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Ultrafast Vibrational Spectroscopy of Aqueous Solution of Methylamine from First Principles MD Simulations

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We performed Car-Parrinello molecular dynamics (CPMD) simulations of deuterated aqueous solution of methylamine (MA) to investigate the structure, dynamics and time dependent vibrational spectra of water molecules in the first solvation shell. Our results show that the hydrogen bond of DOD…ND$_2$ is the dominant interaction between ND$_2$ and D$_2$O as compared to the D$_2$O…D$_2$N. The hydrogen bond involving DOD…ND$_2$ has longer lifetime (2.6 ps) than both D$_2$O…D$_2$N (1.1 ps) and water-water hydrogen bonds. The residence time of water molecule inside the first solvation shell of ND$_2$ is 5.72 ps. The vibrational spectral diffusion of water molecules in the first hydration shell of the amine nitrogen of methylamine proceeds with three time scales. A short-time relaxation originates from dynamics of amine-water hydrogen bonds without breaking (90 fs), and a slower relaxation (∼1.8 ps) is due to the breaking of amine-water hydrogen bonds. Another longer time constant (∼7 ps) is due to the escape dynamics of water molecules from the first hydration shell of the amine group.

Introduction

Amines play a vital role in chemistry and biology because amine groups are a constituent of peptides, proteins and biopolymers. A simple primary amine like the methylamine (MA) molecule is found in the human body[1–6] and responsible for many biochemical phenomena.[7–9] Methylamine is one of the simplest organic molecules containing both hydrophobic (methyl) and hydrophilic (amine) groups. As most parts of living cells contain water molecules, the biological functions of methylamine and other molecules having amine functional are directly connected to their hydrated structures.[10–15] In an aqueous solution of amines, along with the water-water hydrogen bonds, one can find the water-amine group hydrogen bonding both through nitrogen and hydrogen atoms. Due to the presence of such a hydrogen-bonding environment, MA influences the local structure, dynamics and spectral properties of water molecules inside and outside its solvation shell. The hydration of amines are known to influence amines' basicity in aqueous solution[16,17] and MA shows the most favorable solvation free energy in aqueous solution among ammonia, dimethylamine and trimethylamine.[18,19] Therefore, much attention has been given to reproduction of experimental solvation free energy of MA along with other amines.[20–29] Moreover, the hydration behavior of methylamine in its aqueous solution has

been reported by some computational studies. For example, Dunn et al.[30] studied the aqueous solution of MA by applying Monte Carlo (MC) simulations. They reported that the first hydration shell of the NH$_2$ group has three water molecules. Among the three water molecules, two of them only participate in the hydrogen bond formation with amine group. Another study by Kusalik et al.[20] using Molecular Dynamics (MD) simulations also showed that two water molecules were required to form hydrogen bonds with an amino group in its first hydration shell. Holger and Karsten[31] performed the *ab initio* molecular dynamics simulation of methylamine in water. According to Holger and Karsten, one of the water molecules forms a hydrogen bond with the nitrogen atom, and other two water molecules form hydrogen bonds with the two hydrogen atoms of the amine group. According to an MC simulation,[32] on average NH$_2$ group can be involved in 2.51 hydrogen bonds. But, as per an MD simulation,[25] the amine group can form 1.77 hydrogen bonds with water molecules, while the **reference interaction site model(RISM)**[33] predicted 2.4 hydrogen bonds per the same moiety. Marta et al.[34] studied the structures of the hydrated clusters of methylamine by applying density functional theory (DFT). Marta et al.'s primary goal was to generate hydroxide ions via proton transfer from water to the amino group. Ultimately, they have concluded that there was no proton transfer in the most stable geometry. Sha-Sha et al.[35] reported from DFT calculations that with the increase in size of methylamine-water cluster, the strength of the H$_2$N…H$_2$O hydrogen bonds increase. Although much effort has been made to produce the structural data on hydration, detailed analysis of dynamical and spectral signatures of water molecules in the vicinity of a primary amine group has not been reported.

In this paper, we have considered the hydration of a primary amine group by investigating deuterated methylamine, (CD$_3$ND$_2$), dissolved in liquid water (D$_2$O). The major part of this work enumerates the structure, dynamics and spectral signa-

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ture of water molecules inside first solvation shell of methyl-amine. The vibrational frequency of water molecules in aqueous solution varies because of the fluctuations in the local solvation environment. The ultrafast time-resolved infrared spectroscopy has provided a very powerful experimental means of investigating water dynamics at molecular level, such as the dynamics of breaking and making hydrogen bonds in water[36–49] and aqueous solutions.[50–56] The frequency fluctua-tions of the hydroxyl modes of water molecules can be used to capture the dynamical interactions of the solute with its surrounding water molecules.

We investigate the structure, hydrogen bond dynamics and vibrational spectral diffusion of aqueous methylamine molecule at room temperature using density functional theory (DFT)-based Car-Parrinello molecular dynamics (CPMD) simulations. In particular, we analyzed the hydrogen bond interactions between methylamine and the water molecules by calculating radial distribution functions and hydrogen bond coordination numbers. The dynamics of the hydrogen bond has been calculated through the hydrogen bond auto-correlation func-tion. We also investigated the spectral feature of the first solvation shell water molecules through the time-dependent vibrational stretching frequencies of hydroxyl modes of water molecules calculated from trajectories, by performing wavelet analysis.

Results and Discussion

Structure of solvation shell

In aqueous solution, MA acts as a double donor and single acceptor of hydrogen bonds. Structural features that illustrates the hydration behaviour of methylamine molecule are radial distribution functions; these functions are directly correlated to the structure factors available from neutron diffraction experi-ments. Our focus is mainly on those radial distribution functions (RDF) that are responsible for hydrophilic properties in aqueous methylamine solution. However, the hydrophobic interaction between MA and water can be captured through the study of interaction between methyl group and oxygen of water molecules. First, We will discuss hydration of the ND_2 group. We have calculated RDFs between nitrogen and oxygen, as well as hydrogen atoms of water, ($N-O_w$ and $N-D_w$) and between aminic hydrogen and oxygen of water ($D-O_w$) pairs. The radial distribution functions $g(r_{NOw})$, $g(r_{NDw})$, and $g(r_{DOw})$ are shown in Figure 1 along with the corresponding number integrals (NIs). The atoms with subscript 'w' correspond to water molecules for RDF calculations, to differentiate the D of amine group. For the $N-D_w$ pair correlation function, the first peak appears at 1.64 Å, followed by a broad minimum around 2.34 Å. The depth of the minimum of the $g(N-D_w)$ function reaches up to 0.05. This peak position arises due to the formation of hydrogen bonds between the nitrogen atom and water molecules; it is clear from the first peak position of $g(N-O_w)$. However, the first minimum for the later RDF was not so well defined. The peak position obtained from our work for N-D_w RDF was shorter than the earlier reported values in the
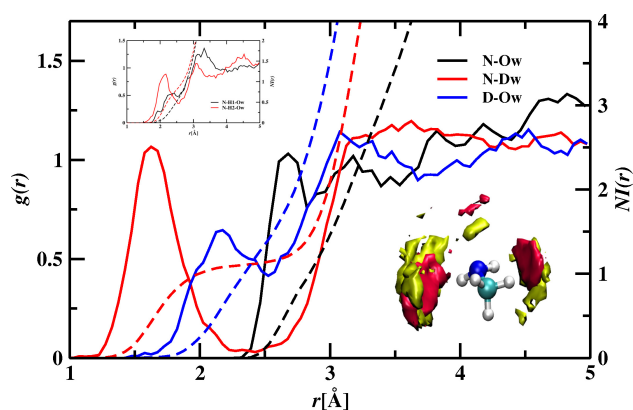
Figure 1. Radial distribution functions for ND_2-D_2O. Solid lines represent the radial distribution functions and dashed lines represents the number integral values. The black, red, and blue solid lines represent the RDFs for N-O$_w$, N-D$_w$ and D-O$_w$ pairs, respectively and the corresponding NI value is shown with dashed lines. The inset figure in the upper part represents RDFs along with NIs calculated individually for two D atoms of ND_2 group. Inset figure (lower) depicts the SDF oxygen and hydrogen atoms around methylamine; red and yellow colored surfaces represents oxygen and hydrogen atoms, respectively. A value of 0.04 was used as the isosurface value for surface plot.

