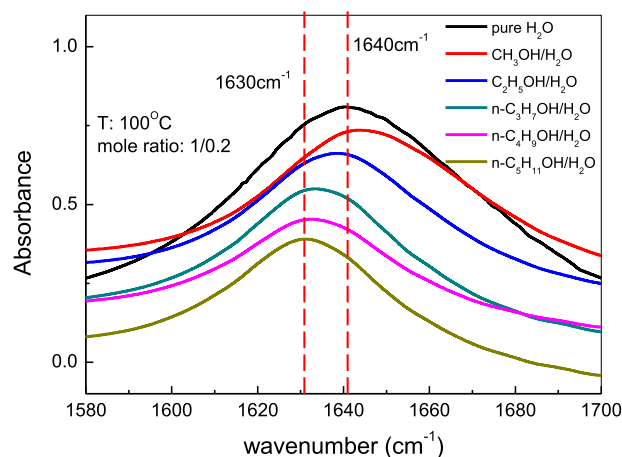


Figure 5. Effect of alcohol chain length on water structural transformation. Infrared spectra of aqueous alcohol solutions at temperature 100 °C with the alcohol/water molar ratio of 1/0.2. The less ordered water structure at high temperature arises in large alcohol solutions.

jump arises, in which the new high-temperature structure (more disordered structure with the peak at about 1630 cm^{-1}) occurs only in the alcohol solutions with the alcohol bigger than ethanol. In the concentrated solutions used in this work, propanol and larger alcohol molecules form aggregations and can produce larger hydrophobic domains than short-chain alcohols.^{2,24} Similar to previous theoretical studies⁴⁷ on protein surfaces, water can swing from ordered to disordered structures on large or flat hydrophobic surfaces in these concentrated alcohol solutions. On smaller hydrophobic domains, such a transformation does not exist.⁴⁷

Dangling OH at Hydrophobic Interfaces. The enhancement of water structure and temperature-dependent water structural transformation imply that a micro phase separation must exist in the alcohol–water solutions. There must be microscopic molecular hydrophobic interfaces arising from the hydration shells. With the solute concentration increasing, the surface topography of molecular hydrophobic interfaces would change. From theoretical studies, Cheng et al.⁴⁷ reported that the

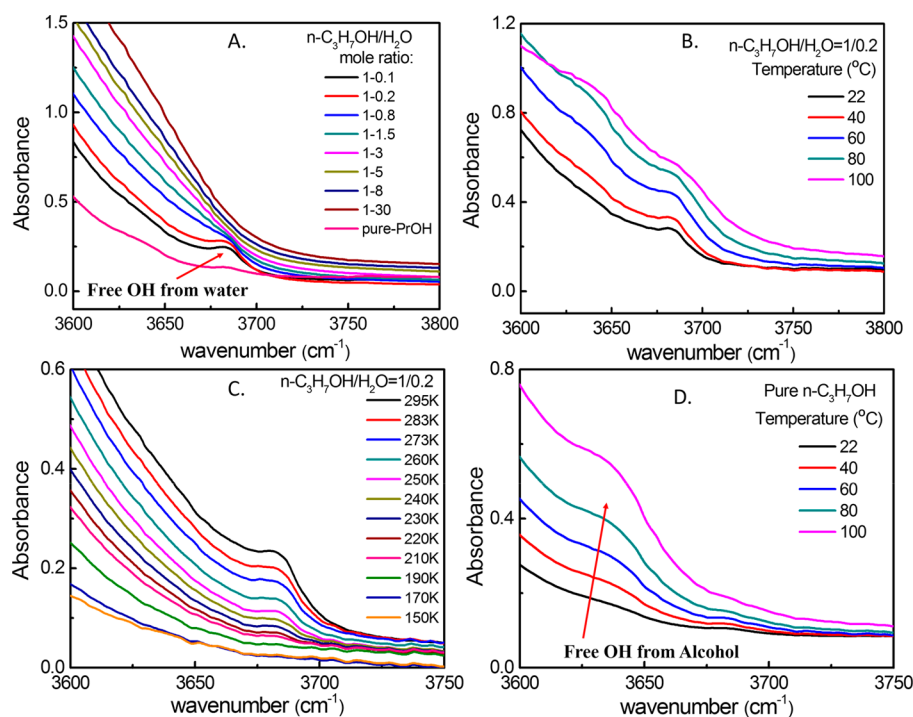


Figure 6. (A) Infrared spectra of the water OH stretching mode region of aqueous *n*-propanol ($n\text{-C}_3\text{H}_7\text{OH}/\text{H}_2\text{O}$) solution with different propanol concentrations. The small peak at 3683 cm^{-1} can be attributed to dangling OH from water. (B) The dangling OH peak decreases as the temperature increases, and the other small peak gradually increases at 3635 cm^{-1} , which can be assigned to dangling OH from propanol. (C) The dangling OH from water decreases with the temperature decrease. (D) The dangling OH from propanol also can be seen at high temperature in the pure propanol.

strong influence of surface topography on the structure and free energy of hydrophobic hydration is likely to hold in general and will be particularly important in various biological, geological, and environmental processes. The dangling OH arising at hydrophobic interfaces is used to further investigate the topography-dependent water structural transformation.

