Structure and Dynamics of the Hydration Shell: Spatially Decomposed Time Correlation Approach

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(Dated: 1 February 2018)

Molecular simulations provide insight into solvation structures and dynamics with unparalleled spatial and temporal resolution. Here, we take advantage of this fact and develop a set of generally applicable computational tools for a detailed analysis of the hydration shell around an ionic or molecular solute. These tools allow us to quantify and visualize orientationally-resolved radial distribution functions as well as distance-resolved orientational time-correlation functions of water molecules surrounding the solute. Such a detailed view of the hydration shells allows us to unravel important structural and dynamical features, which are not accessible when employing standard analysis techniques.

TOC GRAPHIC

I. INTRODUCTION

Many solutes are influenced by the aqueous environment upon hydration, but at the same time they also perturb the surrounding water molecules. Indeed, the structure,1–3 the extent of structural perturbation,4,5 and dynamics6–8 of water around a solute have been major subjects of hydration studies over several decades. The focus of the analyses is then the collection of water molecules located within the first few shells around the solute, meaning often implicitly that spatially resolved information is sought for characterizing hydration properties. Thermodynamic, transport, and most spectroscopic measurements do not refer to a certain shell, though, but provide spatially averaged information with weights for hydration shells being assigned according to respective measurement methods. An opportunity thus exists for theory and simulations to provide insights into the solute’s effects on water by modelling of experimentally observed quantities with atomistic detail.

For decades, water dynamics was explained using a model where water molecules reorient via small diffusive steps.9 This view was challenged a decade ago10 by the introduction of a mechanism involving large amplitude angular jumps, in which a water molecule trades its hydrogen-bond acceptors. Between the jumps, the molecular orientation does not remain frozen, but the water molecules forming the intact hydrogen bond diffusively tumble. These two contributions are combined in the extended jump model10 with the jump contribution to the reorientation being dominant. This model has been applied to explain the general slowdown of water dynamics next to hydrophobic solutes due to the excluded volume effect.8,11 In the vicinity of hydrophilic solutes, water molecules can be either retarded or accelerated, because on top of the general excluded volume effect, the relative hydrogen bond strength with respect to water plays an important role.8,12,13 Recently, path integral simulations of liquid water were also analyzed within this framework.14

The present work is an attempt provide a new perspective using all-atom molecular dynamics simulations and time correlation function theory of statistical mechanics. We focus on rotational dynamics of water molecules around a series of solutes and introduce an analysis scheme based on spatial decomposition of water dynamics. The key development has been to decompose the rotational time correlation function in terms of the distance between the solute and water. This decomposition scheme is exact and does not rely on a particular model of water dynamics. The motivation for this approach is

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twofold. Most importantly, it provides insight into the properties of the system without making any a priori assumption about its structure and dynamics. Further, it allows the use of molecular simulations to decompose and interpret experimental results, where only total, unresolved, signals are available for most techniques. The scheme of spatial decomposition was previously employed to analyze energetics and volumetrics in hydration.\textsuperscript{15–18} The corresponding thermodynamic quantities were then expressed as integrals of molecular distribution functions over the whole space. The extents of spatial localization of the solute’s effect on water in these quantities were assessed by examining the convergence behaviors of the integrals. Dynamic properties were treated similarly and statistical-mechanical frameworks were provided to investigate the ion-pair contribution to the electrical conductivity\textsuperscript{19,20} and the solvation-shell contributions to spectroscopic data.\textsuperscript{21–24}

![Image](Image317x666 to 562x740)

FIG. 1. An illustration of the definitions of the angles $\theta_{\text{DM}}$ and $\theta_{\text{OH}}$. Note that $\theta_{\text{OH}}$ is defined for both OH bonds and thus there are two contributions for each water molecule, corresponding to the same position of the oxygen atom but different OH bond directions.