range 1.73-1.90,[20,30] but in well agreement with the MD simulation reported by Hesske et al.[31] According to our calculations, the NI value of a N-D$_w$ pair up to first minimum is 1.11. This implies that the nitrogen atom of methylamine can form approximately one hydrogen bond with water. Our obtained NI value is in good agreement with several MD simulations,[20,31,32] but differs with the value of 1.77, reported from other MD study.[25] The ND_2 moiety contains three hydrogen bonding sites, one acceptor (N atom) and two donor sites (D atoms). Therefore, the amine group can be involved in formation of two types of hydrogen bonds. One type is N…D$_w$-O$_w$ that has been already discussed. Another type is D…O$_w$ (the D belongs to the aminic group). The D-O$_w$ RDF pair gives the first peak at 2.15 Å, followed by a minimum at 2.53 Å. The position of the first peak indicates the hydrogen bond formation between aminic hydrogen and water molecules. The depth of the minimum of the D-O$_w$ RDF pair comes down up to 0.40 that gives the evidence of formation of weaker hydrogen bonds when compared to N…D$_w$ and O$_w$…D$_w$ types of hydro-gen bonds in aqueous solution (RDFs for water-water are not shown). The position of our peak for the D-O$_w$ pair agrees well with the value of 2.10 Å calculated from other MD simula-tions,[23,32] but is greater than the values 1.80 and 1.85 Å, determined from Monte-Carlo simulations[30] and the RISM method[33], respectively. The calculated NI value of D-O$_w$ RDF also matches well with earlier reported values; the first minimum is 1.40 (a value of 0.7 for each hydrogen atom). The earlier reported values showed that each hydrogen atom attached with nitrogen forms 0.5-0.7 hydrogens bond with water.[25,33] In case of the NH$_2$ radical, the amine group interacts with a water molecule through the aminic hydrogen; one of these hydrogen atoms is exposed towards the air.[57] Moreover, our calculated data of N…D$_w$ and D…O$_w$ hydrogen bonded

entities are in qualitative agreement with experimental results.[58] We also calculated pair correlation functions for the individual deuterium atoms of amine group with the oxygen of water to understand their symmetric nature in the aqueous environment. The radial distribution functions calculated separately for both the deuterium atoms (Hereafter D1 and D2) with water are shown in the inset of Figure 1. The D1…O_w RDF shows a small peak position at 1.92 Å, while the D2…O_w RDF shows the first peak at 2.15 Å. From the peak positions of both RDFs we find that the D1 atom makes a relatively stronger hydrogen bond than the D2 atom. The NI value of the D2-O_w RDF pair is showing 0.90 up to the first minimum. The probability of finding two hydrogen bonds through two N—D bonds in symmetrical manner with respect to N of amine group is smaller. Adding together the NI values obtained from N-D_w and D-O_w RDFs pairs, it is found that the ND_2 moiety makes on average 2.55 hydrogen bonds with water. This number is higher than earlier reported values.[32,33] We have further shown the three-dimensional environment of amine solvation shell depicted by the spatial distribution function (SDF) plot in the inset graphics of Figure 1. This SDF representation also shows the interaction of water hydrogen atoms towards the nitrogen atom and the relatively unsymmetrical hydrogen bonding nature of the two N—D bonds of the amine group.

We calculated combined distribution function (CDF) for the proper understanding of the structure of hydrogen bonds made by aminic nitrogen and deuterium atoms with water molecules. In CDF contour plot, the x-axis represents RDF and y-axis represents the angular distribution function. The graphical model of the considered distance and angle is shown in the inset of Figure 2. The CDF for N-O_w distance and the angle that originates from two vectors O_w-D_w and N-D_w are presented in the top panel of the same figure. This angle primarily represents the hydrogen bond angle between the acceptor and donor. The bottom panel of Figure 2 represents the CDF of N-O_w distance and the hydrogen bond angle that originates from N—D and D-O_w vectors. In case of N…D_w interaction, the most probable angle lies around 165°, and the preferred distance is 260 (2.6) to 270 pm (2.7 Å). This distance corresponds to the first peak position of N-O_w RDF. In case of D…O_w interaction, the most probable angle value is 165°, and the D-O_w distance is 280 pm (2.8 Å). However, some structures with different angles and distances are also evolving from the analysis of the contour plot with a lower probability. Moreover, we have the assessment from the analysis of CDF contour plots that N…D_w hydrogen bonds are stronger than D…O_w.

Vibrational frequencies of water inside and outside the first solvation shell of methylamine

The hydrogen bond network of water molecules is affected by the presence of an amine group. In aqueous solution, the stretch frequencies of water molecules (OD modes) vary due to the fluctuations in the involved solute-water and water-water hydrogen bonds. We examined such fluctuations in the solvation shell in the vicinity of amine group. We also considered the N—D modes of MA. In Figure 3 (left panels), we
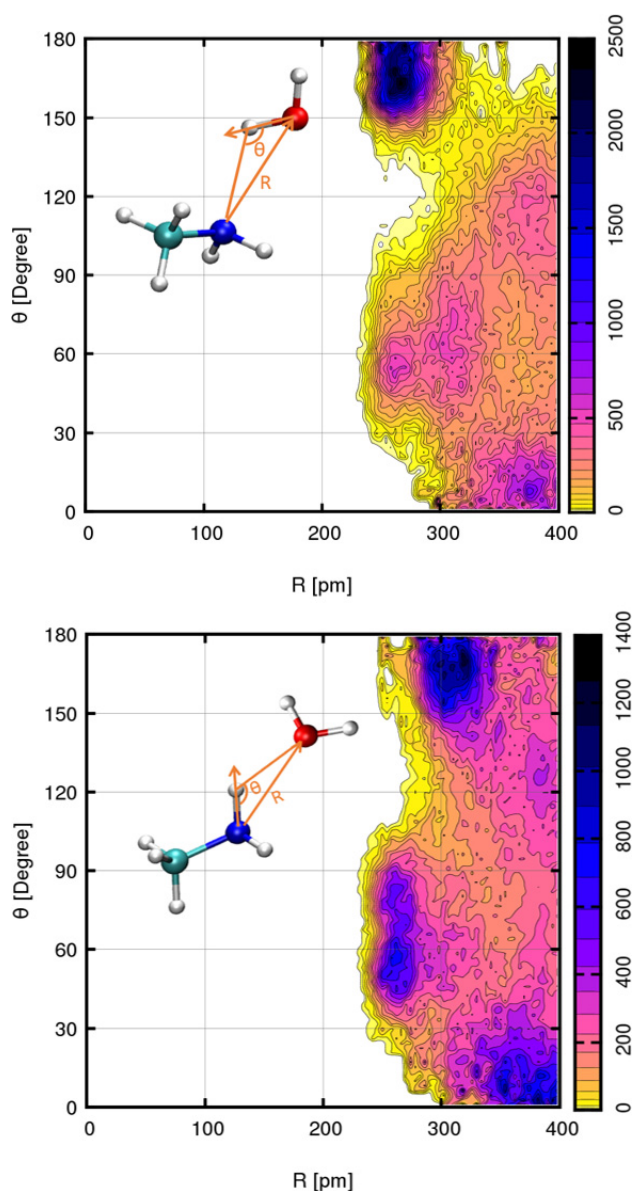

Figure 2. Contour plots of hydrogen bond angle vs distance. The x-axis represents N-O_w distance (in Pico meter) and the y-axis represents the hydrogen bond cut-off angle originated from two vectors points O_w-D_w and D_w-N.

