Dynamic and thermodynamic anomalies of water at low temperatures: from bulk water to reverse micelles and DNA hydration layer

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Liquid water is known to exhibit remarkable thermodynamic and dynamic anomalies, ranging from solvation properties in supercritical state to an apparent divergence of the linear response functions at a low temperature. Anomalies in various dynamic properties of water have also been observed in the hydration layer of proteins, DNA grooves and inside the nanocavity, such as reverse micelles and nanotubes. Here we report studies on the molecular origin of these anomalies in supercooled water, in the grooves of DNA double helix and reverse micelles. The anomalies have been discussed in terms of growing correlation length and intermittent population fluctuation of 4- and 5-coordinated species. We establish correlation between thermodynamic response functions and mean squared species number fluctuation. Lifetime analysis of 4- and 5-coordinated species reveals interesting differences between the role of the two species in supercooled and constrained water. The nature and manifestations of the apparent liquid–liquid transition under confinement are found to be markedly different from that in the bulk. We find an interesting ‘faster than bulk’ relaxation in reverse micelles which we attribute to frustration effects created by competition between the correlations imposed by surface interactions and that imposed by hydrogen bond network of water.

Keywords: Dynamic and thermodynamic anomalies, DNA hydration layer, reverse micelles.

Introduction

Liquid water continues to draw immense attention from scientists working in all branches of natural sciences. Different groups remain interested in different aspects of this liquid. Although some study ‘structured water’ in micelles and reverse micelles, some study its properties in protein and DNA hydration layers, there are still others who study it in carbon nanotubes, while for some attention remains focused on electrolyte solutions, and for many bulk water itself poses unlimited puzzles to keep them engaged over a lifetime. Many books and reviews have been devoted to water and their number seems to be increasing every year.

One can list the large number of anomalies that water exhibits in different environments. The list continues to grow. More recently a considerable amount of attention has been devoted to water at temperatures below the freezing temperature of 273 K. Not only does water at such a low temperature exhibit certain amazing anomalies, it is also hoped that this can serve as a key to understand properties at higher temperatures. Notable anomalies are the divergent-like growth of the linear response functions (heat capacity, isothermal compressibility, etc.) as the temperature is decreased. Several explanations of these anomalies have been put forward. The explanations in terms of the re-crossing of the gas–liquid spinodal at lower temperature (spinodal retracing) and in terms of the negative slope of the temperature maximum density line in the (P, T) plane (singularity-free scenario) are only partly successful in explaining the experimental results. The most recent and promising approach in this area is in terms of liquid–liquid phase transitions. In this scenario, water is hypothesized to exhibit a phase transition in the region of deeply supercooled water, at higher than ambient pressure, from high-density liquid (HDL) to low-density liquid (LDL). This liquid–liquid critical point in water is estimated to be located at a pressure P ≈ 100 MPa and temperature T ≈ 220 K. Beyond this critical point, one can draw a line of the maximum density fluctuation in the (P, T) plane owing to the remnant effect of the criticality and such a line is termed as Widom line. In this scenario, water is hypothesized to exhibit a phase transition in the region of deeply supercooled water, at higher than ambient pressure, from high-density liquid (HDL) to low-density liquid (LDL). This liquid–liquid critical point in water is estimated to be located at a pressure P ≈ 100 MPa and temperature T ≈ 220 K. Beyond this critical point, one can draw a line of the maximum density fluctuation in the (P, T) plane owing to the remnant effect of the criticality and such a line is termed as Widom line. The anomalous increase in the response functions upon cooling at the ambient pressure can be a manifestation of the crossing of the Widom line. This hypothesis not only explains the response functions anomalies of water but also explains the polymorphism of glassy water and seems at present to be the most consistent with experiments. Moreover, liquid–liquid (L–L) phase transition scenario is also consistent with the presence of a crossover in the dynamics found in recent experiments in the nano-confined water.