II. THEORY

A. Orientation-resolved radial distribution functions

Water dynamics around a solute is also a long-standing target of experimental studies such as NMR spectroscopy,\textsuperscript{25–27} dielectric spectroscopy,\textsuperscript{28–30} quasi-elastic neutron scattering\textsuperscript{31} or ultrafast IR spectroscopy.\textsuperscript{7,32,33} In these studies, it is often implicitly considered that the water molecules in the first shell around the solute determine the response of water dynamics to solute insertion. For example, NMR measurements of dilute solutions, where individual hydration shells do not overlap, use the concentration dependence of the signal and the a priori knowledge of the size of the hydration shell to infer the hydration-layer contributions water dynamics. This entails the assumption that the response is localized within the first shell, which is difficult to verify within the experiments only. The spatial decomposition analysis presented here can check the validity of this assumption by examining the spatial extent of the solute’s influence on water dynamics. The importance of these correlation functions stems further from the fact that they correspond to various (typically spectroscopic) observable quantities.\textsuperscript{34,35} For complex condensed systems, they can be efficiently evaluated using molecular dynamics simulations. In the rest of this article we take advantage of this fact. First, we present the theory behind orientationally resolved radial distribution functions and conditional time correlation functions, as well as simulation details. Next, we introduce the software tools that were developed to perform the analysis discussed here and were made available to the community as software. Finally, we present and discuss the major findings concerning the detailed spatial and temporal structures around ionic and neutral solutes, before summarizing the findings in the concluding remarks.

First, we want to characterize the structure of the solvation shell around a solute in a way that includes information on the orientation of the solvent molecules relative to the solute. For this purpose, we define the orientation-resolved radial distribution function (OR-RDF) of $N$ water molecules around a solute as

$$g(r, \theta) = \frac{N}{4\pi r^2 \sin \theta} \frac{2}{\cos \theta} \langle \delta(r-r') \delta(\theta-\theta') \rangle, \quad (1)$$

where the additional normalization factor $2/\sin \theta$ ensures that the value of $g(r, \theta)$ becomes 1.0 in the uncorrelated limit. For water molecules the angle $\theta$ can be taken as any direction defined by the three atoms (resulting in different OR-RDFs), but in the examples below, we focus specifically on the OH bond direction and the dipole moment direction (Figure 1). These static structural distribution functions can then serve as the $t=0$ basis for dynamical behavior of the solvent, namely its reorientation dynamics. We can perform integration of $g(r, \theta)$ over a range of angles to obtain an unresolved RDF,

$$\int_{\theta_1}^{\theta_2} \sin \theta \frac{d\theta}{2} g(r, \theta) = g(r). \quad (2)$$

The special case of $\theta_1=0$, $\theta_2=\pi$ yields the usual unresolved RDF. Integrating, for example, only up to $\theta_2=\pi/2$ results in an RDF only for vectors “pointing towards the solute”. While the above OR-RDF is specific to the radial coordinate, analogous orientation-resolved distribution functions can be defined for other coordinates, like the distance from an interface, for example. While similarly resolved distribution functions were employed in previous work to analyze the details of structure of aqueous systems\textsuperscript{36} or dynamics right at the interface,\textsuperscript{37–39} here we focus on OR-RDFs as the starting point for the analysis of orientational dynamics of water molecules along the entire continuous radial coordinate.
B. Conditional time correlation functions

The orientational dynamics of a molecule can be described with the orientation correlation functions

$$C_n(t) = \langle P_n (u(t_0) \cdot u(t_0 + t)) \rangle_{u,t_0},$$  \hspace{1cm} (3)

where $P_n$ is the $n^{th}$ order Legendre polynomial, $u$ is a unit vector given by the geometry of the molecule, and angle brackets denote averaging over all equivalent vectors $u$ and all time origins $t_0$ along a trajectory.\textsuperscript{34,35} The total autocorrelation time is then defined as

$$\tau_n = \int_0^\infty C_n(t) dt. $$  \hspace{1cm} (4)

The vector $u$ can describe any direction given by the geometry of a molecule, but here we focus specifically on the direction vectors of the OH bond and the dipole moment in a water molecule. In the following text, we will omit the subscript $n$, as the formulation applies to all orders in the same way. Results are then presented specifically for $n=2$.

The correlation function defined above only provides summary information for the whole system. The averaging is performed over the whole length of the trajectory and over all equivalent molecules. However, we would like to get more detailed information that is local in time and space in order to be able to attribute changes or differences in these time correlation functions to specific configurations of the system of interest. For this purpose, we define the conditional time correlation function (CTCF), a decomposition of the above $C_n(t)$, as

$$C_n(r,t) = \langle P_n (u(t_0) \cdot u(t_0 + t)) \delta(r - r(t_0)) \rangle_{u,t_0},$$  \hspace{1cm} (5)