Figure 6A shows infrared spectra of the free OH stretching mode region of aqueous *n*-propanol ($n\text{-C}_3\text{H}_7\text{OH}/\text{H}_2\text{O}$) solutions with different propanol concentrations. A small OH stretch peak around 3683 cm^{-1} arises with the increase of solute concentration and disappears in the pure *n*-propanol solution. This small peak is the dangling OH from water. The dangling alcohol OH is at about 3635 cm^{-1} (Figures S12 and 6D). The dangling water OH stretch peak is also observed in the concentrated ethanol solutions and *n*-butanol solutions (Figure 3B) but is not observed in the concentrated methanol solutions (Figures S10 and S11). Figure 3B shows the intensity of the dangling OH band generally increases with increasing alkyl size in solutions of the same concentration (1/0.2).

The dangling OH peak has a frequency of 3683 cm^{-1} and a width of $\sim 16\text{ cm}^{-1}$. The results are different from that observed by Ben-Amotz and co-workers, in which the dangling OH peak has a frequency of 3661 cm^{-1} and a width of 33 cm^{-1} in a dilute solution,^{48,49} but similar to the dangling OH stretch peaks previously observed at macroscopic water–monolayer interfaces, in which the dangling OH peaks are centered at $\sim 3680\text{ cm}^{-1}$ with a bandwidth of 17 cm^{-1} .⁵⁰ In the concentrated alcohol solutions, the hydrophobic groups aggregate to form large clusters and produce large hydrophobic surfaces. Longer-chain alcohols are likely to produce larger hydrophobic domains than short-chain alcohols. This is why the dangling OH peak is more pronounced in a solution with

large alcohols (Figure 3B). However, in the dilute alcohol solutions, the dangling OH bonds are associated with single hydrophobic groups rather than aggregates. This means that the hydrophobic surface is convex, like a ball. Thus, the dangling OH in dilute solutions has a different feature (peak at 3661 cm^{-1} and a width of 33 cm^{-1} , as observed by Ben-Amotz and co-workers).^{48,49} The results also suggest that the size and curvature of the exposed hydrophobic surface can influence the water's propensity to form dangling OH.

With the increase of temperature, the water dangling OH peaks become broader, as shown in Figure 6B (the feature is clearer in Figure S13). The water dangling OH has a width of about 30 cm^{-1} at $100\text{ }^\circ\text{C}$. This is because the water molecules on interfaces change from an ordered structure to disordered structures with the temperature increase, as revealed by the bending spectra in Figure 4. The inhomogeneous distribution of disordered structures widens the peak of water dangling OH.

With temperature decreasing from room temperature to 150 K , the intensity of water dangling OH decreases (Figure 6C). This is different from that observed in the ice–monolayer or ice–solid interfaces, in which the peaks of dangling OH become sharper as the temperature decreases.⁵¹ With temperature decreasing, some water molecules begin to freeze and form ice. Alcohol molecules are squeezed to form bigger clusters, resulting in a smaller total area of hydrophobic interface (water–monolayer-like interface). This leads to the decrease of the total amount of dangling OH. It is interesting that there is hardly a shift of dangling OH peak position, compared with the pronounced blue shifts of water bend spectra (Figure S14) as temperature decreases. The difference is because the two observations deliver different information.

The bending spectra reflect the overall water structural change, but the dangling OH represents only the change on interface. Water structure becomes ordered (more tetrahedral and stronger hydrogen bonds) at low temperature, and accordingly we observe blue shifts in the bending spectra. However, water in the hydrophobic shell is already very ordered at room temperature because of the hydrophobic effect. Thus, lowering the temperature cannot order the water on the interface as much, so that the dangling OH at hydrophobic interfaces has a very limited frequency shift.

