Water Jump Reorientation: From Theoretical Prediction to Experimental Observation

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CONSPECTUS

L iquid water is remarkably labile in reorganizing its hydrogen-bond (HB) network through the breaking and forming of HBs. This rapid restructuring, which occurs on the picosecond time scale, is critical not only for many of the pure liquid's special features but also for a range of aqueous media phenomena, including chemical reactions and protein activity. An essential part of the HB network reorganization is water molecule reorientation, which has long been described as Debye rotational diffusion characterized by very small angular displacements. Recent theoretical work, however, has presented a starkly contrasting picture: a sudden, large-amplitude jump mechanism, in which the reorienting water molecule rapidly exchanges HB partners in what amounts to an activated chemical reaction. In this Account, we first briefly review the jump mechanism and then discuss how it is supported by a series of experiments. These studies range from indirect indications to direct characterization of the jumps through pioneering two-dimensional infrared spectroscopy (2D-IR), the power of which accords it a special focus here.

The scenarios in which experimental signatures of the jump mechanism are sought increase in complexity throughout the Account, beginning with pure water. Here 2D-IR in combination with theory can give a glimpse of the jumps, but the tell-tale markers are not pronounced. A more fruitful arena is provided by aqueous ionic solutions. The difference between water—water and water—anion HB strengths provides the experimental handle of differing OH stretch frequencies; in favorable cases, the kinetic exchange of a water between these two sites can be monitored. Sole observation of this exchange, however, is insufficient to establish the jump mechanism. Fortunately, 2D-IR with polarized pulses has demonstrated that HB exchange is accompanied by significant angular displacement, with an estimated jump angle similar to theoretical estimates.

The Janus-like character of amphiphilic solutes, with their hydrophobic and hydrophilic faces, presents a special challenge for theory and experiment. Here a consensus on the 2D-IR interpretation has not yet been achieved; this lack of accord impedes the understanding of, for example, biochemical solutes and interfaces. We argue that the influence of hydrophobic groups on water jumps is only modest and well accounted for by an excluded volume effect in the HB exchange process. Conversely, hydrophilic groups have an important influence when their HB strength with water differs significantly from that of the water—water HB. The power of 2D-IR is argued to be accompanied by subtleties that can lead to just the opposite and, in our view, erroneous conclusion. We close with a prediction that a hydrophobic surface offers an arena in which the dynamics of “dangling” water OHs, bereft of a HB, could provide a 2D-IR confirmation of water jumps.

1. Introduction

Among liquid water’s numerous remarkable features, a unique property is the great lability of its hydrogen-bond (HB) network, which constantly rearranges by breaking and forming HBs on a picosecond time scale.1–4 This reorganization dynamics plays a key role in a wide range of fundamental processes, such as $S_N2$ and proton transfer reactions, proton transport, and protein activity where
the labile water HB network facilitates conformational transitions. Rearrangements of this HB network involve the reorientation of individual water molecules, long commonly described as an angular Brownian motion of the water molecule through very small angular steps.

In stark contrast with this Debye rotational diffusion picture, a theoretical study recently proposed a very different molecular mechanism, where water reorientation mainly proceeds through sudden large amplitude angular jumps. In this new picture, large jumps occur when a water hydroxyl (OH) group trades HB acceptors, providing the elementary mechanism of HB network rearrangement. Subsequent simulation work suggested these angular jumps to be a universal feature of liquid water, since they occurred not only in neat water but also in a wide range of aqueous environments, including aqueous solutions of ions and amphiphilic solutes, confining geometries, and biomolecular hydration layers.

Because the first suggestion for the presence of these jumps came from theoretical work (and despite the picture’s robustness vis-à-vis changes in the water force field), a legitimate concern is whether their existence can be evidenced experimentally. In this Account, after a brief description of the jump mechanism, we will see how the existence of these jumps is supported by a series of experiments, from indirect indications to direct characterization of the jumps through pioneering two-dimensional infrared (2D-IR) spectroscopy measurements on isotopic mixtures of water. We then describe how these jumps are affected by a solute’s presence and how the jump model provides a predictive theoretical framework to understand how a solute alters the surrounding water’s dynamics illustrated by recent ionic and amphiphilic aqueous solution examples.