The corresponding reorientation time decomposed with respect to the given coordinate is then simply

$$\tau(r) = \int_0^\infty C(r,t) dt$$  \hspace{1cm} (6)

and its long-distance limit, i.e. a value unperturbed by the solute,

$$\tau_\infty = \lim_{r \to \infty} \tau(r),$$  \hspace{1cm} (7)

serves as a baseline for the influence of the solute. To understand how the contribution of a given solute accumulates, we define the excess reorientation time as

$$\Delta \tau(r) = \int_0^r dr' \rho(r') (\tau(r') - \tau_\infty),$$  \hspace{1cm} (8)

where $\rho(r)$ is the normalized probability distribution of the coordinate $r$. In the case of the radial coordinate, this is proportional to $g(r)r^2$, but in a numerical simulation in periodic boundary conditions also includes finite size effects at distances larger than half the box size. The total excess reorientation time is the limit of the above cumulative quantity, or equivalently the difference between the total reorientation time in a simulation with a single solute and the unperturbed reorientation time,

$$\Delta \tau = \lim_{r \to \infty} \Delta \tau(r) = \tau - \tau_\infty. $$  \hspace{1cm} (9)

This quantity provides a complementary perspective to that provided by the ratio of the reorientation time to the bulk value and at the same time can be robustly linked to experimental observables, as detailed in the Appendix.

Thanks to the way it is defined, the CTCF fulfills what we call the “sum rule” — averaging over the conditioning coordinate yields the original unresolved correlation function,

$$C(t) = \int dr \rho(r) C(r,t). $$  \hspace{1cm} (10)

This sum rule is a crucial feature of this approach, as it enables a full decomposition of the time correlation function into unique contributions, with no parts missing and no double counting. By extension, this then allows the decomposition of experimental observables that are given by these time correlation functions. For example, the NMR signal can be related to the $\tau_2$ correlation time. The connection of $\Delta \tau$ to experimentally determined coefficients\textsuperscript{26,27} as well as the intricacies associated with $\tau_\infty$, are described in Appendix A.

The application of the condition that allows us to decompose the correlation function in Equation 5 only at delay time $t_0=0$ means that with increasing delay, spatial resolution is gradually lost. As orientation of a given molecule changes in time, it decorrelates with its initial orientation, but at the same time, its distance from the solute also changes, making the resolution at $t=0$ less relevant. Therefore, in the long-time limit all the autocorrelation functions started at different distances eventually become identical. An alternative approach would be to try and select only molecules that spend the whole delay interval in a selected range of reference distances, but that has limitations that make it less useful. Namely, the narrower the interval of interest is, the more difficult it becomes to collect sufficient statistics of water molecules that do not leave that interval of reference distances for the whole autocorrelation time of interest, usually units to tens of picoseconds. Furthermore, this selection would artificially collect contributions only from molecules with slower dynamics, as those would be more likely to stay within the given narrow interval.\textsuperscript{12} Finally, as this would make it necessary to discard molecules that leave the interval, it would not be possible to use the sum rule discussed above. For these reasons, we have not used this alternative approach and only apply the spatial condition at $t_0=0$. 

III. COMPUTATIONAL METHODOLOGY

A. Molecular dynamics simulations

Molecular dynamics simulations were performed using the GROMACS program. 508 water molecules and one solute molecule were simulated in periodic boundary conditions with interactions given by the SPC/E water model, ion parameters by Smith and Dang, and methane parameters from the united-atom OPLS force field. Three different solutes were used in separate simulations — a sodium cation, a chloride anion and a methane molecule in a united-atom description. Water molecules were held rigid using the SETTLE algorithm. All simulations were performed with a time step of $\Delta t = 1$ fs for a total time of 500 ns. Initial conditions were sufficiently equilibrated in previous simulations. Configurations were saved every 100 fs, which thus also determines the resolution of time correlation functions. A temperature of 300 K was maintained using a global stochastic velocity rescaling thermostat with a time constant of 50 ps, while a pressure of 1 atm was maintained using the Berendsen barostat with a time constant of 50 ps. To collect statistics for time correlation functions, we use multiple time origins along a single weakly coupled trajectory, rather than a set of constant energy trajectories.

B. Analysis tools

Separate programs for the calculation of orientation-resolved distribution functions and conditional time correlation functions were written as GROMACS analysis tools. The analysis can be readily performed on the output from GROMACS itself or any another program, as long as the trajectory file is in a compatible format, and running it is no more complicated than using one of the standard GROMACS analysis tools. Python scripts to plot the results are also provided. The code is available at https://github.com/OndrejMarsalek/water-orientation-dynamics and needs a working GROMACS 5.1 installation and a C++ compiler.

IV. RESULTS AND DISCUSSION

To illustrate the approach outlined above, we examine three typical hydration situations — a sodium cation, Na$^+$, a chloride anion, Cl$^-$, and a methane molecule as a simple hydrophobic solute. All systems are studied at pseudo infinite dilution, meaning that only a single solute is present in each simulation.