have shown the instantaneous frequency fluctuation (upper panel) of the hydroxyl modes of a water molecule, which was initially not hydrogen-bonded with nitrogen and then subsequently formed a hydrogen bond with it. We have presented the fluctuation of corresponding N-D_w distances with the time in the lower left panel. In the upper right panels of same figure, we have shown the instantaneous fluctuation of the N—D mode of methylamine associated with the hydrogen bonding with water molecules. The lower panel represented the fluctuation in N—O_w distance. It is seen that there is a significant decrease in the frequencies of both the OD bonds when a tagged water molecule makes a hydrogen bond with corresponding atoms of MA. On average, the OD covalent frequency
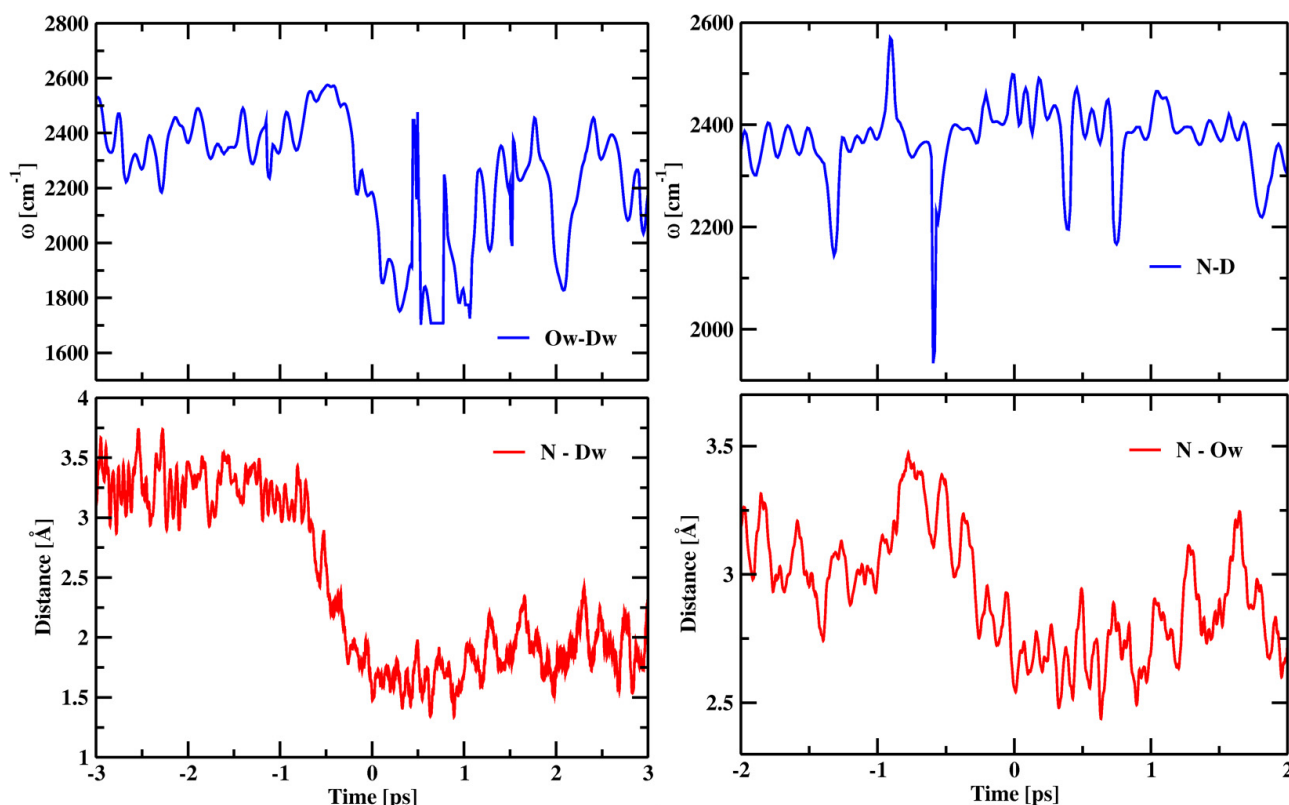
Figure 3. (Left panels) Time dependence of the fluctuating frequency of an OD bond of water as it makes hydrogen bonded to nitrogen atom to which it was not hydrogen bonded initially. The time when $N-D_w$ distance less than 1.80 Å (first time during observation period of 6 ps) is taken to be $t=0$. The upper panel represents time dependence of the frequency of the OD bond and the lower panel represents the corresponding $N-D_w$ distance. (Right panels) Time dependence of the fluctuating frequency of ND bond of methylamine as it makes hydrogen bonded to hydrogen atom of water molecule to which it was not hydrogen bonded initially. The time when $N-O_w$ distance approaches 2.60 Å is taken to be $t=0$. The upper panel represents time dependence of the frequency of the ND bond and the lower panel represents the corresponding $N-O_w$ distance.

increases somewhat with an increase in the associated hydrogen bond distance with water molecules. However, this effect is not observed in the frequency of ND. As the distance of the nitrogen atom of the amine group increases from a particular oxygen of a water molecule, the ND_2 can be in a similar environment with other water molecules. In Figure 4, we have shown the frequency distribution of the OD bonds which are inside the solvation shell of ND_2 group, hydrogen bonded to nitrogen atom, and those are outside the solvation shell, or bulk water. We have also shown the frequency distribution for N—D modes of MA in the same figure; the average frequency of N—D modes is 2370 cm^{-1}. Due to aqueous solvation this mode is red shifted as compared to gas phase ND frequency.[59] The existence of hydrogen bonds between donor and acceptor atoms is determined by the simple geometric criterion that the distance should be less than the corresponding first minimum of RDF pair. The corresponding water molecule should be in the solvation shell of amine group having a $N-O_w$ distance less than 3.2 Å. The cut-off distance of 2.45 Å for hydrogen bonded OD modes around the amine group has been chosen according to the first minimum of $N-D_w$ RDF pairs. The average frequencies OD modes in the hydration shell of an ND_2 group and the bulk are found to be 2395 and 2365 cm^{-1}, respectively.
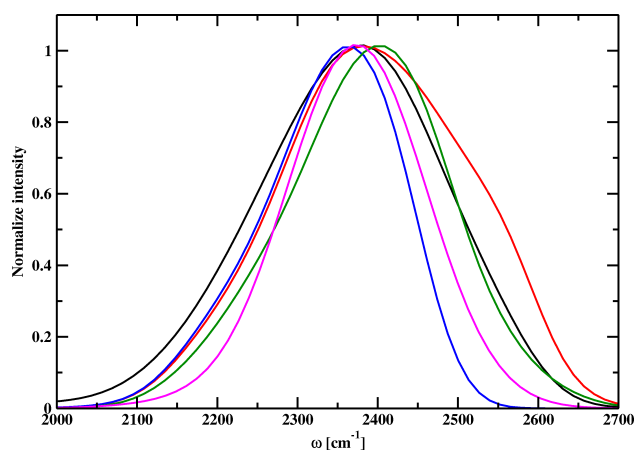
Figure 4. The distributions of OD stretch frequencies of the solvation shell OD modes in the first hydration shell of amine nitrogen of MA, and hydrogen bonded OD modes with nitrogen inside the solvation shell are represented in red and blue lines, respectively. The distribution of dangling OD modes around the hydrophobic methyl group is shown in green line. Black line represents the distribution of frequencies OD modes that are outside the solvation shell. We have also shown the frequency distribution of N—D modes of MA in pink color line. Each distribution is normalized to the maximum value 1.

A blue shift is observed in the frequencies of hydration shell OD modes as compare to those of bulk modes. The present value of the average frequency of the bulk OD is less than the pure water (2380 cm^{-1}).[60] The red shift is observed for hydrogen bonded OD mode with the nitrogen atom; the average value for hydrogen bonded OD modes is found to be 2335 cm^{-1}. This shift of frequency can be correlated to the fact that the strength of hydrogen bond N…D$_w$ is stronger than water-water hydrogen bonds, as we concluded from our structural analysis. We also performed the gas phase cluster calculation of the hydrated cluster of methylamine having a single water molecule following optimization procedure using the B3LYP[61,62] method with 6–311+G(d,p) basis set as implemented in Gaussian 09 software.[63] We found that water binds the nitrogen center most favorably with an interaction energy of −7.5 as compared to −5.2 kcal/mol of water-water binding energy. The red shift of the vibrational frequencies of the elongated proton donating H–O bond, and the shortening of the N…H intermolecular distance with the addition of water molecules to the hydrated cluster were also observed from an *ab initio* simulation study.[35] These tendencies were not found for the hydrated cluster containing five water molecules. We have also calculated the distribution of dangling O–D modes around the methyl group; these modes essentially contribute towards the hydrophobic interaction of MA with water molecules. The average frequency (2385 cm^{-1}) of these modes is higher than both bulk and solvation shell hydrogen bonded modes with shifting of peak position towards higher frequencies indicating the weak solute-solvent interaction through the hydrophobic group.

