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# Hydrophobic Molecules Slow Down the Hydrogen-Bond Dynamics of Water

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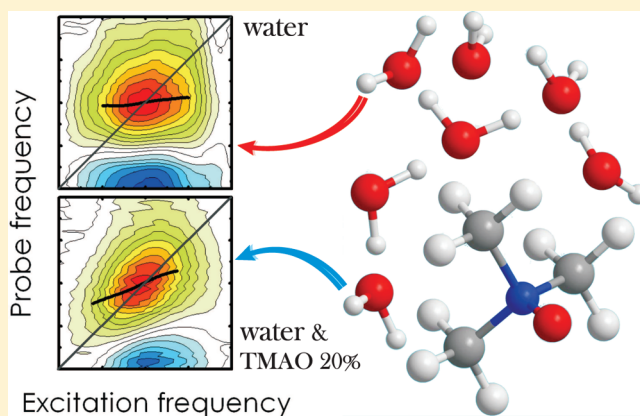
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S Supporting Information

**ABSTRACT:** We study the spectral and orientational dynamics of HDO molecules in solutions of tertiary-butyl-alcohol (TBA), trimethyl-amine-oxide (TMAO), and tetramethylurea (TMU) in isotopically diluted water (HDO:D<sub>2</sub>O and HDO:H<sub>2</sub>O). The spectral dynamics are studied with femtosecond two-dimensional infrared spectroscopy and the orientational dynamics with femtosecond polarization-resolved vibrational pump–probe spectroscopy. We observe a strong slowing down of the spectral diffusion around the central part of the absorption line that increases with increasing solute concentration. At low concentrations, the fraction of water showing slow spectral dynamics is observed to scale with the number of methyl groups, indicating that this effect is due to slow hydrogen-bond dynamics in the hydration shell of the methyl groups of the solute molecules. The slowing down of the vibrational frequency dynamics is strongly correlated with the slowing down of the orientational mobility of the water molecules. This correlation indicates that these effects have a common origin in the effect of hydrophobic molecular groups on the hydrogen-bond dynamics of water.



## I. INTRODUCTION

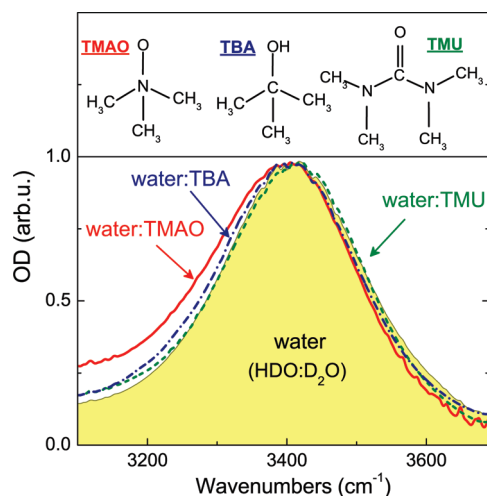
The aggregation of hydrophobic (water fearing) molecular groups in aqueous environments plays an important role in the structuring and chemical reaction dynamics of biological systems. Examples are the folding of proteins, the formation of membrane bilayers, and the binding of substrates to enzymes. Thermodynamic measurements showed that the introduction of a hydrophobic solute in water is associated with a negative excess entropy and a strong increase in heat capacity, thus suggesting a structuring of the liquid and an increase of the strength of the hydrogen-bond interaction. These thermodynamics effects have been explained by Frank and Evans with a model that is often referred to as the “iceberg model”.<sup>1</sup> According to this model the water surrounding the hydrophobic solute acquires a well-ordered (clathrate) structure (explaining the negative excess entropy) that melts when the temperature is increased (explaining the large heat capacity). More recently, Pratt and Chandler developed models for hydrophobic hydration in which the temperature dependence of the entropy and enthalpy changes associated with hydrophobic hydration could be well accounted for using macroscopic parameters of liquid water.<sup>2–4</sup>

Molecular scale studies did not find evidence that the structure of water surrounding hydrophobic groups would be different from bulk liquid water. For instance, in neutron scattering studies the oxygen–oxygen distances of the solvating water molecules were observed to be similar as in bulk liquid water.<sup>5–8</sup> Interestingly, the *dynamics* of water molecules surrounding hydrophobic groups were observed to be different from those of bulk liquid water. With nuclear magnetic resonance (NMR),<sup>9–13</sup> dielectric relaxation,<sup>14–16</sup> and femtosecond mid-infrared spectroscopy,<sup>17–19</sup> it was observed that solvating water molecules show slower orientational dynamics than the molecules in bulk liquid water. In a femtosecond infrared study of the reorientation of water hydrating tertiary-butyl-alcohol (TBA) and tetramethylurea (TMU), a slowing down of the solvating water molecules by a factor  $\sim 4$  was reported.<sup>19</sup> In a recent dielectric relaxation study of aqueous TMU solutions, the reorientation of the water molecules solvating TMU was found to slow down by a factor of 3–10, and

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**Figure 1.** Structural formulas of tertiary-butyl-alcohol (TBA), trimethylamine-oxide (TMAO), and tetramethylurea (TMU) and linear absorption spectra of the O–H stretch vibration of HDO for solutions of TBA, TMA, and TMU in 4% HDO:H<sub>2</sub>O and for pure 4% HDO:H<sub>2</sub>O. The concentration of the solutions is 10 water molecules per solute molecule ( $w = 0.1$ ).

the amount of slowing down was observed to increase with the concentration of TMU.<sup>16</sup> These results are consistent with the average slowing down of the water molecules in solution as observed with NMR.<sup>9–13,20</sup> Interestingly, the strong slowing down of the reorientation in the hydrophobic hydration shells is not reproduced by molecular dynamics simulations.<sup>21,22</sup> In a classical MD study (using SPC/E water) the reorientation of OH groups tangential to hydrophobic methyl groups was calculated to slow down only by a factor of  $\sim 1.4$  at low solute concentrations.<sup>21</sup>