In summary, the water structural transformation in concentrated alcohol–water solutions is studied in this work, and the water structure on the hydrophobic surface is observed to be enhanced at room temperature in alcohol–water liquids. Theoretical studies⁴⁷ suggested that water structure toward the hydrophobic surface depends strongly on the surface topography: clathrate-like structures dominate the convex hydrophobic surface, whereas the hydration shell near the flat surface fluctuates between clathrate-like and less-ordered or inverted structures. In the methanol solutions, the hydrophobic interface is convex because it is difficult for methanol to form large clusters, whereas the hydrophobic interface is nearly flat in solutions of large alcohols (like *n*-propanol or *n*-butanol) because of severe clustering. Thus, the transformation from a more ordered to a less ordered water structure was observed only in the large alcohol solutions. The probability of forming a dangling OH increases as the hydrophobic chain length increases and concentration increases, also confirming the curvature of the interface plays important roles in the water structural transformation. Our experimental results show that the length of the alkyl chain is important in determining the properties of the hydrophobic surface. Clustering is also critical, because in the concentrated *n*-propanol solutions water can swing from clathrate-like to inverted structure (Figure 4), but only the clathrate-like structure was observed on the surface of a single *n*-propanol chain in the dilute solution.¹⁸ Though our spectroscopic observations suggest the enhancement of water structure in the hydrophobic shell at room temperature, the enhanced hydrogen-bond structure cannot be truly ice-like. The dangling OH feature in the solutions is very different from that in the ice–air or ice–monolayer interface,⁵¹ and the OH bend spectra are much broader in ice than what we observed in the solutions.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at <https://pubs.acs.org/doi/10.1021/acs.jpcllett.9b03429>.

Detailed description of the experimental methods, Figures S1–S14, Tables S1 and S2, and references (PDF)

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Notes

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■ REFERENCES

- (1) Ball, P. Water as an Active Constituent in Cell Biology. *Chem. Rev.* **2008**, *108*, 74–108.
- (2) Chandler, D. Interfaces and the Driving Force of Hydrophobic Assembly. *Nature* **2005**, *437*, 640–647.
- (3) Franks, F.; Ives, D. J. G. The Structural Properties of Alcohol–Water Mixtures. *Q. Rev., Chem. Soc.* **1966**, *20*, 1–44.
- (4) Franks, F.; Desnoyers, J. E. Alcohol–Water Mixtures Revisited. *Water Sci. Rev.* **1985**, *1*, 171–232.
- (5) Frank, H. S.; Evans, M. W. Free Volume and Entropy in Condensed Systems. 3. Entropy in Binary Liquid Mixtures - Partial Molal Entropy in Dilute Solutions - Structure and Thermodynamics in Aqueous Electrolytes. *J. Chem. Phys.* **1945**, *13*, 507–532.
- (6) Li, I. T. S.; Walker, G. C. Signature of Hydrophobic Hydration in a Single Polymer. *Proc. Natl. Acad. Sci. U. S. A.* **2011**, *108*, 16527–16532.
- (7) Petersen, C.; Tielrooij, K. J.; Bakker, H. J. Strong Temperature Dependence of Water Reorientation in Hydrophobic Hydration Shells. *J. Chem. Phys.* **2009**, *130*, 214511.
- (8) Zhang, X. Y.; Zhu, Y. X.; Granick, S. Hydrophobicity at a Janus Interface. *Science* **2002**, *295*, 663–666.
- (9) Lum, K.; Chandler, D.; Weeks, J. D. Hydrophobicity at Small and Large Length Scales. *J. Phys. Chem. B* **1999**, *103*, 4570–4577.
- (10) Matysiak, S.; Debenedetti, P. G.; Rossky, P. J. Dissecting the Energetics of Hydrophobic Hydration of Polypeptides. *J. Phys. Chem. B* **2011**, *115*, 14859–14865.
- (11) Laage, D.; Stirnemann, G.; Hynes, J. T. Why Water Reorientation Slows without Iceberg Formation Around Hydrophobic Solutes. *J. Phys. Chem. B* **2009**, *113*, 2428–2435.
- (12) Raschke, T. M.; Levitt, M. Nonpolar Solutes Enhance Water Structure Within Hydration Shells While Reducing Interactions between Them. *Proc. Natl. Acad. Sci. U. S. A.* **2005**, *102*, 6777–6782.
- (13) Garde, S.; Patel, A. J. Unraveling the Hydrophobic Effect, One Molecule at a Time. *Proc. Natl. Acad. Sci. U. S. A.* **2011**, *108*, 16491–16492.
- (14) Dixit, S.; Crain, J.; Poon, W. C. K.; Finney, J. L.; Soper, A. K. Molecular Segregation Observed in a Concentrated Alcohol–Water Solution. *Nature* **2002**, *416*, 829–832.
- (15) Laaksonen, A.; Kusalik, P. G.; Svishchev, I. M. Three-Dimensional Structure in Water–Methanol Mixtures. *J. Phys. Chem. A* **1997**, *101*, 5910–5918.
- (16) Meng, E. C.; Kollman, P. A. Molecular Dynamics Studies of the Properties of Water Around Simple Organic Solutes. *J. Phys. Chem.* **1996**, *100*, 11460–11470.
- (17) Fidler, J.; Rodger, P. M. Solvation Structure Around Aqueous Alcohols. *J. Phys. Chem. B* **1999**, *103*, 7695–7703.
- (18) Davis, J. G.; Gierszal, K. P.; Wang, P.; Ben-Amotz, D. Water Structural Transformation at Molecular Hydrophobic Interfaces. *Nature* **2012**, *491*, 582–585.
- (19) Galamba, N. Water's Structure Around Hydrophobic Solutes and the Iceberg Model. *J. Phys. Chem. B* **2013**, *117*, 2153–2159.