2. Jump Reorientation Mechanism in Bulk Water

a. Jump Mechanism. Molecular dynamics (MD) simulations suggest that large angular jumps occur when a water OH group trades HB acceptors. This exchange process, which can be viewed very fruitfully as a chemical reaction, is depicted in Figure 1. The first step is the initial HB’s elongation while a new water oxygen acceptor approaches, in most cases from the second shell. Once the initial and final oxygen acceptors are equidistant from the rotating water oxygen, the water OH can suddenly execute a large-amplitude angular jump from one acceptor to another; at the transition state for this HB exchange, the rotating water forms a symmetric bifurcated HB with its initial and final water acceptors. The HB with the new partner eventually stabilizes, while the initial partner leaves. This jump mechanism’s free energy barrier was shown from simulations to originate not only from the initial HB’s elongation, but also from the new partner’s penetration into the first shell; this jump barrier is smaller than the free energy cost to fully break the initial HB due to the mechanism’s concerted nature.

The mechanism shown in Figure 1 is obviously to be understood as an average, simplified, but nonetheless representative mechanism. Actual paths are distributed around this typical mechanism, as illustrated by the wide jump angle distribution found around the average amplitude of \(68^\circ\). A natural question is now whether the existence of these jumps, first suggested by simulations, can be supported by experiments.
b. Anisotropy Decay and Extended Jump Model. Since the jumps lead to the reorientation of water molecules, a first place to seek a signature of them is in the time-correlation function of the molecular orientation. For a given body-fixed vector such as the water OH bond, this function tracks how fast memory of the initial orientation is lost. Its definition is $C_n(t) = \langle P_n(u(0) \cdot u(t)) \rangle$, where $P_n$ is the $n^{th}$ order Legendre polynomial, and $u(t)$ is the molecular orientation at time $t$. Ultrafast polarized pump–probe infrared spectroscopy experiments measure the anisotropy decay, approximately proportional to $C_2(t)$.13,15 Beyond an initial regime (< 200 fs) where water molecules partially reorient due to fast librational motions, that is, rotations hindered by the restoring torques imposed by the HB network, $C_2(t)$ decays exponentially with a characteristic time $\tau_2$.

The characteristic reorientation time resulting from a reorientation through large jumps can be determined through the jump model developed by Ivanov, which generalizes the diffusive angular Brownian motion picture to finite amplitude jumps.3,6 Assuming that the jumps have a constant amplitude $\Delta \theta$, are uncorrelated, and occur with a frequency of $1/\tau_{\text{jump}}$ around axes distributed isotropically, the (second-order) reorientation time is $\tau_2 = \tau_{\text{jump}}(1 - 1/5[n(5\Delta \theta/2)/\sin(\Delta \theta/2)])^{-1}$. The two features of the jumps, their amplitude $\Delta \theta$ and their frequency $1/\tau_{\text{jump}}$, can be determined from simulations. The jump frequency $1/\tau_{\text{jump}}$ is now identified as the forward rate constant for the reaction that breaks an initial stable HB to form a new different stable HB.3,6

However, this simple model needs extension, since it incorrectly assumes fixed molecular orientation between jumps. This would imply that while a water OH bond retains the same HB acceptor, the OH direction remains frozen. This is not the case, due to the intact HB axis reorientation through a tumbling motion of the local molecular frame. The dominant jump contribution is combined with the minor frame component within an extended jump model (EJM).3,6 leading to an overall EJM reorientation time

$$1/\tau_{\text{EJM}} = 1/\tau_{\text{jump}} + 1/\tau_{\text{frame}}$$

The EJM provides an excellent description of the $\tau_2$ reorientation times measured by pump–probe and NMR spectroscopies and calculated from simulations.3,6 However, if one ignores the results of simulations for the moment and only considers the experimental anisotropy measurements, these cannot unambiguously demand that the Debye rotational diffusion picture could be replaced by the jump mechanism, since the former can within experimental uncertainties often provide a comparably satisfactory description of these results.3,6 although with a very different underlying molecular interpretation. The measured smooth exponential decay of $C_2(t)$ could result either from sharp large amplitude jumps averaged over a great number of water molecules jumping at different times or from infinitesimal reorientations for each water molecule. The ratio of the second-order time $\tau_2$ with the first- or third-order times would be needed to furnish an answer,3,6 but these times are at present not experimentally accessible. Other direct and incisive experimental evidence is thus necessary.