FIG. 2. Orientation-resolved radial distribution functions around an Na$^+$ ion. The top panel shows the OR-RDF for the oxygen atom of a water molecule and its dipole moment vector, while the bottom panel shows the same with the OH bond vector. Both panels also contain plain RDFs (labeled on the right) obtained by integrating the OR-RDF over a range of angles. The dotted line indicates a value that corresponds to the maximum of the OR-RDF color scale, which is shown at the top of the plot.

A. Solvent Structure

Let us first investigate the detailed structure of water around the solute as a starting point for the subsequent study of the spatially-resolved dynamics of the hydration shell. Figures 2, 3, and 4 show the orientationally resolved radial distribution functions (OR-RDFs), as defined by Equation 1, around the three different solutes. The value of the correlation function is indicated using the color scale shown at the top of the plots. In each case, the top panel decomposes the oxygen-solute RDF with respect to $\theta_{DM}$, the angle between the dipole moment vector of the water molecule and the line connecting its oxygen atom with the solute. The middle panel then decomposes the same oxygen-solute RDF with respect to $\theta_{OH}$, the angle between each OH bond vector and the line connecting its oxygen atom with the solute. The middle panel then decomposes the same oxygen-solute RDF with respect to $\theta_{OH}$, the angle between each OH bond vector and the line connecting its oxygen atom with the solute. Both angles are illustrated in Figure 1. An angle of 0° corresponds to a vector pointing towards the solute.

The OR-RDF is normalized so that integrating over the angle yields the standard RDF, which means that it has a constant value of 1.0 in the uncorrelated limit. We can further split each RDF into two components by integrating separately over angles below and above 90° i.e., with the given vector pointing towards or away from the solute (labeled as RDF “in” and “out” in the plots). While the full information is contained in the 2D OR-RDF, the partially integrated RDFs have the advantage
of direct comparison to the full RDF. Figures 2, 3 and 4 show RDFs obtained this way, both fully and partially integrated.

Looking now specifically at the features of the sodium cation OR-RDFs in Figure 2, we can see a clearly separated peak due to the water molecules in the first hydration shell around 2.4 Å. The angular distributions reveal that, as expected, the water molecules in the first shell are oriented with the dipole moment pointing directly away from the ion. The main feature of the second shell (between 4 Å and 5 Å) repeats the orientation of the first shell, but there is also a contribution from water molecules hydrogen bonded to those in the first shell (the feature at around 30°). The partially integrated RDFs summarize the structure of the hydration shell well, showing complete polarization of the first peak in the case of the dipole moment vector almost complete polarization in the case of the OH bond vector. Polarization is also present, but less pronounced, for the second peak.

In the case of the chloride anion in Figure 3, we can again see a clearly defined first hydration shell around 3.2 Å, although its orientation is different. Each water molecule points one OH bond directly towards the ion, while the direction of the other bond is determined by the rigid H-O-H angle. The seemingly different magnitude of the two peaks that correspond to the two OH bonds is due to the angle-dependent normalization factor of the distribution function; the populations of the two peaks are identical. Note that because of the 90° boundary for the partially integrated RDFs, there is seemingly no polarization in the direction of the OH bond vector. As the full distribution reveals, this is because, on average, one OH bond of each water molecule points “in”, while the other one points “out”. However, the partially integrated RDFs for the water dipole vector exhibit full polarization. This illustrates the limited utility of the partially integrated RDFs and the importance of examining the full OR-RDF for the understanding of the structure of the hydration shell. For both ions, the effect of longer-range polarization, fully disappearing just below 10 Å, can be seen in the OR-RDFs. This is due to the interaction of the central charge with the dipole moments of the hydrating water molecules.

Methane shows the weakest structure in the OR-RDFs in Figure 4, but there are still some noticeable features. The first shell is not as clearly separated as in the case of the two ions, but it does have distinct peaks that correspond to a water molecule “straddling” the solute. There is almost no polarization visible in the partially integrated RDFs. Still, the full OR-RDF shows clear orientational features. Both the dipole moment and OH bond favor specific orientation when the water molecule is in the first shell, and the first-shell orientation is influential for the OH bond direction in the second shell. Finally, due to the lack of net charge there is no long-range polarization around this neutral solute.
FIG. 5. Orientation autocorrelation function resolved with respect to the distance from a Na$^+$ ion. The second-order orientation autocorrelation function of the dipole moment vector and the OH bond vector resolved with respect to the distance from the solute, $C_2(r, t)$ as defined by Equation 5, is shown in the top and middle panel, respectively. The color scale for these two panels is shown at the top of the plot. Dotted lines indicate cuts at selected distances which are then shown in the bottom panel. Symbols mark corresponding lines. All data is shown on logarithmic scale.