More insight into the effects of hydrophobes on water can be obtained by probing the hydrogen-bond dynamics of water surrounding hydrophobic molecular groups. In recent years it was demonstrated that valuable information on the hydrogen-bond dynamics of liquid water can be obtained with third-order vibrational spectroscopic techniques like spectral hole burning, echo-peak shift spectroscopy and two-dimensional (2D) vibrational spectroscopy.<sup>23–27</sup> With these methods it was found that the hydrogen-bond network of water shows dynamics on different time scales, ranging from tens of femtoseconds up to picoseconds. Here we use 2D vibrational spectroscopy and polarization-resolved pump–probe spectroscopy to study the hydrogen-bond and reorientation dynamics of water molecules interacting with hydrophobic groups of three amphiphilic solutes.

## II. EXPERIMENTAL SECTION

We perform two-dimensional vibrational spectroscopy (2D-IR) and polarization-resolved pump–probe experiments on HDO molecules of solutions of tertiary-butyl-alcohol (TBA), trimethylamine-oxide (TMAO), and tetramethylurea (TMU) (Aldrich, 99% pure), in isotopically diluted water. These amphiphilic solutes have 3 (TBA, TMAO) or 4 (TMU) hydrophobic methyl groups and one hydrophilic group arranged in a similar geometry (Figure 1). The hydrophilic groups of these solutes are quite different: TMAO possesses a very polar N<sup>+</sup>O<sup>−</sup> group, while TBA possesses an hydroxyl group that is very similar to water hydroxyl groups. The solute concentrations are defined

with a parameter  $w$  that is equal to the ratio  $w$  of the number of TBA/TMAO/TMU and water;  $w$  was ranging from 0 to 0.2 for TBA and TMAO (because of solubility reasons), and from 0 to 1 for TMU. As the absorption of the hydroxyl group of TBA overlaps with the absorption spectrum of HDO, this hydroxyl group may form a small contribution to the measured signal. At the highest studied concentration of TBA of  $w = 0.2$ , this contribution will still be less than 10%. In all experiments the concentration of HDO molecules is kept sufficiently low (less than 1:20) to avoid resonant (Förster) energy transfer between the O–H/O–D groups.<sup>28–30</sup> The experiments are performed at a temperature of 295 K.

The probing of the OH/OD stretch modes of HDO:D<sub>2</sub>O/HDO:H<sub>2</sub>O has several advantages and disadvantages. A disadvantage of probing the OH stretch mode is that its vibrational lifetime of 0.7 ps is  $\sim 2$  times shorter than the vibrational lifetime of the O–D stretch mode. As a result, the dynamics can be followed over a longer time interval for the O–D vibration. An advantage of probing the OH stretch vibration is that the spectral dynamics of the OH stretch vibration are slower than those of the OD stretch vibration (owing to a slower D<sub>2</sub>O bath), and that the absorption band of the OH stretch vibration is less motionally narrowed than that of the OD stretch vibration,<sup>31</sup> making the spectral diffusion dynamics of the OH clearer and easier to measure with the 2D-IR technique. Therefore, the 2D-IR experiments were performed on the O–H vibration of HDO for solutions in HDO:D<sub>2</sub>O and the polarization-resolved studies on the O–D vibration of HDO for solutions in HDO:H<sub>2</sub>O.

The 2D-IR experiment is a heterodyne detected three-pulse photon echo experiment.<sup>26,27,32,34</sup> In this experiment a pair of optical pulses creates a frequency-modulated population grating in the sample with a finesse determined by the pulse separation  $\tau_{12}$ . This grating evolves during a waiting time  $T$  during which hydrogen-bond fluctuations wash out the frequency fringes. The third pulse is scattered off the remaining population grating, thus producing the signal. The signal amplitude is determined by the extent of memory loss for the initial frequencies of fringes and dissipation during the waiting time  $T$ . The dependence of the signal on the excitation frequency  $\omega_1$  is obtained by performing many experiments in which  $\tau_{12}$  is varied. Fourier transform of all these signals gives the dependence of the signal on  $\omega_1$ . The probing frequency axis is acquired by interferometric superposition of the echo signal with a fourth laser pulse that acts as a local oscillator. The ( $\omega_3$ ) frequency dependence of the heterodyned echo signal is obtained by dispersing the signal and the fourth pulse with a polychromator. The light is detected with a 64 elements mercury–cadmium–telluride (MCT) array.

Detailed information on the spectral dynamics can be obtained by plotting the frequency  $\omega_{3,\text{max}}$  of the maximum probe response at a given excitation frequency  $\omega_1$  and by calculating the slope of the  $\omega_{3,\text{max}}(\omega_1)$  function:<sup>32,33</sup>

$$S(T) = \left. \frac{\partial \omega_{3,\text{max}}}{\partial \omega_1} \right|_T \quad (1)$$

When  $S(T)$  has its maximum value of 1, the excitation and probing frequency are fully correlated, meaning that there has been no spectral diffusion; when  $S(T)$  becomes equal to zero, the correlation has completely decayed, indicating that the spectral equilibration is complete. The slope analysis was initially developed for the case of Gaussian frequency dynamics. However, even if the dynamics are not Gaussian, the slope value can still

serve as a measure for spectral equilibration, but it can no longer be directly associated with a single frequency-frequency correlation function.<sup>35</sup>

The light source for 2D-IR experiments is an optical parametric amplifier (OPA)<sup>36</sup> providing 70 fs pulses centered around the OH stretching mode of the HDO molecule at 3420 cm<sup>-1</sup>. The procedure of data acquisition and processing was similar to the procedure described before.<sup>37</sup> The sample is a thin ~40–80 μm film in a wire-guided jet.<sup>38</sup> The optical density is <0.4. The 2D-IR experiment on the O–H stretch mode of HDO:D<sub>2</sub>O provides information about the spectral dynamics up to waiting times of 2 ps. At later times the 2D spectrum is too much dominated by the thermal response that results from the relaxation and equilibration of the excitation energy over the focal volume.