c. Experimental Support: Quasi-Elastic Neutron Scattering and Two-Dimensional Infrared Spectroscopy. Some first experimental support of the jump model comes from the analysis of quasi-elastic neutron scattering spectra (QENS), which are sensitive to both the first- and second-order reorientation times. The surprising 2-fold difference between the second-order reorientation times obtained through QENS and those from NMR and ultrafast infrared spectroscopies disappears when the angular jump model replaces the rotational diffusion assumption to interpret the spectra.16

But among the many experimental techniques applied to the study of water HB dynamics, including QENS16 and NMR spectroscopy,17 the most recent, and arguably most powerful, has been 2D-IR spectroscopy. Numerous discussions of 2D-IR are available; our presentation addresses the key relevant aspects for water HB dynamics.18–23 This technique follows the time fluctuations of vibrational frequencies and yields the correlation between the frequencies at two instants separated by a given delay. As described elsewhere,21–23 2D-IR shares many similarities with the 2D-NMR method, although its characteristic time scale is much shorter (picosecond vs longer than nanosecond). Its application to water13 provides detailed information about the HB dynamics,20 since the water OH stretch vibration is a sensitive probe of the hydrogen-bonding interaction. An OH engaged in a strong HB vibrates at a lower frequency: the OH bond is weakened by stabilizing interaction with the HB acceptor, inducing an average OH frequency red shift; conversely, a weakly hydrogen-bonded OH exhibits a blue-shifted frequency. 2D-IR probing of the OH frequency time evolution therefore reports on HB network fluctuations and HB breaking and forming events. It has already been successfully employed for water HB dynamics in a broad gamut of contexts, from the bulk case2,4,19,20 to, for example, ionic aqueous solutions,22,24,25 confining environments,26 and biomolecular hydration.19
What insight can be provided by 2D-IR on the presence of angular jumps? The jump transition state (TS) determined from MD simulations is a bifurcated HB structure where the reorienting water OH donates two weak HBs to two acceptors, resulting in a blue shift of the OH stretch vibrational frequency. OH frequency changes during the jump thus make 2D-IR spectroscopy a promising technique to investigate the presence of angular jumps in water, exploiting its ability to selectively follow systems with given initial and final vibrational frequencies.

A first indirect support of the jump picture can be found in a 2D-IR study performed prior to the theoretical proposal of jumps. Focusing on the spectral relaxation of blue-shifted OH frequencies corresponding to very weak or broken HBs, this work first evidenced the transient and unstable character of non-HB states, which very quickly (<200 fs) relax to form a HB. This is fully consistent with the jump mechanism where HB acceptor exchanges occur through the concerted breaking and forming of HBs, in contrast with a sequential mechanism involving a long-lived broken HB state.

However, most blue-shifted OHs do not lie at the jump mechanism TS, since most do not execute a jump between HB acceptors. Simulations indicate that most waters (∼80%) only experience a transient HB break and quickly return to their initial HB acceptor and orientation without any jump and formation of a HB with a new acceptor; the OHs jumping from one acceptor to another only represent a minor (∼20%) part. This implies that water molecules close to the jump TS cannot be selectively excited using a blue-shifted infrared excitation. Further, the frequency dynamics measured by 2D-IR cannot distinguish the contributions from jumps and from librations: the OH frequency dynamics is similar for a successful jump forming a new HB with a different water acceptor and for an unsuccessful jump (i.e., a large amplitude libration) reforming a HB with the initial acceptor; the OHs jumping from one acceptor to another only represent a minor (∼20%) part.