B. Solvent Dynamics

Let us now proceed to examining the details of rotational dynamics of the solvent around the individual solutes. Figures 5, 6, and 7 show second-order orientation autocorrelation functions of the dipole moment direction vector and the OH bond direction vector of water molecules decomposed with respect to the distance from the solute, $C_2(r, t)$, as defined by Equation 5. The bottom panel shows cuts through the data in the two panels above at various fixed distances, as indicated by dotted lines. For the sodium cation, Figure 5, the dipole moment vector direction exhibits substantially slower decay (compared to bulk water behavior) at distances within the first solvent shell and marginally slower decay in the second solvent shell. The OH bond direction shows a less pronounced slowing down. The reorientation of both vectors is clearly accelerated between the first and second solvation shell, suggesting that water molecules reside in configurations at these distances only transiently. Note that the positions of the peaks in the RDF do not correspond exactly to distances at which extrema of slowing down or acceleration occur. For example, the largest slowing down of the dipole moment vector occurs at the lower edge of the first solvent shell, not at its peak. The bottom panel of Figure 5 shows cuts through the dipole moment CTCF at distances of 2.1 and 3.1 Å to show the extrema of the influence of the ion. It also shows cuts through both the dipole moment and OH bond vector CTCF at the distance of 9.5 Å to provide a reference correlation function unperturbed by the ion. In the case of the chloride anion, Figures 6, there is a similar slowing down, but the situation is reversed — the reorientation of the OH bond vector is slowed down more than that of the dipole moment vector. The acceleration between the first and second shell is almost non-existent here and a dip only appears because of the contrast with the surrounding correlation functions in the first and second solvation shells. Here, the bottom panel shows cuts for the OH bond vector at the distances of 3.1 and 3.9 Å as well as 9.5 Å for both vectors, again to provide a reference for the deviations. Finally, the hydrophobic solute shown in Figures 7 represents a different situation. We observe a general slowing down of the reorientation of both vectors at distances that correspond to the diffuse first hydration shell in the radial distribution function, but no separate contribution of the second shell or an acceleration between the shells is apparent. Cuts are shown through both the dipole moment and OH bond vector CTCF at 3.8 and 9.5 Å.

The above data can be summarized by calculating the
FIG. 7. Orientation autocorrelation function resolved with respect to the distance from a methane molecule. The second-order orientation autocorrelation function \( C_2 \) of the dipole moment vector and the OH bond vector resolved with respect to the distance from the solute, \( C_2(r, t) \) as defined by Equation 5, is shown in the top and middle panel, respectively. The color scale for these two panels is shown at the top of the plot. Dotted lines indicate cuts at selected distances which are then shown in the bottom panel. Symbols mark corresponding lines. All data is shown on logarithmic scale.

The total integrated autocorrelation time at each distance. This is shown in the top panels of Figures 8, 9, and 10 for the three solute species. This separation-dependent reorientation time \( \tau(r) \) is then referenced against the reorientation time of the corresponding vector at infinite distance from the solute, \( \tau_{2,\infty} \), i.e. in the solvent unperturbed by the solute. The limiting value is the same as that obtained from a simulation of the neat solvent and serves as a baseline for \( \tau(r) \), indicating whether the orientational dynamics at a given distance is slowed down or sped up. Although we can see that in all cases the reorientation time quickly approaches the limiting unperturbed value, the magnitude of contributions from different distances only becomes apparent once we take into account the populations at those distances. In the case of the radial distance from the solute considered here, the contribution at distance \( r \) is weighted by the factor \( g(r)\tau^2 \), while in the general case we would simply consider the probability distribution of the given coordinate.