In the polarization-resolved pump–probe experiments, the O–D vibration of HDO:H<sub>2</sub>O with the lifetime of 1.8 ps is probed, which allows the measurement of the anisotropy over an 8-ps long time interval. The O–D vibration of HDO:H<sub>2</sub>O has a strong absorption around 4 μm (2500 cm<sup>-1</sup>). The mid-infrared light pulses are generated via parametric amplification processes in β-barium borate (BBO) and potassium niobate (KNbO<sub>3</sub>) crystals that are pumped with the pulses from a commercial Ti:sapphire amplifier system (Hurricane, Spectraphysics: 800 nm, 100 fs, 1 mJ, 1 kHz). We obtain pulses at 4 μm with a duration of 150 fs and a pulse energy of ~3 μJ.

Probe and reference pulses are generated by reflecting small fractions of the generated 4 μm pulses by a wedged CaF<sub>2</sub> window. The main transmitted light beam forms the pump beam. The polarization of the pump is rotated using a λ/2 plate to 45° with respect to that of the probe beam. The pump excites a few percent of the O–D stretch vibration to the first excited vibrational state. This excitation results in an increased transmission at the frequency of the fundamental  $\nu = 0 \rightarrow 1$  transition and an induced absorption at the  $\nu = 1 \rightarrow 2$  transition. These transmission changes are monitored with the probe pulse that is delayed by a time  $T$  with respect to the pump. After the sample, the probe and reference beams are focused onto the entrance slit of a spectrometer, which disperses the beams onto a 2 × 32 liquid-nitrogen-cooled MCT array. Before entering the spectrometer, the probe beam passes through a polarizer allowing the selection of either its parallel or perpendicular polarization component with respect to the pump polarization. This selection results in transient absorptions  $\Delta\alpha_{||}(T)$  and  $\Delta\alpha_{\perp}(T)$ , respectively. The signals  $\Delta\alpha_{||}(T)$  and  $\Delta\alpha_{\perp}(T)$  are used to construct the so-called rotational anisotropy parameter

$$R(T) = \frac{\Delta\alpha_{||}(T) - \Delta\alpha_{\perp}(T)}{\Delta\alpha_{||}(T) + 2\Delta\alpha_{\perp}(T)} \quad (2)$$

which is a quantity whose decay reflects the reorientation of the observed vibration.

### III. RESULTS

Figure 1 presents linear absorption spectra of the O–H band of pure HDO:D<sub>2</sub>O and solutions of TBA, TMAO, and TMU in HDO:D<sub>2</sub>O with  $w = 0.1$ . It is seen that the O–H absorption spectra look quite similar, in spite of the high concentration of solute. This finding indicates that the introduction of the amphiphilic solutes keeps the hydrogen bonds between the water molecules intact. The O–H absorption spectrum of the TMAO

solution possesses a small red wing, indicating that the average hydrogen-bond is stronger in this solution as a result of the interactions between water and the polar N<sup>+</sup>O<sup>-</sup> group.<sup>39,40</sup>

Figure 2 presents 2D-IR spectral contour plots at different waiting times for pure HDO:D<sub>2</sub>O and for solutions of TBA, TMAO, and TMU in HDO:D<sub>2</sub>O, with  $w = 0.1$ . At a waiting time of 0 ps, the 2D-IR contour is elongated along the diagonal, which means that there is a strong correlation between the frequency at which the O–H stretch vibration is excited and the frequency at which the vibration is probed. This observation demonstrates that the O–H absorption line contains significant inhomogeneous broadening. For the TMU solution the 2D-IR spectrum also shows a small negative feature at frequencies above the fundamental transition. This signal is due to an induced phase modulation effect that is only present when the laser pulses overlap ( $T \approx 0$ ). This signal is observed only for the TMU solution because for this system the sample is relatively thick: the thickness was always adjusted to form a stable wire-guided jet, and for solutions of high viscosity a thicker jet was needed.

For pure HDO:D<sub>2</sub>O, the spectral contour acquires an asymmetric shape at short waiting times ( $T = 0.1, 0.25$  ps). It is seen that the response in  $\omega_3$  is very broad in case the O–H band is excited in the blue wing (high  $\omega_1$ ), and that the response remains relatively narrow if the absorption band is excited in the center or in the red wing (low  $\omega_1$ ). This phenomenon has been observed before and has been explained from rapid hydrogen-bond dynamics.<sup>41,42</sup> At a longer waiting time of ~1 ps, the spectral contour measured for pure HDO:D<sub>2</sub>O acquires a broad, symmetrical circular shape, which shows that after this time the spectral equilibration between strongly and weakly hydrogen-bonded water molecules is nearly complete.

For the solutions containing TBA, TMAO, or TMU, the spectral contour possesses a similar asymmetry at early waiting times as was observed for pure HDO:D<sub>2</sub>O. However, in contrast to pure HDO:D<sub>2</sub>O, the asymmetry is still present at a waiting time of 1 ps, demonstrating that the spectral equilibration of the different water molecules in this solution is much slower. For all waiting times, pumping in the blue wing results in a much narrower response in  $\omega_3$  than observed for pure HDO:D<sub>2</sub>O, indicating that the hydrogen-bond dynamics have slowed down significantly.