Amine–water hydrogen bonds and escape dynamics of water from first solvation shell

The stability of amine-water hydrogen bonds has been explored using time dependent population correlation function. We have calculated continuous hydrogen bond correlation function[64–71] to study the breaking dynamics of hydrogen bonds which describes the probability that an initially hydrogen bonded pair remains bonded all times up to t. The continuous hydrogen bond time correlation function $S_{HB}(t)$, is defined as

$$S_{HB}(t) = < h(o) H(t) > / < h(o)^2 > \qquad (1)$$

where $< … >$ denotes an average over all the corresponding hydrogen bonded pairs. Clearly, $S_{HB}(t)$ describes the probability that an initially hydrogen bonded pair remains bonded at all times up to t. The associated integrated relaxation time gives the average lifetime of the hydrogen bond between two hydrogen bonding sites. Here, we have considered N and D atoms of amine group as the hydrogen bond accepting and donating sites, respectively. The existence of hydrogen bonds between ND$_2$ and water was considered by taking the cut-off distances obtained from the first minima of corresponding RDFs. The cut-off distances for N…D$_w$ and D…O$_w$ hydrogen bonds are taken to be 2.45 and 2.43 Å, respectively. The

computed lifetime obtained from decay rate of correlation function for DOD…ND$_2$ is slower than that of DND…OD$_2$. The lifetime of N…D$_w$ pair is 2.6 ps while the lifetime of D…O$_w$ is 1.1 ps. This N…D$_w$ hydrogen bond lifetime is longer than the lifetimes of hydrogen bonds in pure water.[60] Thus the average number of hydrogen bonds, strength, CDF and lifetime of the hydrogen bonds show that the interaction between ND$_2$ and water is dominated by DOD…ND$_2$ hydrogen bond interaction. Our reported lifetime value of the D…O$_w$ hydrogen bond is higher than the amide hydrogen−water hydrogen bonds for an aqueous solution of N-methylacetamide,[72] but close to the value obtained for formamide.[73] Along with the hydrogen bond lifetimes of the solute-water system, we have calculated residence time[74] of water molecules in the hydration shell of ND$_2$ group. We have calculated the probability that a water molecule which was in the hydration shell of nitrogen of methylamine at time t=0, remains continuously in the same hydration shell up to time t. Here, we have considered the N…O$_w$ distance to describe the hydration shell of amine group. The associated integrated relaxation time τ_R gives the average residence time of the water molecule inside the solvation shell. We have calculated the residence time from the residence time correlation decay, by fitting with bi-exponential decay. The long time scale of this bi-exponential decay gives the residence time. The residence time of the water molecule in the hydration shell of an amine group is found to be 5.72 ps. The decay of the residence correlation function is shown in Figure 5. Earlier
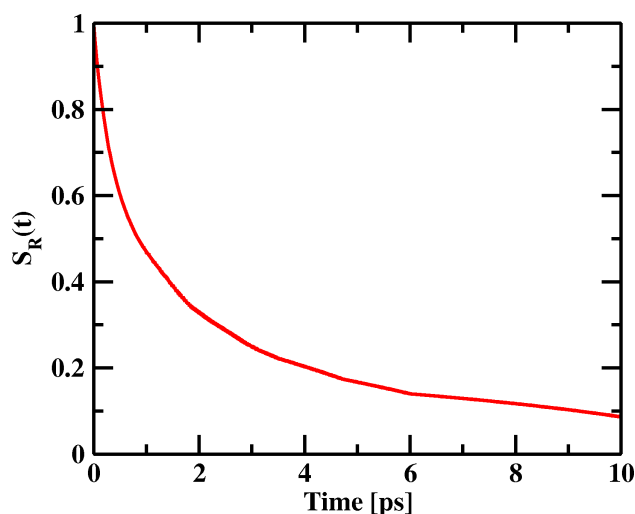
Figure 5. The decay of time dependent continuous residence time correlation functions for water molcules in the first solvation of amine group.

first principles simulation study showed that the one water molecule was strongly hydrogen bonded through N atom of amine while both amine hydrogen atoms were only involved in weak hydrogen bonds.[31] Furthermore, the water molecules were observed to exchange faster when weakly bonded by amine hydrogen. However, the exchange of the water molecule with interaction through the nitrogen atom was not found within the simulation time of 10 ps. The authors[31] reported the

residence time (major) of 1.5 ps due to hydrogen bonded water molecules, which is lower than our reported value. We did not see the exchange of water molecules during our arbitrarily chosen 10 ps trajectory from the total trajectory. In Figure 6, we
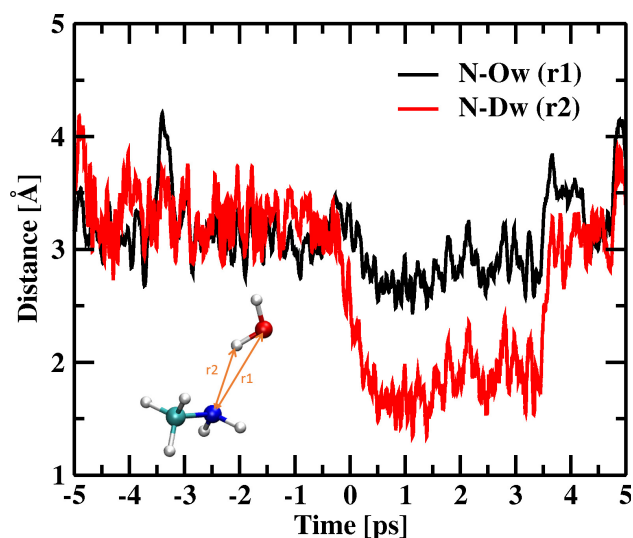
Figure 6. Escape trajectory of water molecule from the first solvation shell of amine group.

have shown the fluctuating distances of the oxygen and hydrogen atoms of the nearest water molecule from the nitrogen atom of the amine group. In this figure, 0 ps is the start of observation time. Though, the N–O_w distance fluctuates around 3.3 Å, the formation of the hydrogen bond is found between 0 to 3.5 ps. The specific water molecule essentially stays inside the solvation shell of amine group, occasionally escaping from the shell by breaking the existing hydrogen bond. So, our reported residence time of 5.7 ps is well complemented by the observations obtained from distance fluctuation.

**Vibrational spectral diffusion of first solvation shell water molecules**

We have calculated the frequency time correlation function and hole dynamics in the OD stretching vibrational states in the first solvation shell of the amine group. These functions are directly correlated to time dependent infrared signals available from experiments. The spectral diffusion of water molecules is described through the frequency-frequency time correlation function,

$$C_{\omega}(t) = \frac{\langle \delta\omega(t)\delta\omega(0)\rangle}{\langle \delta w(0)^2\rangle} \qquad (2)$$

where $\delta\omega(t)$ is the fluctuation from the average frequency at time t. The fluctuation of frequency (vibrational states) with time, observed by time dependent infrared spectroscopic

studies,[44,45,47,60,75–86] occurs for water in bulk and solvation shell environment depends upon the aqueous environment.