In the bottom panels of Figures 8, 9, and 10, we plot the change in the reorientation time of a water molecule due to the presence of a solute that takes into account these populations. Specifically, we plot the excess contribution to the reorientation time from water molecules within a distance \( r \) of the solute, \( \Delta\tau(r) \), as defined by Equation 8. This offers a perspective on how the excess contribution converges as we consider an increasingly larger surrounding of the solute and highlights differences between the three types of solutes that are not readily apparent from the decomposed correlation functions or decomposed reorientation times considered above. For the sodium cation, we observe a large difference between the overall slowdowns of the reorientation of the two vectors in the bottom panel of Figure 8 — the dipole moment vector is slowed down substantially more. At the same time it is clear that the bulk of the contributions comes from the first solvation shell, while further distances contribute very little. In contrast, the data for the chloride...
anion in the bottom panel of Figure 9 shows a clear contribution to the excess reorientation time of both vectors from the second solvation shell, even for this monovalent anion. Although the OH vector is slowed down more than the dipole moment vector in this case, the difference is not as pronounced as for the sodium cation. Finally, the hydrophobic solute exhibits the largest overall excess reorientation times as well as their slowest convergence with respect to the distance of the water molecule from the solute. In fact, a large part of the total contribution comes from distances larger than the conventional boundary of the first solvent layer, taken as the first minimum of the radial distribution function. Both vectors are slowed down by approximately the same amount.

The slow-down effect of the investigated ions on water is consistent with previous studies by some of the authors based on the jump model of water reorientation,\textsuperscript{11,48} as well as with experimental observables, whenever available.\textsuperscript{49} Note that, unlike in simulations, in experiments on salt solutions the cationic and anionic effects are hard to disentangle. One of the innovative aspects of the present approach is that it explicitly and systematically accounts for all solvent molecules, not just the first solvent shell around the solute. The example of the chloride anion shows how a substantial part of the total contribution only appears in the second solvent shell, while the total contribution around the neutral methane solute accumulates gradually over distances up to about 9 Å. It is important to consider the motion (and therefore change of distance from the solute) of the water molecule as the delay time increases. In Section S1 of the SI we examine this issue in detail by calculating resolved reorientation times accumulated over limited delay time. This clearly shows that the overall shape of $\Delta \tau(r)$, including the positions of local minima and maxima, does not change with an increasing delay, confirming that the existence of contributions beyond the first shell is not an artifact of the analysis method.

V. CONCLUSIONS

In this paper, we present a set of computational tools, which are generally applicable for a detailed analysis of structural and dynamical aspects of hydration shells of ionic and molecular solutes. In particular, we evaluate orientationally-resolved radial distribution functions and distance-resolved orientational time-correlation functions, which render a comprehensive picture of the behavior of water molecules in the hydration shells of solutes. Compared to the existing approaches, the present analyses provide a fine-grained insight into the local structural as well as dynamical aspects of the solvent response to ionic and molecular solutes. Both the structural and dynamic analyses are implemented as GROMACS analysis tools and available as free software. This makes them immediately available to the large community of users of GROMACS, as well as other simulations packages, as long as trajectory data is available in a compatible format.

To illustrate the above methodology, we apply it to investigate the spatially resolved radial distribution functions and orientation correlation functions of water molecules around a sodium cation, a chloride anion, and a methane molecule. We thus obtain a detailed structural and dynamical characterization of hydration shells around a typical atomic cation, anion, and a small hydrophobe. The analysis reveals the spatial extent and structure of their hydration shells in the sense of both structure and dynamics of the solvent. Thus, the validity of the assumption of contributions to localized to the first solvent shell can be explicitly checked. This enables the interpretation of experimental observables related to hydration shells of various other small solutes.

Future plans include extending the present approach to inhomogeneous environments, such as surfaces and interfaces, and to finite concentrations of solutes, as well as to linking directly to infra-red, Raman, NMR, and other spectroscopics.

Appendix A: Connection of $\Delta \tau$ to the experimental observable and the asymptotics of $\tau(r)$

Equations 8 and 9 introduce the excess reorientation time $\Delta \tau$ through integration over the space. In this Appendix, we provide the connection of $\Delta \tau$ to the experimental observable which is often called “$B$ coefficient”.\textsuperscript{26,27} When $\tau$ is a single-molecule quantity such as NMR reorientation correlation time, it is measured as an average over all the water molecules in the system and
is expressed as

$$\tau = \frac{1}{N_w} \sum_i \tau_i, \quad (A1)$$

where $\tau_i$ is the $\tau$ of the $i$th water molecule and $N_w$ is the total number of solvent molecules. Let us have $N_u$ solute molecules, and $\tau_i$ is spatially decomposed in terms of the relative position from each solute as

$$\tau_i = \int dr_1 \ldots dr_{N_u} P_i(r_1, \ldots, r_{N_u}) \tau_i(r_1, \ldots, r_{N_u}), \quad (A2)$$

where $r_j$ is the position of the $j$th solute ($j = 1, \ldots, N_u$). Actually, not all of $r_j$ are independent, but the dependencies between them are taken into account by setting $P_i = 0$ then, where $P_i$ is the probability of finding the $i$th solvent at the set of positions $(r_1, \ldots, r_{N_u})$. We also let $\tau_\infty$ be the value of $\tau_i$ far separated from all the solutes. This exists when the solute is dilute. A more rigorous specification of $\tau_\infty$ will be given at the end of the Appendix.