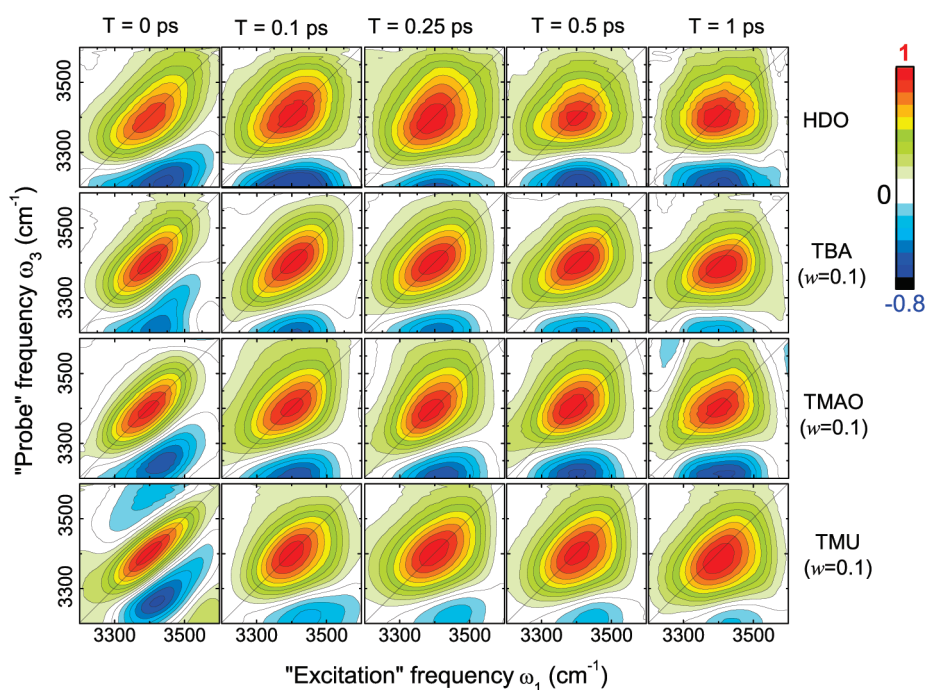
Figure 3a presents the average slope of the 2D spectra within a range of  $\pm 50$  cm<sup>-1</sup> around the absorption maximum as a function of waiting time for different solutions of TMU in HDO:D<sub>2</sub>O. In this analysis we did not correct for the contribution of the excited state absorption. This approach is justified because of the large anharmonicity of the O–H stretch vibration. For all solutions the slope shows an initial rapid decay and then appears to saturate at a nonzero level. This level increases with increasing concentration of TMU. We cannot measure the slope values at waiting times >2 ps because of the limited lifetime of the O–H stretch vibration and the rise of a thermal signal. The increase of the slope values at 2 ps with TMU concentration shows that for a significant fraction of the water molecules that solvate TMU the spectral diffusion is much slower than for bulk liquid water.

To quantize the slowing down effect of the solutes on the water spectral dynamics, we fit the slope  $S(T)$  for all measured solutes and concentrations with the following expression

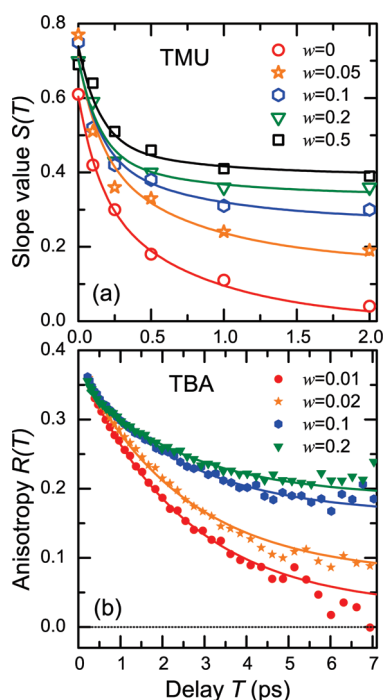
$$S(T) = A_1 e^{-T/\tau_1} + A_2 e^{-T/\tau_2} + A_0 \quad (3)$$

where  $A_1$  and  $A_2$  represent the fast and the slow spectral dynamics that are observed for pure liquid water. These time constants





**Figure 2.** Two-dimensional correlation spectra of pure HDO:D<sub>2</sub>O and of solutions of TBA, TMAO, and TMU in HDO:D<sub>2</sub>O with  $w = 0.1$ , measured at different waiting times. Positive signals (red color) correspond to bleaching of and stimulated emission from the fundamental transition while the excited state absorption is represented by negative values (blue color). Each 2D spectrum is normalized onto its maximum. The equilateral contours are drawn in 10% steps of the maximum amplitude.



**Figure 3.** Slope value  $S(T)$  (a) and anisotropy  $R(T)$  (b) as a function of the delay  $T$  for different concentrations. The slope values are calculated as an average over the range  $\pm 50 \text{ cm}^{-1}$  from the absorption maximum. The curves represent biexponential fits to the data using eqs 3 and 4.

have been assigned to local librational and O–O translational motions of the water molecules ( $\tau_1$ ), and more collective diffusional hydrogen-bond dynamics ( $\tau_2$ ), while  $A_0$  represents the fraction of water showing slow spectral dynamics. As we can measure