The frequency time correlation functions are shown in Figure 7. In order to get time constants, we have fitted the
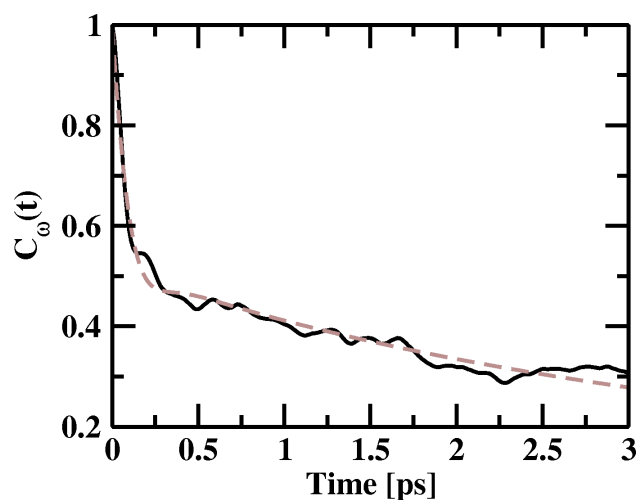
Figure 7. Time dependent frequency correlation function of OD modes inside the first solvation shell of ND_2 group.

decay of the frequency correlation functions to the following function[60,83]

$$f(t) = a_0 \cos \omega_s t e^{-\frac{t}{\tau_0}} + a_1 e^{-\frac{t}{\tau_1}} + (1 - a_0 - a_1)e^{-\frac{t}{\tau_2}} \qquad (3)$$

in which the first term will contribute to the shorter time dynamics related to intact hydrogen-bonded pairs. The relaxation times and the weights of solvation shell OD are tabulated in Table 1. We observe a fast decay and an oscillation

Table 1. Spectral diffusion data for the hydration shell OD modes. Time scales and the frequencies are in ps, and cm^{-1} units, respectively.

Quantity	Excitation	τ_0	τ_1	τ_2	ω_s	a_0	a_1
$C_{\omega}(t)$	-	0.09	1.77	6.95	50.67	0.48	0.12
$\Delta\bar{\omega}_h(t)$	Blue	0.06	1.96	7.10	119.60	0.74	0.14
$\Delta\bar{\omega}_r(t)$	Blue	0.07	0.89	7.29	119.32	0.46	0.10
$\Delta\bar{\omega}_h(t)$	Red	0.07	1.99	5.10	119.57	0.38	0.17
$\Delta\bar{\omega}_r(t)$	Red	0.07	1.71	2.80	94.20	0.70	0.20

at short time followed by slower decay extending to a few picoseconds. The oscillation in the short time delays (0.09 ps) are coming from the under-damped motion of the intact hydrogen bonds; i. e. from the dynamics of MA-water hydrogen bonds without breaking. Two slow relaxation times (1.77 and 6.95 ps) of the frequency correlation function correspond to the lifetimes of amine-water hydrogen bonds and the residence time of water in the amine hydration shell, respectively. Our calculated long-range time scales from the frequency fluctua-
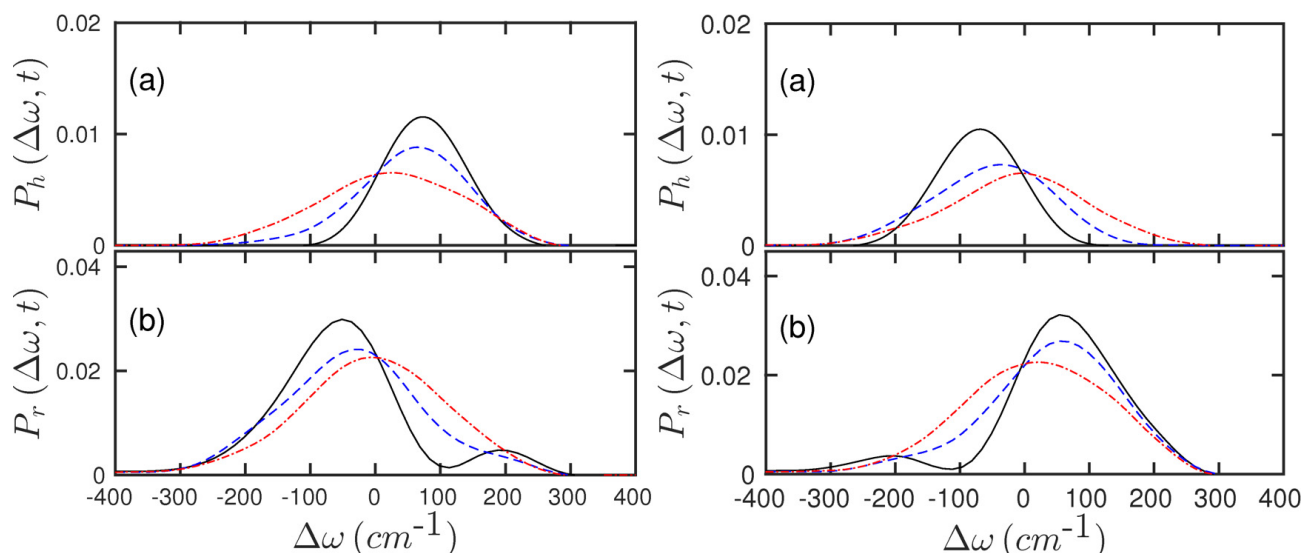
Figure 8. (Left panels) The time variation of the distribution of (a) hole and (b) remaining modes after hole creation in the blue side at time t = 0. The solid, dashed and dashed-dotted curves are for times t = 10 fs, 50 fs and 125 fs. (Right Panels) The time variation of the distribution of (a) hole and (b) remaining modes after hole creation in the red sides at time t = 0. The solid, dashed and dashed-dotted curves are for times t = 10 fs, 50 fs and 125 fs.

tion agrees well with the lifetime of amine-water hydrogen bonds (statistically averaged over both sites) and residence times calculated separately from population correlation functions. The average hydrogen bond lifetime of the ND_2-D_2O pair is around 1.70 ps. Our observations of the fast time scale corresponding to intermolecular vibrations of intact amine-water hydrogen bonds, and two slow time scales corresponding to hydrogen life and residence times, are in general agreement with the results of earlier studies of aqueous solution.[75]

We then focused on the frequency fluctuations of the OD modes in the hydration shell of amines. This is another way to investigate the dynamics of spectral diffusion by performing the so called hole dynamics calculations, where the dynamics of a hole, that is created by the removal of several OD modes of selected frequencies from the total OD bonds for the first hydration shell water molecules, is followed until the equilibrium is reached. The time evolution of such an initially-created non-equilibrium distribution is closely related to the dynamics of pump-probe signals of time dependent infrared spectroscopic experiments on vibrational spectral diffusion. It is assumed that at time t = 0, a laser pump pulse having Gaussian frequency profiles burns a hole in the ground state, having a frequency distribution of the form

$$P_h(\omega, 0) = P_{eq}(\omega)\frac{(\omega - \omega_p)^2}{2\sigma^2} \qquad (4)$$

where ω_p indicates the pulse center frequency and $P_{eq}(\omega)$ denotes the equilibrium distributions of all OD frequencies present in the system hydration shell. Clearly, the initial distribution of the remaining frequencies in the ground state is equal to $P_{eq}(\omega) - P_h(0)$. For the given system, we have calculated time evolution of the nonequilibrium distribution of

the remaining modes $(P_r(\omega, t))$, and also the hole modes $(P_h(\omega, t))$, after the hole is created at t = 0 of hydration shell water in the vicinity of a ND_2 group of methylamine. The average frequencies of the remaining modes and hole modes are calculated from the following relations