This frequency-dependent version of the EJM (FD-EJM) has been developed to interpret such 2D anisotropy diagrams and identify angular jump signatures. This extension describes the jump probability's moderate dependence on the initial HB strength and thus on the OH vibrational frequency. The free energy barrier to reach the jump TS was shown to be mostly due to the concerted elongation of the initial HB and penetration of the new partner within the rotating water's first shell, with similar free energy costs. An initially blue-shifted frequency corresponds to a water OH, which has already weakened its initial HB, but does not imply that a
new HB partner is available to effect a jump. This therefore explains that the jump probability increases with vibrational frequency blue shift but that this increase is very moderate.\(^6\),\(^28\)

The FD-EJM predicts that angular jumps should lead to a faster anisotropy decrease for blue-shifted frequencies, as long as memory of the initial frequency is retained.\(^28\) Such accelerated reorientation has already been observed in frequency-resolved pump–probe studies,\(^29\) and it can be rigorously connected to the presence of jumps through the FD-EJM. Future polarization-resolved 2D-IR measurements should lead to a more detailed characterization.

### 3. Ionic Aqueous Solutions

We now turn to ionic aqueous solutions, which have been used to furnish a much more direct characterization of the angular jumps through 2D-IR experiments.\(^22\),\(^24\),\(^25\) A key feature of ions is breaking of the symmetry of the jump between initial and final HB acceptors. In neat water, these two configurations are experimentally indistinguishable: the OH group donates a HB to a water oxygen in both cases, which leads to the difficulties described above in distinguishing failed and successful jumps. In the presence of a salt, simulations indicate that some jumps occur from an initial state where a HB is donated to an anion to a final state with a HB to a water molecule.\(^7\) If the anion accepts very weak HBs (e.g., BF\(_4^-\) or ClO\(_4^-\)),\(^22\),\(^24\),\(^25\) the vibrational frequency of the water OH bonded to the anion is sufficiently blue shifted to become distinct from the broad distribution of vibrational frequencies observed for OH groups bonded to a water. In the linear infrared spectrum, this results in two distinct OH stretch bands (Figure 3), but no dynamical information can be extracted; 2D-IR spectroscopy is required for this.

This spectroscopy’s great strengths are to reveal and measure the kinetics of the chemical exchange between these two states: hydrogen-bonded to an anion and to a water oxygen. As detailed in recent studies, chemical exchange between two states usually manifests itself in 2D-IR spectra through the presence of two distinct diagonal peaks and the progressive growth of off-diagonal peaks.\(^21\)–\(^23\),\(^25\)

The latter correspond to OH groups in the same state when the system is first excited and after a delay \(T\) when the correlation is measured (Figure 3). As \(T\) is increased, exchange between the two populations causes these two diagonal peaks to decrease, while off-diagonal peaks progressively grow. These off-diagonal peaks correspond to OH groups that have undergone exchange and thus have different initial and final frequencies (Figure 3). Two-dimensional IR experiments on concentrated salt solutions (5.5 M NaBF\(_4\)\(^22\) and 6 M NaClO\(_4\))\(^25\) measured the exchange time for a water OH to go from an anion acceptor to a water acceptor.\(^13\) Within the EJM terminology, this time corresponds to the jump time. The experimental values (7 ps\(^22\) and 6 ps,\(^25\) respectively) agree well with the time determined from a simulation study of a different salt solution (3.6 ps in a 3 M NaCl solution), considering the different anion nature and more importantly the strong concentration dependence of the jump time, which dramatically increases for increasing salt concentrations.\(^7\)

These pioneering 2D-IR measurements provided the first time-resolved observation of chemical exchange between different HB acceptors but could not yet establish unambiguously that exchanges occur through large angular jumps. It is only very recently that polarization-resolved 2D-IR experiments have provided a quantitative measure of the reorientation associated with HB exchange.\(^24\) Comparison of spectra acquired with parallel and perpendicular polarizations evidenced that systems that exchange between the two states (off-diagonal peaks) experience a much larger reorientation than those that remain in the same state (diagonal peaks). Spectral analysis through a kinetic model leads to an average jump angle of 49°.\(^24\) This value is in quite good agreement with the distributions of jump angles determined from MD simulations of various aqueous solutions, whose average lies between 60° and 70°.\(^3\),\(^7\),\(^8\),\(^11\),\(^12\)