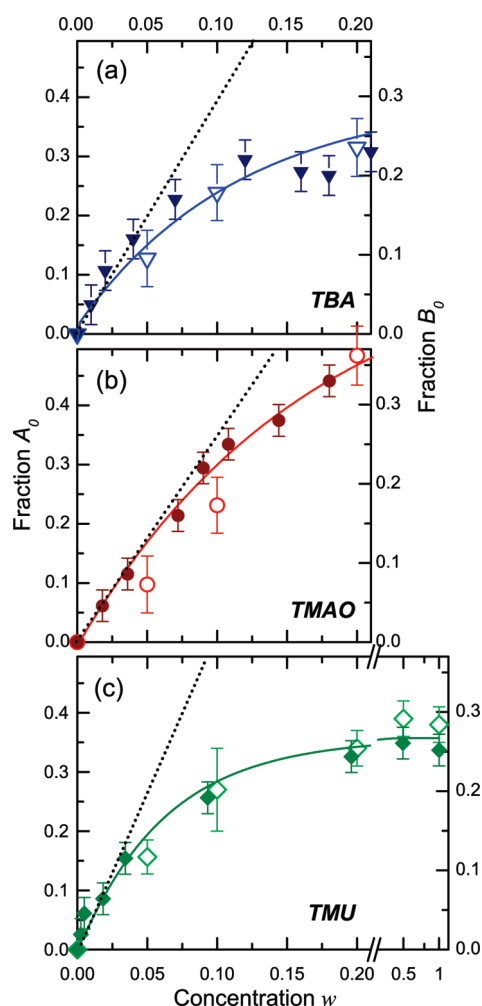
the slope value only with good quality up to a waiting time of 2 ps, we cannot determine the time constant of the slow spectral diffusion process; we estimate it to be longer than 5 ps. This implies that this spectral diffusion process is  $>4$  times slower than the main spectral diffusion component of bulk liquid water, for which a time constant  $\tau_2$  of 1.2 ps has been reported.<sup>25</sup> As we cannot determine the precise time constant of the slow spectral diffusion process, we model it as an offset with amplitude  $A_0$ .

We perform a global fit of eq 3, with the restriction that the parameters  $A_1$ ,  $\tau_1$ , and  $\tau_2$  are the same for all solutions (see Supporting Information for details). The amplitude  $A_1$  does not depend on the solute concentration because the hydrophobes primarily affect the hydrogen-bond network reorganization represented by  $A_2$ , and not the local librational and O–O translational motions represented by  $A_1$ . This result is consistent with the fact that the average hydrogen-bond strength (which restricts the librations and O–O translations) hardly changes with solute concentration. We find time constants  $\tau_1 = 0.15 \text{ ps}$  and  $\tau_2 = 0.78 \text{ ps}$ , which agree very well with literature data for HDO:D<sub>2</sub>O.<sup>25</sup> The fit results for TMU are represented by the solid curves in Figure 3a. With increasing solute concentration the amplitude  $A_2$  decreases while the amplitude  $A_0$  associated with the slow water molecules increases.

Figure 3b presents the anisotropy measured with polarization-resolved pump–probe spectroscopy as a function of the delay  $T$  for four different concentrations of TBA. The anisotropy shows a nonexponential decay as a function of the delay time  $T$ , similar to the observations for the slope  $S(T)$ . Likewise, the decay  $R(T)$  is described as

$$R(T) = B_1 e^{-T/\tau_{\text{or}}} + B_0 \quad (4)$$

where  $B_1$  represents the contribution to the observed anisotropy of the water molecules possessing fast orientational dynamics



**Figure 4.** Fraction  $A_0$  (left axis, open symbols) representing water molecules showing slow spectral diffusion, and the fraction  $B_0$  of slowly reorienting water molecules (right axis, filled symbols) as a function of solute concentration  $w$  for solutions of TBA (a), TMAO (b), and TMU (c). The values of  $A_0$  and  $B_0$  are obtained from fits to the data using eqs 3 and 4. The dotted lines represent linear fits to the low-concentration ( $w < 0.05$ ) anisotropy data. The anisotropy data for the TMAO and TMU solutions are obtained from previous work.<sup>17,18</sup>

with time constant  $\tau_{\text{or}}$  and  $B_0$  the contribution of water molecules showing a much slower reorientation. For all concentrations we obtain a good fit with  $\tau_{\text{or}} = 2.5$  ps, which is the same reorientation time constant as is observed for pure  $\text{HDO}:\text{H}_2\text{O}$ . The reorientation time of the solvation shell water varies from roughly 10 ps at low concentrations to 30 ps for TMU solutions with  $w > 0.2$ .<sup>19</sup> In this study we model the reorientation dynamics of the water molecules in the hydration shell as an offset, to allow for a quantitative comparison with the spectral dynamics that are measured in the 2D-IR experiments.

Figure 4 presents the values of  $A_0$  (open symbols) as a function of concentration for the solutions of TBA, TMAO, and TMU. For all three solutions  $S(T)$  shows a steep linear increase with solute concentration at low concentrations, and starts to saturate for concentrations  $w > 0.1$ . At low concentrations, the increase is steeper by a factor  $\sim 1.3$  for TMU than for TBA and TMAO, which demonstrates that the slow spectral dynamics is associated with water molecules solvating the hydrophobic part of TMU and TMAO (TMU has four methyl groups while TBA

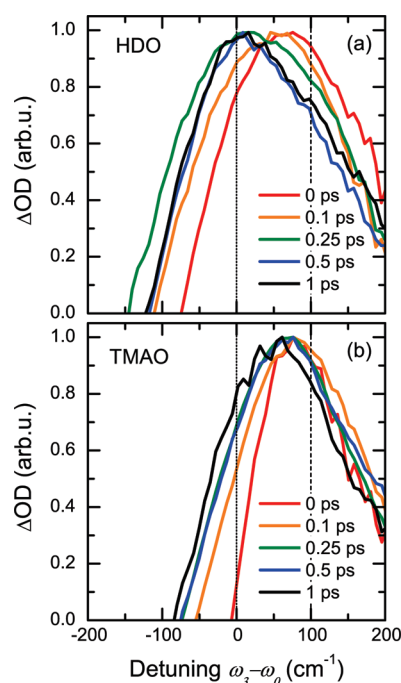
and TMAO have three methyl groups). It should be noted here that the size of the hydration shell of the hydrophobic part of the molecule does not need to scale rigorously with the number of methyl groups. The hydration shells of individual methyl groups overlap, thus possibly leading to a somewhat slower increase of the hydrophobic hydration shell with the number of methyl groups. The present results also demonstrate that the hydrophilic part of the molecule does not play an important role in the water hydrogen-bond dynamics. TBA and TMAO strongly differ in their hydrophilic part, but nevertheless show a similar increase of  $A_0$  at low concentrations ( $w \leq 0.1$ ).