$$\omega_i(t) = \frac{1}{N_i} \int \omega P_i(\omega, t)d\omega \qquad (5)$$

where i = r and i = h for the remaining modes and hole modes, respectively, and $N_i = \int d\omega P_i(\omega, 0)$. To study the dynamics, we have created a hole in two different frequency regions: one centered at the red side at $\omega_P = \bar{\omega} - 100$ cm^{-1} and the other one cantered at $\omega_P = \bar{\omega} + 100$ cm^{-1} where $\bar{\omega}$ is the average frequency of all the OD modes present in the hydration shell of the amine group. We employed a Metropolis Monte Carlo like algorithm to create a hole of the chosen distribution in the red and blue regions, and at different initial times. A more extended explanation of this procedure can be found in earlier publications.[60,75] The distribution of holes and remaining modes after the hole creation is represented in Figure 8. We have shown the temporal evolution of the average hole and remaining frequency hole created at the higher frequency (blue) region and lower frequency (red) region. We have calculated average frequencies of hole and remaining modes from the time dependent distribution. The results are shown in Figure 9. The figure also contains results of decay pattern of the normalized frequency shifts. It is seen that when the hole is created in the higher frequency (blue) region, the average hole frequency shifts toward the lower frequency side until the average equilibrium value is attained. The average frequency of remaining modes shift toward the blue side with time, as the hole in the blue region is filled gradually, and finally the distribution adopts a nearly symmetric shape around the
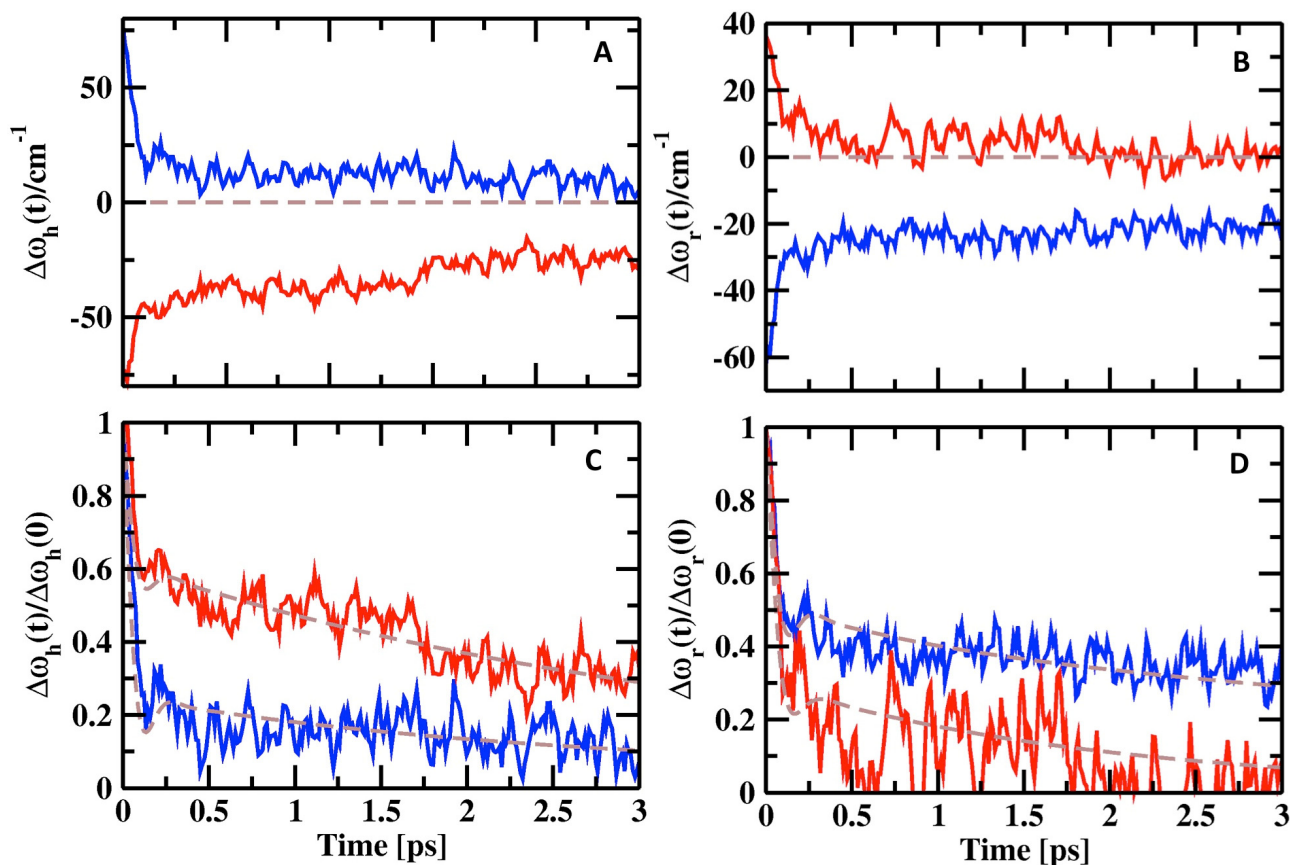
Figure 9. Time dependence of the (upper panel, A) average frequency shifts of the hole modes after they are selected in the blue and red sides of the hydration shell of OD modes. The corresponding results for the blue and red excitations after normalization by the initial frequency shift are shown in bottom panel, C. The corresponding data for remaining modes are shown in panels B and D. The dotted gray solid curves in C and D represent the fits by a function of Eq. 3.

average frequency. It is clear from panels A and B that the opposite behaviour is found when the hole is created in red side. It is seen that the overall decay pattern of the frequencies is similar to that frequency time correlation function shown in Figure 7. We have fitted decay of the average frequency shifts to function of equation 3, and the results of the relaxation times and weights are included in Table 1. From the analysis of time constants, we observe a fast decay and an oscillation at short times, followed by slower decay. It is evident that the initial oscillation in the range 0.06-0.09 ps are likely due to the under-damped motion of the hydrogen bonded OD groups with ND_2 moiety. The longer time scale around 1.77 ps arises due to the average hydrogen bond lifetime of ND_2-D_2O pair. From the hydrogen bond autocorrelation function, the average hydrogen bond lifetime of ND_2-D_2O pair is found to be 1.90 ps. The relatively large time scales are due to the escape dynamics of water molecules from the amine hydration shell.

Conclusions

We have presented a combined study of first principles molecular dynamics simulations and wavelet analysis to gain insight into the hydration, hydrogen bonding, exchange dynamics and vibrational spectral diffusion in aqueous solution of Methylamine. The former method was used to generate the trajectories; we have used the later one to do the time series analysis of fluctuating vibrational frequencies. The simulations have been carried out using a BLYP density functional with the dispersion correction. The water molecule forms the stronger hydrogen bond with the nitrogen atom of MA than the deuterium of amine group. This hydrogen bond is stronger than the water-water one. The amine deuterium-water hydrogen bond is the weakest among all types of possible hydrogen bonds existing in an aqueous solution of MA. On average, the amine group is found to form 2.5 hydrogen bonds with water. The average frequency of OD modes in the first solvation shell of amine is lower than that of pure D_2O molecules, confirming the relative strength of the formed hydrogen bonds. Due to presence of a hydrophobic group like the methyl group, the average frequency of OD modes in its solvation shell is higher than other OD modes; this is due to the non-hydrogen bonded or dangling OD modes of water molecules. The vibrational spectral diffusion of the OD stretch modes of water molecules is investigated through frequency correlation function and hole-dynamics calculations. The vibrational spectral diffusion of OD modes in the first hydration shell of amine group are found

to have a very fast time scale of ~80 fs, and two slower time scales of ~2 and ~7 ps. The time scale of ~2 ps can be assigned to the lifetime of amine-water hydrogen bonds. The longest time scale is correlated to the escape dynamics of water from the first hydration shell of the amine group.

Computational Methodology Section

The DFT based first principles molecular dynamics simulations have been carried out by employing the Car-Parrinello method[87] implemented in CPMD code.[88] The present system contains a single methylamine molecule dissolved in a solvent of 31 water molecules. Periodic boundary conditions were applied in all three dimensions, and the electronic structure of the extended system was represented by the Kohn-Sham (KS)[89,90] formulation of density functional theory within a plane wave basis. A kinetic energy cut off of 80 Ry was used for the plane wave expansion of the orbitals, and the core electrons were treated via the atomic pseudo potentials of Troullier-Martins.[91] BLYP[61,92] functional along with dispersion correction introduced by Grimme[93,94] has been used in the present study. The BLYP functional is known to reproduce the water density approximately 20% lower than the experimental value at ambient condition,[95] but the addition of dispersion correction improves the predicted density value close to the experimental one. Therefore, the volume of the cubic simulation box was taken corresponding to experimental density to generate water density of 1 gm/cc with inclusion of dispersion correction. In the present system, a fictitious mass of $\mu = 700$ atomic unit was assigned to the electronic degrees of freedom and the system dynamics was integrated by using a time step of 5 a.u. (~0.12 fs). All hydrogen atoms were assigned the mass of deuterium to make sure that electronic adiabaticity and energy conservation are maintained throughout the simulations. Essentially, we simulated the deuterated MA dissolved in D_2O. We generated the initial configuration by performing classical molecular dynamics simulation. The system was equilibrated for 2 ns at NVT ensemble. With CPMD, the system was equilibrated for 20 ps using separate Nose-Hoover thermostats[96–98] for the ionic and electronic degrees of freedom to control the adiabatic separation in the canonical ensemble.[99] After switching off the thermostat, the simulation was continued for another 25 ps by controlling temperature within the limit of ±20 K corresponding to the target temperature. The average temperature during the production run is 297 K. We utilized the last 20 ps of the trajectories for calculation of various average properties. The configurations at the interval of 10 steps (50 a.u) were collected for the analysis. We didn't find any event of complete protonation of methylamine from the structural analysis. The radial distribution functions and combine distribution functions (CDF) were computed using a bin width of 0.04 Å. We have also studied the spectral signature of water molecules around hydrogen bonding sites of a methylamine. It is well known that the vibrational frequency of water molecules in the vicinity of solute fluctuates due to the fluctuations in its interactions with the surrounding molecules in aqueous solution. In the current study, the time dependent vibrational frequencies of water