![Figure 3. Schematic representation, for a concentrated ionic aqueous solution, of (a) the linear infrared spectrum and (b) a 2D-IR spectrum after a few picoseconds, with growing off-diagonal peaks due to exchanges.](image-url)
Two-dimensional IR spectroscopy thus appears as an exquisite technique to follow water HB exchange kinetics and very clearly supports the existence of angular jumps. One could therefore hope to extend these measurements to other aqueous environments in order to assess how the jump mechanism is altered and compare with theoretical predictions. However, several limitations exist for the applicability of 2D-IR. Perhaps most importantly, a large fraction of the water hydroxyls bonded to solute acceptors is required in order to obtain a visible spectral peak (especially for blue-shifted frequencies, which suffer from smaller transition dipoles due to non-Condon effects). Experiments on very dilute solutions (<1 M) available for instance in NMR measurements are still inaccessible. It is all the more unfortunate that water HB dynamics is extremely sensitive to the solute concentration, so that dilute solution behavior cannot be easily inferred from concentrated solution measurement. These 2D-IR studies additionally require spectrally distinct populations, that is, the vibrational frequency shift between the two states should exceed the frequency fluctuations within each state. This is not the case for most monovalent anions, for example, halides, for which 2D-IR cannot be used to directly follow the HB exchanges, although information on spectral diffusion is still provided.

4. Solutions of Amphiphilic Solutes

a. Transition-State Excluded Volume Model. Simulations indicate that water also reorients through large angular jumps in a very different context, next to hydrophobic groups. The jump mechanism and amplitude are nearly identical to those found in bulk water, although the jump time, \( \tau_{\text{jump}} \), is longer. This was explained through a transition-state excluded-volume (TSEV) effect for HB exchange (Figure 4a), which provided the first quantitative treatment of a hydrophobic group’s influence on the surrounding water HB and reorientation dynamics. Briefly, the hydrophobe’s presence hinders a new water partner’s approach for the HB exchange. For hydrophobic hydration shell water molecules, the TSEV slowdown factor in the jump time (compared with bulk) is directly related to the local fraction of space occupied by the solute. For usual hydrophobic groups (radius 3–5 Å), this fraction is smaller than 1/2 and the TSEV slowdown factor is close to 1.4. Such a moderate slowdown quantitatively

![FIGURE 4. Schematic representations of the (a) TSEV and (b) TSHB effects of a solute on the water jump rate constant.](image)

![FIGURE 5. Simulated 2D-IR spectra at several delays for a series of solutions (pure HOD/H2O and concentrated (8 mol/kg) aqueous solutions of TMU, TMAO, and TBA), together with the solutes' chemical structures and the vibrational frequency shift direction for the water bonded to the hydrophilic head.](image)
agrees with dilute solution studies using a broad range of techniques, including NMR,\textsuperscript{17} dielectric relaxation,\textsuperscript{31} Kerr effect spectroscopy,\textsuperscript{32} and MD simulations (both with classical force fields\textsuperscript{8} and ab initio\textsuperscript{33}). This clearly shows that a single hydrophobic group has a limited effect on water dynamics.

\textbf{b. 2D-IR Spectra.} Can 2D-IR spectroscopy provide an experimental characterization of these jumps next to hydrophobic groups? Recent experiments\textsuperscript{34–36} and calculations\textsuperscript{9} have been performed on a series of amphiphilic solutes containing hydrophobic methyl groups, namely, tetramethylurea (TMU), tert-butyl alcohol (TBA), and trimethylamine N-oxide (TMAO) (see structures in Figure 5). The computed spectra\textsuperscript{9} (Figure 5) compare very well with experiment.\textsuperscript{34–36} While in a dilute (1 mol/kg) solution the 2D spectra are very similar to those of bulk water, in the concentrated (8 mol/kg) case the spectral relaxation is much slower, with a frequency correlation persisting over several picoseconds.\textsuperscript{9,13,34} This very retarded spectral relaxation was interpreted by the spectroscopy group as revealing a dramatic intrinsic effect on water dynamics induced by hydrophobic groups: suppression of HB acceptor jumps and “immobilization” of the orientation of some water molecules in their hydration layer, in line with previous controversial conclusions reached by pump–probe anisotropy experiments\textsuperscript{37} on these solutes. But such a picture contrasts radically with the moderate retardation shown by simulations and other experiments and rationalized by the EJM/TSEV models. How can one then decide what happens to the angular jumps next to hydrophobic groups? We now show how this disagreement can be resolved through a careful interpretation of 2D-IR spectra, leading to a picture fully consistent with the moderate hydrophobic effect predicted by the EJM/TSEV model.