In Figure 4 we also plot the fraction  $B_0$  (filled symbols) of slowly reorienting water molecules as a function of concentration. For TMAO and TMU this fraction is obtained from earlier studies.<sup>17,18</sup> To facilitate the comparison between the concentration dependencies of  $A_0$  and  $B_0$ , we use a scaling factor of 0.8 that is the same for all solutes and all concentrations. For all three solutes we observe a perfect correlation between the dependencies of  $A_0$  and  $B_0$  on the concentration  $w$ .  $A_0$  and  $B_0$  show the same linear increase at low concentrations ( $w < 0.1$ ) and the same saturation behavior at high concentrations ( $w > 0.1$ ).

#### IV. DISCUSSION

The large and rapid changes in frequency observed in the blue wing of the O–H stretch vibration of bulk  $\text{HDO}:\text{D}_2\text{O}$  have been explained from the fast evolution of the molecules absorbing in the blue wing to a weakly hydrogen-bonded structure.<sup>41,42</sup> This weakly hydrogen-bonded structure has been assigned to a configuration in which the H atom of the O–H group forms a bifurcated hydrogen bond with the oxygen atoms of two other water molecules.<sup>42–45</sup> The bend character makes these hydrogen bonds very weak, with the result that the O–H frequency has a high value. By rapid contraction of one of the branches of the bifurcated hydrogen bond with simultaneous breakage of the other branch, the bifurcated configuration rapidly evolves to a structure in which there is only one strong hydrogen bond between the H atom of the O–H with one oxygen atom of a neighboring water molecule. This change of the hydrogen-bond structure is accompanied by a large and rapid change of the frequency of the O–H stretch vibration, thus leading to a broad response in  $\omega_3$  in the 2D spectrum. These structural dynamics were also proposed to form the mechanism for the reorientation of liquid water.<sup>43–46</sup> The return from the bifurcated state to a single strong hydrogen bond can involve the reformation of the original hydrogen bond, or lead to the formation of a hydrogen bond to the new partner, i.e., a switching or jumping event.<sup>42–46</sup> In case the original hydrogen bond is reformed, the transition through the bifurcated configuration corresponds to a large librational motion of the O–H group. In case a new hydrogen bond is formed, the O–H group has rotated over  $\sim 60^\circ$ .<sup>43,45</sup>

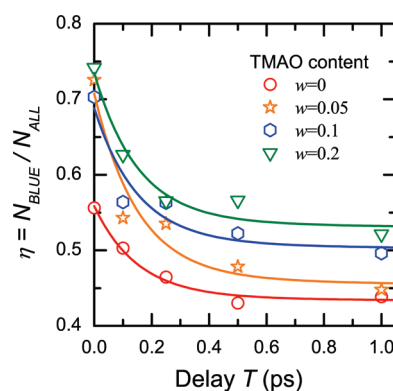
For the spectral dynamics it does not make a difference whether a new hydrogen bond is formed (successful switch) or whether the original hydrogen bond is reformed (unsuccessful switch). In both cases the frequency of the OH stretch strongly changes, giving rise to a broad response in  $\omega_3$ . Classical MD calculations predict that  $\sim 25\%$  of the molecules in the blue wing of the spectrum will make a successful switch within 125 fs.<sup>45</sup> Most of the water molecules will return to the original hydrogen bond, meaning that they have undergone a large-amplitude libration. For the solutions of TBA, TMAO, and TMU in  $\text{HDO}:\text{D}_2\text{O}$  we observe a much narrower and slower response



**Figure 5.** Cross sections through the 2D spectra (Figure 2) for pure HDO:D<sub>2</sub>O (a), and a solution of TMAO in HDO:D<sub>2</sub>O with  $w = 0.2$  (b) measured for  $\omega_1 - \omega_0 = 100$  cm<sup>-1</sup>. Only the positive part (i.e., due to the ground-state bleach and excited-state stimulated emission) of the cross sections is presented. The dashed and dotted lines show frequencies of the on-diagonal excitation and equilibration, respectively.

in  $\omega_3$  than for pure HDO:D<sub>2</sub>O, indicating that for a significant fraction of the water molecules in these solutions the evolution to the bifurcated hydrogen-bond state is strongly hindered. Figure 5 depicts the cross sections through the 2D spectra at the frequency of  $\omega_1 - \omega_0 = 100$  cm<sup>-1</sup> for pure HDO:D<sub>2</sub>O and a TMAO solution with  $w = 0.2$  in HDO:D<sub>2</sub>O at different waiting times. For pure HDO:D<sub>2</sub>O (Figure 5a), the spectra are broadened and shifted from the on-diagonal position within 0.1 ps<sup>42</sup> and for a waiting time of  $T = 0.25$  ps the spectra already peak at zero detuning. Also, the decrease of the on-diagonal amplitude (i.e., at the frequency of  $\omega_3 = \omega_1$ ) is clearly visible when the waiting times increase to 1 ps. These features are characteristic for the rapid hydrogen-bond dynamics of molecules in the blue wing of the absorption of pure HDO:D<sub>2</sub>O.<sup>41,42</sup> In sharp contrast to neat water, the TMAO solution demonstrates a completely different behavior (Figure 5b). After some initial broadening (within 0.1 ps), there are very little subsequent dynamics both in terms of spectral shift and broadening. This observation indicates that the evolution to the bifurcated hydrogen-bonded structure has slowed down substantially.