molecules have been carried out by time series analysis of the first principles molecular dynamics trajectories using the wavelet method.[60,75,100–102] The vibrational degrees of freedom of organic molecules and correlation functions have been used in thermopower and superconductivity models, respectively.[103,104] After getting the frequency of individual OD bonds of water, the frequency distribution, and spectral diffusion were calculated for the purpose. The same procedure was followed for calculation of other stretching modes presented in this work. The software package, TRAVIS[105] was used for presentation of SDF and CDF data.

Conflict of interest

The authors declare no conflict of interest.

[1] K. Blau, *Biochem. J.* **1961**, *80*, 193–200.
[2] G. A. Lyles, S. A. Mcdougall, *J. Pharm. Pharmacol.* **1989**, *41*, 97–100.
[3] S. Baba, Y. Watanabe, F. Gejyo, M. Arakawa, *Clin. Chim. Acta* **1984**, *136*, 49–56.
[4] A. M. Asatoor, D. N. S. Kerr, *Clin. Chim. Acta* **1961**, *6*, 149–156.
[5] Y. Zhang, J. Mao, P. H. Yu, S. Xiao, *Anal. Chim. Acta* **2012**, *752*, 106–111.
[6] S. Xiao, P. H. Yu, *Anal. Biochem.* **2009**, *384*, 20–26.
[7] R. W. Schayer, R. L. Smiley, E. H. Kaplan, *J. Biol. Chem.* **1952**, *198*, 545–551.
[8] M. S. Dar, P. L. Morselli, E. R. Bowman, *Gen. Pharmacol. Vasc. Syst.* **1985**, *16*, 557–560.
[9] S. H. Zeisel, J. S. Wishnok, J. K. Blusztajn, *J. Pharmacol. Exp. Ther.* **1983**, *225*, 320–324.
[10] K. Teilum, J. G. Olsen, B. B. Kragelund, *Biochim. Biophys. Acta* **2011**, *1814*, 969–976.
[11] S. N. Timasheff, *Annu. Rev. Biophys. Biomol. Struct.* **1993**, *22*, 67–97.
[12] D. R. Canchi, A. E. García, *Annu. Rev. Phys. Chem.* **2013**, *64*, 273–293.
[13] H.-X. Zhou, T. A. Cross, *Annu. Rev. Biophys.* **2013**, *42*, 361–392.
[14] A. C. Fogarty, E. Duboué-Dijon, F. Sterpone, J. T. Hynes, D. Laage, *Chem. Soc. Rev.* **2013**, *42*, 5672–5683.
[15] E. Duboué-Dijon, D. Laage, *J. Chem. Phys.* **2014**, *141*, 22D529.
[16] M. S. B. Munson, *J. Am. Chem. Soc.* **1965**, *87*, 2332–2336.
[17] C. Reichardt, T. Welton, *Solvents and Solvent Effects in Organic Chemistry*, Wiley, **2011**.
[18] F. M. Jones, E. M. Arnett, in *Prog. Phys. Org. Chem.* (Eds.: A.S. Jr, R.W. Taft), John Wiley & Sons, Inc., **1974**, pp. 263–322.
[19] A. Ben-Naim, Y. Marcus, *J. Chem. Phys.* **1984**, *81*, 2016–2027.
[20] P. G. Kusalik, D. Bergman, A. Laaksonen, *J. Chem. Phys.* **2000**, *113*, 8036–8046.
[21] B. G. Rao, U. C. Singh, *J. Am. Chem. Soc.* **1989**, *111*, 3125–3133.
[22] D. J. Tannor, B. Marten, R. Murphy, R. A. Friesner, D. Sitkoff, A. Nicholls, B. Honig, M. Ringnalda, W. A. Goddard, *J. Am. Chem. Soc.* **1994**, *116*, 11875–11882.
[23] P.-Y. Morgantini, P. A. Kollman, *J. Am. Chem. Soc.* **1995**, *117*, 6057–6063.
[24] Y. Ding, D. N. Bernardo, K. Krogh-Jespersen, R. M. Levy, *J. Phys. Chem.* **1995**, *99*, 11575–11583.
[25] E. C. Meng, P. A. Kollman, *J. Phys. Chem.* **1996**, *100*, 11460–11470.

[26] T. S. Hofer, H. T. Tran, C. F. Schwenk, B. M. Rode, *J. Comput. Chem.* **2004**, *25*, 211–217.

[27] C. Oostenbrink, D. Juchli, W. F. van Gunsteren, *ChemPhysChem* **2005**, *6*, 1800–1804.

[28] C. J. Cramer, D. G. Truhlar, *J. Comput. Aided Mol. Des.* **1992**, *6*, 629–666.

[29] D. Liu, T. Wyttenbach, M. T. Bowers, *Int. J. Mass Spectrom.* **2004**, *236*, 81–90.

[30] W. J. Dunn, P. I. Nagy, *J. Phys. Chem.* **1990**, *94*, 2099–2105.

[31] H. Hesske, K. Gloe, *J. Phys. Chem. A* **2007**, *111*, 9848–9853.

[32] R. C. Rizzo, W. L. Jorgensen, *J. Am. Chem. Soc.* **1999**, *121*, 4827–4836.

[33] M. V. Fedotova, S. E. Kruchinin, *Russ. Chem. Bull.* **2012**, *61*, 240–247.

[34] M. Sánchez-Lozano, E. M. Cabaleiro-Lago, J. M. Hermida-Ramón, C. M. Estévez, *Phys. Chem. Chem. Phys. PCCP* **2013**, *15*, 18204–18216.

[35] S.-S. Lv, Y.-R. Liu, T. Huang, Y.-J. Feng, S. Jiang, W. Huang, *J. Phys. Chem. A* **2015**, *119*, 3770–3779.

[36] R. Laenen, C. Rauscher, A. Laubereau, *Phys. Rev. Lett.* **1998**, *80*, 2622–2625.

[37] R. Laenen, K. Simeonidis, A. Laubereau, *J. Phys. Chem. B* **2002**, *106*, 408–417.

[38] S. Woutersen, U. Emmerichs, H. J. Bakker, *Science* **1997**, *278*, 658–660.

[39] S. Woutersen, H. J. Bakker, *Phys. Rev. Lett.* **1999**, *83*, 2077–2080.

[40] G. M. Gale, G. Gallot, F. Hache, N. Lascoux, S. Bratos, J.-C. Leicknam, *Phys. Rev. Lett.* **1999**, *82*, 1068–1071.

[41] S. Bratos, G. M. Gale, G. Gallot, F. Hache, N. Lascoux, J.-C. Leicknam, *Phys. Rev. E* **2000**, *61*, 5211–5217.

[42] Z. Wang, A. Pakoulev, Y. Pang, D. D. Dlott, *Chem. Phys. Lett.* **2003**, *378*, 281–288.

[43] A. Pakoulev, Z. Wang, D. D. Dlott, *Chem. Phys. Lett.* **2003**, *371*, 594–600.

[44] J. B. Asbury, T. Steinel, C. Stromberg, S. A. Corcelli, C. P. Lawrence, J. L. Skinner, M. D. Fayer, *J. Phys. Chem. A* **2004**, *108*, 1107–1119.