\textbf{c. Slow Spectral Dynamics Does Not Imply That Jumps Are Suppressed.} Next to the hydrophobic portion of solutes (here amphiphilic), water molecules tend to form HBs with other water molecules, since these solute groups can neither donate nor receive HBs. In the vicinity of hydrophobic groups, jumps therefore occur between water oxygens. This is the same type of symmetric jump discussed above, where it was explained that 2D-IR could not discriminate spectral dynamics due to transient HB breaking/reforming and to actual jumps between HB acceptors. The 2D-IR spectra calculated in the total absence of jumps (Figure 2) also show that even if jumps were fully suppressed, the spectral decay would change very little, since it is dominated by the transient HB breaks.\textsuperscript{9} The 2D-IR slow spectral decay for solutions of amphiphilic solutes is thus unlikely to originate from suppressed jumps due to water immobilization by hydrophobic groups.

\textbf{d. Amphiphilic Solutes Lead to Hidden Exchange in 2D-IR Spectra.} This slow spectral decay actually arises from the other moieties of these solute molecules, which as noted above are amphiphilic\textsuperscript{8,17,28,34,37} and contain an HB accepting hydrophilic group. This implies that as for ionic solutions, two states are possible for each water OH: HB donation either to a water oxygen or to a hydrophilic headgroup. Depending on the HB strength with the hydrophilic head, these two populations have distinct vibrational frequency dynamics.

Because these hydrophilic heads are not so different from a water oxygen, the frequency shift between the water-hydrogen-bonded and solute-hydrogen-bonded OH populations is limited (at most 30 cm\textsuperscript{-1}), leading to a single broad band in the linear IR spectrum.\textsuperscript{9,36} In the 2D-IR spectra, the two frequency distributions are also too close to be resolved separately, and the characteristic signatures of exchange discussed above for ionic solutions are not visible. Nonetheless, exchange between these two populations plays a key role in the spectral relaxation, as now discussed.

Spectral relaxation in these two-component systems proceeds via two mechanisms.\textsuperscript{13} The first, faster contribution is similar to the mechanism in neat water discussed above, involving transient HB breaking and making events.\textsuperscript{1,27} These HB breaks occur without any HB acceptor exchange and thus do not lead to an exchange between the two populations. The resulting spectral relaxation time only moderately depends on the HB strength, and is thus similar in the two states. After \textsim 1 ps, the 2D-IR spectra have decayed from the sum of two diagonally elongated bands to the sum of two round peaks. When these two peaks do not exactly overlap, the resulting 2D-IR spectra remain diagonally elongated,\textsuperscript{9,21} which explains the observed incomplete spectral relaxation. Full spectral relaxation then requires a second, slower contribution coming from exchanges between the two peaks, that is, HB jumps between water oxygens and solute hydrophilic heads. The magnitude of this second component scales with the frequency shift between the peaks. This is clearly illustrated by the progressive disappearance of the slow exchange contribution when going from TMAO (which induces a large red shift) to TMU (which leads to a small blue shift) and finally to TBA (whose induced frequency-shift is negligible) (Figure 5). For the last solute, the frequency distributions in the two populations are nearly superimposed, and exchange is not necessary to sample the entire frequency range.
To conclude this description of the subtle effects induced by amphiphilic solutes in 2D-IR spectra, it is important to stress that the same chemical group can have radically different impacts on the water reorientation dynamics and on the water spectral dynamics. While a hydrophobic group slows down the reorientation of the surrounding water molecules by a factor less than 2 (cf section 4.a), it has nearly no effect on water spectral relaxation, since it does not produce a new HB population; spectral relaxation remains almost bulk-like, proceeding through transient HB breaks, which are nearly unaffected by the hydrophobic group. Hydrophilic HB acceptor groups can also have very different impacts on the water HB exchange and thus reorientation dynamics. A hydrophilic group accepting a HB stronger than a water–water HB leads to a slowdown in the reorientation dynamics (potentially much more pronounced than that induced by hydrophobic groups\textsuperscript{12}); conversely, weak HB acceptors lead to an accelerated water reorientation; both effects are quantitatively described through a transition-state hydrogen-bond model\textsuperscript{12} (Figure 4b). Contrasting with this wide range of possible effects on water reorientation, all hydrophilic HB acceptors lead to a new HB type and therefore to an additional slow component in the water spectral relaxation associated with chemical exchanges between HB acceptors (except when the two populations have superimposable frequency distributions). Some weak HB acceptors can therefore accelerate the water reorientation dynamics while retarding the spectral relaxation.