- (20) Graziano, G. Comment on "Water's Structure around Hydrophobic Solutes and the Iceberg Model. *J. Phys. Chem. B* **2014**, *118*, 2598–2599.
- (21) Dixit, S.; Soper, A. K.; Finney, J. L.; Crain, J. Water Structure and Solute Association in Dilute Aqueous Methanol. *Europhys. Lett.* **2002**, *59*, 377–383.
- (22) Tsai, J.; Gerstein, M.; Levitt, M. Keeping the Shape But Changing the Charges: A Simulation Study of Urea and Its Iso-Steric Analogs. *J. Chem. Phys.* **1996**, *104*, 9417–9430.
- (23) Dixit, S.; Poon, W. C. K.; Crain, J. Hydration of Methanol in Aqueous Solutions: a Raman Spectroscopic Study. *J. Phys.: Condens. Matter* **2000**, *12*, L323–L328.
- (24) Wakisaka, A.; Komatsu, S.; Usui, Y. Solute-Solvent and Solvent-Solvent Interactions Evaluated Through Clusters Isolated From Solutions: Preferential Solvation in Water-Alcohol Mixtures. *J. Mol. Liq.* **2001**, *90*, 175–184.
- (25) Ni, Y. C.; Skinner, J. L. IR and SFG Vibrational Spectroscopy of the Water Bend in the Bulk Liquid and at the Liquid-Vapor Interface, Respectively. *J. Chem. Phys.* **2015**, *143*, 014502.
- (26) Zelent, B.; Nucci, N. V.; Vanderkooi, J. M. Liquid and Ice Water and Glycerol/Water Glasses Compared by Infrared Spectroscopy From 295 to 12 K. *J. Phys. Chem. A* **2004**, *108*, 11141–11150.
- (27) Falk, M. Frequencies of H-O-H, H-O-D and D-O-D Bending Fundamentals in Liquid Water. *J. Raman Spectrosc.* **1990**, *21*, 563–567.
- (28) Devlin, J. P.; Sadlej, J.; Buch, V. Infrared Spectra of Large H₂O Clusters: New Understanding of the Elusive Bending Mode of Ice. *J. Phys. Chem. A* **2001**, *105*, 974–983.
- (29) Pavlovic, M.; Baranovic, G.; Lovrekovic, D. Raman Study of the Bending Band of Water. *Spectrochim. Acta, Part A* **1991**, *47*, 897–906.
- (30) Ashihara, S.; Fujioka, S.; Shibuya, K. Temperature Dependence of Vibrational Relaxation of the OH Bending Excitation in Liquid H₂O. *Chem. Phys. Lett.* **2011**, *502*, 57–62.
- (31) Freda, M.; Piluso, A.; Santucci, A.; Sassi, P. Transmittance Fourier Transform Infrared Spectra of Liquid Water in the Whole Mid-Infrared Region: Temperature Dependence and Structural Analysis. *Appl. Spectrosc.* **2005**, *59*, 1155–1159.
- (32) Falk, M. The Frequency of the H-O-H Bending Fundamental in Solids and Liquids. *Spectrochim. Acta, Part A* **1984**, *40*, 43–48.
- (33) Chuntunov, L.; Kumar, R.; Kuroda, D. G. Non-Linear Infrared Spectroscopy of the Water Bending Mode: Direct Experimental Evidence of Hydration Shell Reorganization? *Phys. Chem. Chem. Phys.* **2014**, *16*, 13172–13181.
- (34) Laage, D.; Stirnemann, G.; Sterpone, F.; Hynes, J. T. Water Jump Reorientation: From Theoretical Prediction to Experimental Observation. *Acc. Chem. Res.* **2012**, *45*, 53–62.
- (35) Stirnemann, G.; Hynes, J. T.; Laage, D. Water Hydrogen Bond Dynamics in Aqueous Solutions of Amphiphiles. *J. Phys. Chem. B* **2010**, *114*, 3052–3059.