To analyze the spectral dynamics on the blue wing for the water and TMAO solutions more quantitatively, we present in Figure 6 the temporal evolution of the fraction  $\eta$  of high-energy oscillators with respect to high- and average-energy oscillators for different TMAO concentrations after excitation in the blue wing ( $\omega_1 - \omega_0 = 100$  cm<sup>-1</sup>). To this purpose, we integrated the positive part of the response in the regions where the relatively weakly hydrogen-bonded water molecules ( $50 < \omega_3 - \omega_0 < 150$  cm<sup>-1</sup>) and the relatively strongly hydrogen-bonded water molecules ( $-50 < \omega_3 - \omega_0 < 50$  cm<sup>-1</sup>) absorb. The parameter  $\eta$  is calculated as the ratio between the first integral and the sum of



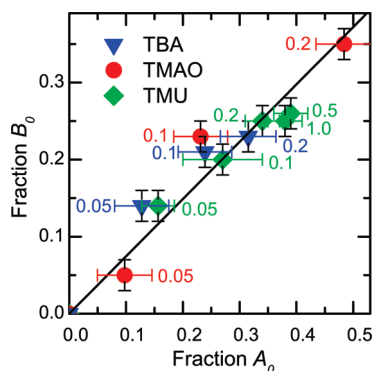
**Figure 6.** Fraction  $\eta$  of high-energy oscillators after excitation at  $\omega_1 - \omega_0 = 100$  cm<sup>-1</sup> as a function of waiting time  $T$  for four different solutions of TMAO dissolved in HDO:D<sub>2</sub>O. The lines are guides to the eye.

both integrals. This procedure is similar to the one used by Fayer and co-workers in the analysis of chemical exchange processes.<sup>47</sup> The value of  $\eta$  represents the relative OH signal amplitude that remains in the blue region after a certain time. If there were no frequency variations of the cross-section (non-Condon effect), the parameter  $\eta$  would represent the relative number of OH oscillators that keep their initial excitation frequency in the blue region after a certain time. However, as the cross-section has been shown to vary substantially across the OH stretching band,<sup>48</sup> this identification is not rigorous. For pure HDO:D<sub>2</sub>O, the fraction  $\eta$  is small already at short time delays and decays quickly with a time constant of  $\sim 0.2$  ps. Already after 0.5 ps  $\eta$  reaches a value of 0.43 which is close to the value of  $\sim 0.4$  of the equilibrium spectrum at room temperature. With increasing TMAO concentration, the parameter  $\eta$  acquires a higher initial value and shows an increasingly slower decay.

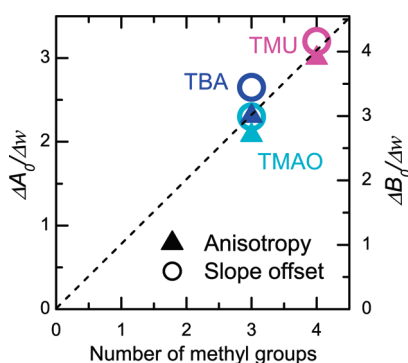
The results of Figures 2–6 demonstrate that the addition of TBA, TMAO, and TMU to HDO:D<sub>2</sub>O leads to a strong slowing down of the spectral dynamics, especially for the molecules that absorb in the blue wing of the spectrum. This slowing down indicates that the solute molecules hinder the water molecules solvating TBA, TMAO, and TMU in evolving to the bifurcated hydrogen-bond configuration. As this bifurcated hydrogen-bond state also forms the transition state for molecular reorientation<sup>43</sup> (successful switch), the slowing down of the spectral dynamics is expected to be strongly correlated with the slowing down of the molecular reorientation.

In Figure 4 it is seen that the concentration dependence of the fraction  $A_0$  water molecules showing slow spectral diffusion perfectly correlates with that of fraction  $B_0$  of slowly reorienting water molecules. To explore the correlation between the spectral diffusion and the reorientation in more detail, we plot in Figure 7  $B_0$  as a function of  $A_0$  for all measured solutions. The resulting points can be fitted well with a straight line, with a Pearson correlation coefficient of 0.97. This near-perfect correlation demonstrates that the slowing down of the spectral diffusion and the reorientation have a common origin. The solute molecules hinder the evolution to the bifurcated hydrogen-bonded structure, thereby preventing both rapid spectral diffusion (successful and unsuccessful switches) and rapid molecular reorientation (successful switches only). Probably, by filling the cavities in the hydrogen-bond network of water, hydrophobic solutes kinetically inhibit the collective reorganizations of the water liquid that would lead to the formation of bifurcated hydrogen-bonded configurations.





**Figure 7.** Fraction  $B_0$  of slowly reorienting water molecules as a function of the fraction  $A_0$  of water molecules showing slow spectral diffusion, for all measured solutes and concentrations. To obtain  $B_0$  values at the same concentrations at which  $A_0$  was determined, we perform a spline interpolation between the measured  $B_0$  values.



**Figure 8.** Slopes of the dotted lines of Figure 4 ( $=\Delta A_0/\Delta w$ ) as a function of the number of methyl groups contained in the solute ( $\circ$ ). For comparison also the derivative of the fraction  $B_0$  of slowly reorienting water molecules with respect to the concentration ( $=\Delta B_0/\Delta w$ ) is presented ( $\blacktriangle$ ).

A similar correlation between spectral dynamics and reorientation was recently reported for solutions of NaBr.<sup>49</sup> It was observed that the spectral diffusion and the reorientation show a very similar slowing down with salt concentration, which suggests that this slowing down finds a common origin in the influence of the ions on the hydrogen-bond dynamics of water, exactly as we find here for hydrophobic molecular groups.

In Figure 8 we plot the derivatives  $\Delta A_0/\Delta w$  and  $\Delta B_0/\Delta w$  for  $w < 0.1$  of the results presented in Figure 4 as a function of the number of methyl groups contained in the solute. It is seen that these derivatives fall on a line, meaning that the initial increases of  $A_0$  and  $B_0$  scale with the number of methyl groups contained in the solute.