The change in $\tau$ between the systems with $N_u$ solute molecules and without any solute is given by

$$\Delta \tau = \tau - \tau_\infty = \frac{1}{N_w} \sum_i \int dr_1 \ldots dr_{N_u} P_i(r_1, \ldots, r_{N_u}) \left[ \tau_i(r_1, \ldots, r_{N_u}) - \tau_\infty \right]. \quad (A3)$$

This is because the integral of $P_i$ is 1. Now the system is dilute, and all the solutes are well separated to one another. $\tau_i(r_1, \ldots, r_{N_u})$ is then different from $\tau - \tau_\infty$ only when the $i$th solvent molecule is close to one of the solutes, and since the system is dilute, it can be close to only one of the solute molecules at a time. When the water solvent molecule is close to $r_1$, for example, there is no effect from the other solute molecules and $\tau_i(r_1, \ldots, r_{N_u})$ depends only on $r_1$. Further, since all the solute molecules are equivalent, a water molecule can be close to each solute at equal probability and we can rewrite Equation A3 as

$$\Delta \tau = \frac{N_u}{N_w} \int dr_1 \ldots dr_{N_u} P_i(r_1, \ldots, r_{N_u}) \left[ \tau_i(r_1) - \tau_\infty \right] = \frac{N_u}{N_w} \int dr_1 P_i(r_1) \left[ \tau_i(r_1) - \tau_\infty \right]. \quad (A4)$$

We can drop the subscripts $i$ other than 1 in the above due to the equivalence of all the solvent molecules and of all the solute molecules. The solvent density $\rho(r)$ at position $r$ is given then by $N_w P_1(r)$ and we have

$$\Delta \tau = \frac{N_u}{N_w} \int dr \rho(r) \left[ \tau(r) - \tau_\infty \right]. \quad (A5)$$

When the solute concentration is $c$, it is equal to $N_u/V$. The response of $\tau$ to the insertion of solute is experimentally described at infinite dilution by $\partial \tau / \partial c$, leading thus to

$$\left( \frac{\partial \tau}{\partial c} \right)_{T,p} = \frac{\Delta \tau}{N_u/V} = \frac{V}{N_w} \int dr \rho(r) \left[ \tau(r) - \tau_\infty \right] = v_0 \int dr \rho(r) \left[ \tau(r) - \tau_\infty \right] \quad (A6)$$

where $v_0$ is the volume per molecule in pure solvent. This equation provides the connection of $\Delta \tau$ to the experimentally determined coefficient; the “$B$ coefficient” is given by dividing Equation A6 by the $\tau$ value in pure solvent.26,27

Finally, we show that $\tau_\infty$ is the bulk value in pure solvent treated at the same pressure (not the volume). $\tau(r)$ is the time integral of the correlation function $C(t;r)$, and we focus on $C(t;r)$ in the following. When the solute is fixed at the origin, the time derivative of $C(t;r)$ is given by

$$\left( \frac{\partial^n C(t;r)}{\partial t^n} \right)_{t=0} = \int dr_1 \ldots dr_n F_{n+1}(r, r_1, \ldots, r_n) \rho_{n+1}(r, r_1, \ldots, r_n), \quad (A7)$$

where $\rho_{n+1}(r, r_1, \ldots, r_n)$ is the $(n+1)$-body distribution function of the solvent with respect to the solute at the origin and $F_{n+1}(r, r_1, \ldots, r_n)$ denotes a function involving (high-order) derivatives of potential functions. $r$ denotes the position of the solvent molecule that appears in $C(t;r)$ and $\tau(r)$, and the integration is conducted only over $r_1, \ldots, r_n$. $\tau(r) - \tau_\infty$ then corresponds to

$$\left( \frac{\partial^n [C(t;r) - C(\infty)]}{\partial t^n} \right)_{t=0} = \int dr_1 \ldots dr_n F_{n+1}(r, r_1, \ldots, r_n) 	imes \left[ \rho_{n+1}(r, r_1, \ldots, r_n) - \rho_{n+1}(\infty, r_1, \ldots, r_n) \right], \quad (A8)$$