- (36) Yoshida, K.; Ibuki, K.; Ueno, M. Pressure and Temperature Effects on H-2 Spin-Lattice Relaxation Times and H-1 Chemical Shifts in tert-Butyl Alcohol- and Urea-D₂O Solutions. *J. Chem. Phys.* **1998**, *108*, 1360–1367.
- (37) Shimizu, A.; Fumino, K.; Yukiyasu, K.; Taniguchi, Y. NMR Studies on Dynamic Behavior of Water Molecule in Aqueous Denaturant Solutions at 25°C: Effects of Guanidine Hydrochloride, Urea and Alkylated Ureas. *J. Mol. Liq.* **2000**, *85*, 269–278.
- (38) Sato, T.; Buchner, R. The Cooperative Dynamics of the H-bond System in 2-Propanol/Water Mixtures: Steric Hindrance Effects of Nonpolar Head Group. *J. Chem. Phys.* **2003**, *119*, 10789–10800.
- (39) Tielrooij, K. J.; Hunger, J.; Buchner, R.; Bonn, M.; Bakker, H. J. Influence of Concentration and Temperature on the Dynamics of Water in the Hydrophobic Hydration Shell of Tetramethylurea. *J. Am. Chem. Soc.* **2010**, *132*, 15671–15678.
- (40) Rezus, Y. L. A.; Bakker, H. J. Strong Slowing Down of Water Reorientation in Mixtures of Water and Tetramethylurea. *J. Phys. Chem. A* **2008**, *112*, 2355–2361.
- (41) Rezus, Y. L. A.; Bakker, H. J. Observation of Immobilized Water Molecules Around Hydrophobic Groups. *Phys. Rev. Lett.* **2007**, *99*, 148301.
- (42) Bakulin, A. A.; Pshenichnikov, M. S.; Bakker, H. J.; Petersen, C. Hydrophobic Molecules Slow Down the Hydrogen-Bond Dynamics of Water. *J. Phys. Chem. A* **2011**, *115*, 1821–1829.
- (43) Sudo, S.; Shinyashiki, N.; Kitsuki, Y.; Yagihara, S. Dielectric Relaxation Time and Relaxation Time Distribution of Alcohol-Water Mixtures. *J. Phys. Chem. A* **2002**, *106*, 458–464.
- (44) Grossmann, G. H.; Ebert, K. H. Formation of Clusters in 1-Propanol/Water-Mixtures. *Ber. Bunsen-Ges* **1981**, *85*, 1026–1029.
- (45) Privalov, P. L.; Gill, S. J. Stability of Protein-Structure and Hydrophobic Interaction. *Adv. Protein Chem.* **1988**, *39*, 191–234.
- (46) Kauzmann, W. Some Factors in the Interpretation of Protein Denaturation. *Adv. Protein Chem.* **1959**, *14*, 1–63.
- (47) Cheng, Y. K.; Rossky, P. J. Surface Topography Dependence of Biomolecular Hydrophobic Hydration. *Nature* **1998**, *392*, 696–699.
- (48) Perera, P. N.; Fega, K. R.; Lawrence, C.; Sundstrom, E. J.; Tomlinson-Phillips, J.; Ben-Amotz, D. Observation of Water Dangling OH Bonds Around Dissolved Nonpolar Groups. *Proc. Natl. Acad. Sci. U. S. A.* **2009**, *106*, 12230–12234.
- (49) Davis, J. G.; Rankin, B. M.; Gierszal, K. P.; Ben-Amotz, D. On the Cooperative Formation of Non-Hydrogen-Bonded Water at Molecular Hydrophobic Interfaces. *Nat. Chem.* **2013**, *5*, 796–802.
- (50) Tian, C. S.; Shen, Y. R. Structure and Charging of Hydrophobic Material/Water Interfaces Studied by Phase-Sensitive Sum-Frequency Vibrational Spectroscopy. *Proc. Natl. Acad. Sci. U. S. A.* **2009**, *106*, 15148–15153.
- (51) Wei, X.; Miranda, P. B.; Zhang, C.; Shen, Y. R. Sum-Frequency Spectroscopic Studies of Ice Interfaces. *Phys. Rev. B: Condens. Matter Mater. Phys.* **2002**, *66*, 085401.