In a recent classical molecular dynamics simulations study it was claimed that the effects of TBA, TMAO, and TMU on the two-dimensional infrared spectrum of water would in fact be due to the hydrophilic groups instead of the hydrophobic groups of these solutes.<sup>50</sup> For instance, TMAO, which has a strongly polar  $N^+O^-$  group, was calculated to have the largest effect, also larger than TMU, while TBA, which has a hydroxyl group similar to the hydroxyl groups of water, was calculated to have a negligible effect on the spectral dynamics of water. It thus appears that the molecular dynamics simulations underestimate the effects of hydrophobic groups on the hydrogen-bond dynamics of water,

thereby arriving at a relatively more important role of the hydrophilic groups. Clearly these results do not agree with the present findings. The results of Figure 8 show that TBA and TMAO have quite similar effects on the water hydrogen-bond dynamics, which is in line with the similarity of their hydrophobic groups, and which points at a relatively unimportant role for their (different) hydrophilic groups. Figure 8 also shows that TMU has the largest effect, again in line with a dominance of the hydrophobic groups over the hydrophilic groups in affecting the hydrogen-bond dynamics of water. This finding agrees with the results of previous NMR,<sup>9–13</sup> dielectric relaxation,<sup>15,16</sup> and femtosecond mid-infrared<sup>17,51</sup> studies. In all these studies it is found that the effect of the solute molecules on the water dynamics scales with the size of the hydrophobic part of the molecule, and that the hydrophilic group is relatively unimportant. Probably the clearest example of this notion is the comparison of the hydrophilic urea and the amphiphilic tetramethylurea (TMU). Both NMR<sup>12</sup> and femtosecond mid-infrared<sup>51</sup> studies observe that the effect of urea on the reorientation dynamics of water is very small, while the effect of tetramethylurea is very large.<sup>12,18</sup>

For all three solutions it is observed that at high concentrations  $A_0$  and  $B_0$  show a saturation effect due to the sharing of the hydration shells of neighboring solute molecules and aggregation of the solute molecules. For TBA and TMU the saturation effect is very strong, which can be explained from aggregation. Due to aggregation, two different types of water molecules can be distinguished in highly concentrated TBA and TMU solutions: water molecules that are solvating the TBA/TMU molecules and water molecules that are embedded in water nanoclusters. Beyond a certain TBA/TMU concentration, all additionally added TBA/TMU is completely embedded by the TBA/TMU molecules that are already present in the solution. As a result, the fraction of water showing bulklike behavior within the nanoclusters and the fraction of water interacting with TBA/TMU (represented by  $A_0$  and  $B_0$ ) no longer change. The observation of clustering of TBA and TMU at high concentrations agrees with previous findings from neutron scattering studies and NMR.<sup>12,52–54</sup> For TMAO the saturation effects are much less strong, which indicates that the solutions containing TMAO do not show aggregation up to high concentrations.

## V. CONCLUSIONS

We studied the spectral and orientational dynamics of water in solutions of the amphiphilic solutes tertiary-butyl-alcohol (TBA), trimethyl-amine-oxide (TMAO), and tetramethylurea (TMU) in isotopically diluted water, and we compare these dynamics with the dynamics of pure isotopically diluted water. The spectral dynamics are studied with femtosecond two-dimensional mid-infrared spectroscopy of the O–H stretch vibration of HDO in solutions of TBA, TMAO, and TMU in HDO:D<sub>2</sub>O. The reorientation dynamics are studied with polarization-resolved pump–probe spectroscopy of the O–D stretch vibration of HDO in solutions of TBA, TMAO, and TMU in HDO:D<sub>2</sub>O. We observe that the addition of the amphiphilic solutes leads to a strong slowing down of both the spectral and the orientational dynamics.

The spectral and the orientational dynamics of the solutions can be described well with two components. One of these components possesses the same spectral/orientational dynamics as observed for pure isotopically diluted water, while the other component has much slower dynamics. At low concentrations ( $w < 0.1$ ),



the amplitude of the slow component increases linearly with the solute concentration and the number of methyl groups contained in the solute. This result demonstrates that the slow water molecules hydrate the hydrophobic groups of the solute. The similarity of the results obtained at concentrations  $w < 0.1$  for TBA and TMAO demonstrates that the character of the hydrophilic group is relatively unimportant for the water dynamics.

For pure HDO:D<sub>2</sub>O, we observe a fast and rapid spectral broadening following excitation in the blue wing of the absorption spectrum of the O–H stretch vibration, in agreement with previous experimental observations.<sup>41,42</sup> This process has been assigned to the rapid evolution to bifurcated, weakly hydrogen-bonded water structures, and is proposed to play an essential role in the molecular reorientation of liquid water.<sup>43–46</sup> For solutions of TBA, TMAO, and TMU in HDO:D<sub>2</sub>O, we observe a much narrower and slower spectral broadening following excitation in the blue wing, indicating that in these solutions the evolution to the bifurcated hydrogen-bond state is strongly hindered for a significant fraction of the water molecules.

For all three studied solutes, the fraction of water showing slow spectral dynamics and the fraction of slowly reorienting water are highly correlated, showing the same saturation effect at high concentrations. This strong correlation demonstrates that the slow spectral dynamics and the slow molecular reorientation have a common origin. The effect of hydrophobes on the dynamics of water thus appears to be the hindrance of the formation of bifurcated hydrogen-bonded structures, as these structures are essential for both the spectral dynamics and the molecular reorientation.

## ■ ASSOCIATED CONTENT

**S Supporting Information.** Additional details, table, and figure. This material is available free of charge via the Internet at <http://pubs.acs.org>.

## ■ ACKNOWLEDGMENT

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