5. Fast Jumps Next to Hydrophobic Surfaces
While it is difficult for 2D-IR spectroscopy to discern jumps next to hydrophobic groups since they occur between spectrally indistinguishable water oxygens, it fruitfully addresses other aspects of hydrophobic hydration. A very recent Raman study suggested that a small fraction of water OHs in small hydrophobe hydration shells are dangling, that is, pointing toward the solute and unengaged in any HB.\textsuperscript{38} Dangling OHs are better known and characterized around extended hydrophobic surfaces: their presence, due to the surface-imposed sacrifice of some HBs, has been experimentally evidenced by sum frequency generation (SFG) spectroscopy, for example.\textsuperscript{39} While hydrophobic groups retard the reorientation of water OHs lying tangent to the interface,\textsuperscript{11} a theoretical study has proposed that their presence actually accelerates the reorientation of these few dangling OHs compared with the bulk situation.\textsuperscript{11} This can be understood through arguments similar to those given above for weak HB acceptors, where the exchange is facilitated by the reduced cost to elongate the initial HB.\textsuperscript{12} This prediction can be tested experimentally through 2D-IR spectroscopy, since the vibrational frequency of these OHs is strongly blue shifted due to HB absence, leading to a small
but distinct peak on the bulk OH stretch band’s blue edge (Figure 6). When these OHs execute a large (~090°) angular jump to form a HB with another water, then lying tangent to the interface, they experience a large frequency change leading to off-diagonal cross peaks in the 2D-IR spectra. However, these are hardly discernible, since they overlap with the main broad bulk water peak. The dangling-tangent state exchange kinetics is instead more easily determined experimentally from the diagonal blue-shifted peak’s decay11 (Figure 6). This clearly demonstrates that 2D-IR spectroscopy can provide experimental information on HB dynamics next to a surface so far inaccessible except through simulations. Further insight may come from promising developments in SFG–2D-IR, which combines the surface-sensitivity of sum-frequency generation with the time-correlation information provided by 2D-IR.40

6. Conclusions
We have shown that the presence of large angular jumps in water, initially suggested through simulations and analytic models,3 has subsequently received clear support from pioneering 2D-IR spectroscopy measurements.22,24 These jumps appear to be a universal feature of liquid water and have been found in a broad span of environments, including the bulk, the interface with hydrophobic and hydrophilic solutes, and the hydration layer of biomolecules.5 Predictive analytic models have been developed to describe how different chemical groups affect the jump kinetics. Our work has also shown that MD simulations coupled with 2D-IR spectra calculations greatly assist in connecting complex and sometimes ambiguous 2D-IR spectral patterns to a molecular picture.9 Exciting theoretical advances and experimental developments, especially in polarization-resolved 2D-IR24,28 and 3D-IR41 spectroscopies, are anticipated to bring further insight into the fascinating dynamics of water in its various habitats.

FOOTNOTES
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14 Analysis within ignores certain features present in ultrafast IR spectroscopy, including local heating and reorientation and dephasing in vibrationally excited states. These features are not relevant for comparison with NMR experiments.

BIOGRAPHICAL INFORMATION

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18 The special issue of Accounts of Chemical Research on Coherent Multidimensional Optical Spectroscopy, 2009, vol. 42, issue 9, may be consulted.