[45] C. J. Fecko, J. D. Eaves, J. J. Loparo, A. Tokmakoff, P. L. Geissler, *Science* **2003**, *301*, 1698–1702.

[46] J. D. Eaves, J. J. Loparo, C. J. Fecko, S. T. Roberts, A. Tokmakoff, P. L. Geissler, *Proc. Natl. Acad. Sci. U. S. A.* **2005**, *102*, 13019–13022.

[47] C. J. Fecko, J. J. Loparo, S. T. Roberts, A. Tokmakoff, *J. Chem. Phys.* **2005**, *122*, 054506.

[48] S. T. Roberts, J. J. Loparo, A. Tokmakoff, *J. Chem. Phys.* **2006**, *125*, 084502.

[49] J. J. Loparo, S. T. Roberts, A. Tokmakoff, *J. Chem. Phys.* **2006**, *125*, 194521.

[50] M. F. Kropman, H. J. Bakker, *Science* **2001**, *291*, 2118–2120.

[51] M. F. Kropman, H. J. Bakker, *J. Chem. Phys.* **2001**, *115*, 8942–8948.

[52] J. M. Park, A. Laio, M. Iannuzzi, M. Parrinello, *J. Am. Chem. Soc.* **2006**, *128*, 11318–11319.

[53] H.-S. Tan, I. R. Piletic, R. E. Riter, N. E. Levinger, M. D. Fayer, *Phys. Rev. Lett.* **2005**, *94*, 057405.

[54] S. Woutersen, H. J. Bakker, *Phys. Rev. Lett.* **2006**, *96*, 138305.

[55] H.-K. Nienhuys, A. J. Lock, R. A. van Santen, H. J. Bakker, *J. Chem. Phys.* **2002**, *117*, 8021–8029.

[56] M. Rini, B.-Z. Magnes, E. Pines, E. T. J. Nibbering, *Science* **2003**, *301*, 349–352.

[57] J. Zhong, Y. Zhao, L. Li, H. Li, J. S. Francisco, X. C. Zeng, *J. Am. Chem. Soc.* **2015**, *137*, 12070–12078.

[58] T. Steiner, *Angew. Chem.* **2002**, *114*, 50–80.

[59] H. Wolff, *J. Chem. Phys.* **1972**, *56*, 5278.

[60] B. S. Mallik, A. Semparithi, A. Chandra, *J. Phys. Chem. A* **2008**, *112*, 5104–5112.

[61] A. D. Becke, *Phys. Rev. A* **1988**, *38*, 3098–3100.

[62] C. Lee, W. Yang, R. G. Parr, *Phys. Rev. B* **1988**, *37*, 785–789.

[63] M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, B. Mennucci, G. A. Petersson, et al., *Gaussian 09, Revision A.1*, Gaussian, Inc., Wallingford, CT, **2009**.

[64] D. C. Rapaport, *Mol. Phys.* **1983**, *50*, 1151–1162.

[65] A. Luzar, D. Chandler, *Phys. Rev. Lett.* **1996**, *76*, 928–931.

[66] A. Luzar, *J. Chem. Phys.* **2000**, *113*, 10663–10675.

[67] A. Chandra, *Phys. Rev. Lett.* **2000**, *85*, 768–771.

[68] H. Xu, B. J. Berne, *J. Phys. Chem. B* **2001**, *105*, 11929–11932.

[69] S. Balasubramanian, S. Pal, B. Bagchi, *Phys. Rev. Lett.* **2002**, *89*, 115505.

[70] H. Xu, H. A. Stern, B. J. Berne, *J. Phys. Chem. B* **2002**, *106*, 2054–2060.

[71] A. Chandra, *J. Phys. Chem. B* **2003**, *107*, 3899–3906.

[72] V. K. Yadav, A. Chandra, *J. Phys. Chem. B* **2015**, *119*, 9858–9867.

[73] S. Biswas, B. S. Mallik, *J. Mol. Liq.* **2015**, *212*, 941–946.

[74] B. S. Mallik, A. Chandra, *J. Chem. Phys.* **2006**, *125*, 234502.

[75] B. S. Mallik, A. Semparithi, A. Chandra, *J. Chem. Phys.* **2008**, *129*, 194512.

[76] D. Chakraborty, A. Chandra, *Chem. Phys.* **2012**, *392*, 96–104.

[77] D. Chakraborty, A. Chandra, *J. Chem. Phys.* **2011**, *135*, 114510.

[78] H. J. Bakker, J. L. Skinner, *Chem. Rev.* **2010**, *110*, 1498–1517.

[79] H. J. Bakker, M. F. Kropman, A. W. Omta, S. Woutersen, *Phys. Scr.* **2004**, *69*, C14-C24.

[80] E. T. J. Nibbering, T. Elsaesser, *Chem. Rev.* **2004**, *104*, 1887–1914.

[81] J. L. Skinner, B. M. Auer, Y.-S. Lin, in *Adv. Chem. Phys.* (Ed.: S.A. Rice), John Wiley & Sons, Inc., **2009**, pp. 59–103.

[82] R. Rey, K. B. Møller, J. T. Hynes, *J. Phys. Chem. A* **2002**, *106*, 11993–11996.

[83] K. B. Møller, R. Rey, J. T. Hynes, *J. Phys. Chem. A* **2004**, *108*, 1275–1289.

[84] C. P. Lawrence, J. L. Skinner, *Chem. Phys. Lett.* **2003**, *369*, 472–477.

[85] C. P. Lawrence, J. L. Skinner, *J. Chem. Phys.* **2002**, *117*, 8847–8854.

[86] C. P. Lawrence, J. L. Skinner, *J. Chem. Phys.* **2003**, *118*, 264–272.

[87] R. Car, M. Parrinello, *Phys. Rev. Lett.* **1985**, *55*, 2471–2474.

[88] J. Hutter, A. Alavi, T. Deutsch, M. Bernasconi, S. Goedecker, D. Marx, M. Tuckerman, M. Parrinello, *IBM Corp* **1990**, *2007*, 1997–2001.

[89] W. Kohn, L. J. Sham, *Phys. Rev.* **1965**, *140*, A1133-A1138.

[90] P. Hohenberg, W. Kohn, *Phys. Rev.* **1964**, *136*, B864-B871.

[91] N. Troullier, J. L. Martins, *Phys. Rev. B* **1991**, *43*, 1993–2006.

[92] C. Lee, W. Yang, R. G. Parr, *Phys. Rev. B* **1988**, *37*, 785–789.

[93] S. Grimme, *J. Comput. Chem.* **2004**, *25*, 1463–1473.

[94] S. Grimme, *J. Comput. Chem.* **2006**, *27*, 1787–1799.

[95] J. Schmidt, J. VandeVondele, I.-F. W. Kuo, D. Sebastiani, J. I. Siepmann, J. Hutter, C. J. Mundy, *J. Phys. Chem. B* **2009**, *113*, 11959–11964.

[96] S. Nosé, *Mol. Phys.* **1984**, *52*, 255–268.

[97] W. G. Hoover, *Phys. Rev. A* **1985**, *31*, 1695–1697.

[98] G. J. Martyna, M. L. Klein, M. Tuckerman, *J. Chem. Phys.* **1992**, *97*, 2635–2643.

[99] M. E. Tuckerman, M. Parrinello, *J. Chem. Phys.* **1994**, *101*, 1302–1315.

[100] B. Finkenstadt, L. Held, V. Isham, *Statistical Methods for Spatio-Temporal Systems*, CRC Press, **2006**.

[101] L. V. Vela-Arevalo, S. Wiggins, *Int. J. Bifurc. Chaos* **2001**, *11*, 1359–1380.

[102] A. Semparithi, S. Keshavamurthy, *Phys. Chem. Chem. Phys.* **2003**, *5*, 5051–5062.

[103] S. Kruchinin, T. Pruschke, *Phys. Lett. A* **2014**, *378*, 1157–1161.

[104] N. N. Bogolubov, E. N. Bogolubova, S. P. Kruchinin, *Mod. Phys. Lett. B* **2003**, *17*, 709–724.

[105] M. Brehm, B. Kirchner, *J. Chem. Inf. Model.* **2011**, *51*, 2007–2023.