where $\rho_{n+1}(\infty, r_1, \ldots, r_n)$ is equal to the $(n+1)$-body distribution function when the “tagged” solvent molecule is located far from the solute. Some care is needed when it comes to the distribution functions at $r = \infty$. In fact, $\rho_{n+1}(\infty, r_1, \ldots, r_n)$ deviates from the $(n+1)$-body distribution function in pure solvent by $O(1/V)$ in the $NVT$ ensemble and by $o(1/V)$ in $NpT$. This difference between the two ensembles can be simply neglected when the single-point values of the distribution functions at $r = \infty$ are concerned. The integration over $r$ is done over the whole space in Equation A5, however, which is $O(V)$. The $O(1/V)$ deviation survives in the integration and provides an observable effect. The $o(1/V)$ effect is integrated to $o(1)$, on the other hand, and can be safely neglected in the limit of large system size. It is shown in Reference 17 that the issue concerning $O(1/V)$
and $\alpha(1/V)$ accounts for the difference between the iso-
choric and isobaric process of solute insertion. When $\rho_{n+1}(\infty, r_1, \ldots, r_n)$ is taken to be the one far from the
solute in the solution system which actually contains a
solute, Equation A8 corresponds to the one in the iso-
baric insertion of solute, irrespective of the ensemble of
the system (NVT or NpT). In other words, even when $\rho_{n+1}(\infty, r_1, \ldots, r_n)$ is computed as the one far from the solute, instead of
the $(n+1)$-body distribution function in pure solvent.
It should be emphasized again that the difference be-
tween $\rho_{n+1}(\infty, r_1, \ldots, r_n)$ and $\rho_{n+1}(\infty, r_1, \ldots, r_n)$ is
computed in this paper as the one far from the solute, instead of
the $(n+1)$-body distribution function in pure solvent absorbs the ensemble depend-
ence (isochoric vs isobaric) of solute insertion. There-
fore, our procedure to fix $\tau_\infty$ as the flat value at far dis-
tances from the solute can be justified with the asym-
ptotic analysis, and even with an NVT MD, the computa-
tional result of $\Delta T$ should be compared to the experiment
done in $NpT$.

ACKNOWLEDGMENTS

E.P. thanks the Czech Academy of Sciences for the Postdoctoral Fellowship (Grant No. L200401651) P.J. acknowledges support from the Czech Science Foundation (grant no. P208/12/G016). N.M. is further supported by the Grants-in-Aid for Scientific Research (Nos. JP15K13550 and JP26240045) from the Japan Society for the Promotion of Science and by the Elements Strategy Initiative for Catalysts and Batteries and the Post-K Supercomputing Project from the Ministry of Education, Culture, Sports, Science, and Technology. O.M. was sup-
ported by the grant Primus16/SCI/27/247019.

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S1. CONVERGENCE WITH RESPECT TO INTEGRATION TIME

To examine the gradual accumulation of the total autocorrelation time as well as the influence of diffusion on its spatial resolution, we can generalize Equation S1 by considering a finite end of the integration interval,

$$\tau(r, t_{max}) = \int_{0}^{t_{max}} C(r, t) dt. \quad (S1)$$

The result is illustrated in Figure S1 for a series of finite integration times. Curves of increasing color intensity show data for $t_{max}$ going from 1.0 ps in steps of 3.0 ps, where the dotted lines indicate the long-distance limit. Curves for $t_{max} = \infty$ are also shown. Alternatively, the excess reorientation time $\Delta\tau$ in the bottom panel can be rescaled so that all the curves have the same value at maximum separation $r$, which facilitates comparison of the shapes of the curves, rather than absolute values. Figures S2–S4 show data rescaled in this way for both vectors and all three systems studied here.

This analysis shows that for the systems we consider here, diffusion, i.e. the change of the reference distance during the integration time, does not substantially change the interpretation of the results. In general, the excess autocorrelation time $\Delta\tau$ has sharper features for shorter integration times. However, even with these shorter times, it does not saturate faster with respect to the reference distance, indicating that the influence of the second solvation shell, as discussed in the main text, is not an artifact of the way the spatial decomposition is performed.

![FIG. S1. Reorientation distance resolved with respect to the distance from a Na$^+$ ion. Multiple curves are shown for increasing integration time as detailed in the text.](image-url)
FIG. S2. Reorientation time resolved with respect to the distance from a Na\(^+\) ion. Multiple curves are shown for increasing integration time as detailed in the text.
FIG. S3. Reorientation time resolved with respect to the distance from a Cl\(^{-}\) ion. Multiple curves are shown for increasing integration time as detailed in the text.
FIG. S4. Reorientation time resolved with respect to the distance from a methane molecule. Multiple curves are shown for increasing integration time as detailed in the text.