The molecular origin of anomalous behaviour near the Widom line is well-understood in several cases. For example, in the gas–liquid case, it is the correlated den-
susceptibility ($\chi_4(t)$) captures the presence of a growing length scale and the concomitant emergence of dynamical heterogeneity in density fluctuations, we have calculated the same as a function of temperature. We have studied the origin of the enhancement of correlated density fluctuations near Widom line in terms of time evolution of the 4- and 5-coordinated species and calculated the relevant properties to demonstrate the microscopic origin of response function anomalies in supercooled water. A two-state model has been presented which can explain the intermittency in the number fluctuations observed in simulations. We have also calculated the lifetime correlation function and lifetime distribution function of 4- and 5-coordinated species. The theoretical and simulations results seem to suggest that the anomalies are a consequence of an avoided criticality owing to the presence of the 5-coordinated water molecules.

Water in the natural world is often found under constrained and/or restricted environments, in the hydration layer of proteins and micelles, within reverse micelles and microemulsions, in the grooves of DNA duplex and within biological cells, to name a few\textsuperscript{1,3}. Properties of water under such constrained conditions can be quite different from those of bulk, neat water. However, it is likely that even under such restricted conditions water retains some of its unique properties. Study of these unique properties of water, especially in the hydration layer of biomolecules, particularly of proteins and DNA, has been a subject of great interest in recent times. Hydration layer not only provides the stability of the structure of the biomolecules, but also plays a critical role in the dynamic control of biological activity. The intercalation of anti-tumour drugs, such as daunoycin, into DNA involves active participation of water molecules in the grooves\textsuperscript{40}.

The low-temperature (near 200 K) ‘glass-like’ transition of hydrated protein has drawn a great deal of attention in both experimental and computer simulation studies\textsuperscript{41,45}. Above this transition temperature, proteins exhibit diffusive motion and below this temperature the proteins are trapped in localized harmonic modes. An important issue in recent times is to determine the effects of hydration on water on this dynamical transition\textsuperscript{46-50}. Recent studies have shown that dynamics of water in the hydration layer of a protein also exhibits strong temperature dependence around the same temperature and it seems to undergo a fragile-to-strong transition which preempts an otherwise expected glass transition at a lower temperature\textsuperscript{50-53}.

Study of DNA hydration layer has recently indicated interesting dynamical behaviour of water in the grooves\textsuperscript{50,51}. Several recent studies have discussed the origin of the slow component of the solvation dynamics in DNA hydration layer\textsuperscript{54}. A recent computer simulation study by Stanley and co-workers has shown that the L–L transition in water induces a dynamic transition in DNA which has striking resemblance to that of liquid to glass transition\textsuperscript{55}. This study, however, did not explore the dynamics of water in the grooves of DNA.

There are many questions that have remained unanswered regarding dynamics of groove water at low temperature. For example, is there a dynamic transition in the grooves of DNA near the L–L transition of bulk water? Does it in any way resemble the one in protein hydration layer? Note that the remarkable properties of bulk water have recently been attributed to a highly interesting L–L transition at around $T_L \approx 247$ K (refs 56–58). The effects of the bulk water L–L transition on groove water dynamics have not yet been studied.

In this article, we report our finding that water in the grooves of a DNA duplex shows a dynamical transition at a temperature ($T_{GL}$) slightly higher than the temperature ($T_L$), where the bulk water undergoes the L–L transition. The nature and manifestation of the transition in the grooves are stronger than those in the bulk for the same TIP5P potential.

There are several effects of confinement on the properties of liquid water. First, fluctuations with wavelength larger than that of the confining region are suppressed. Second, the surface can induce changes within water. For example, a hydrophobic surface can induce enhanced local order among the water molecules. A hydrophilic surface (such as a micelle or a reverse micelle) can induce frustration among water molecules in the second or third layer\textsuperscript{1,59-61}. Both the surfaces are expected to lower the entropy of hydration layer.

An interesting aspect of water molecules in the DNA grooves is that they are free to exchange with the bulk. Therefore, the entropy–energy balance needs to be maintained. As entropy of water in the hydration layer is signi-
significantly less than that in the bulk, these water molecules must be energetically stabilized by interactions among themselves and also with DNA atoms.

Arrangement of water molecules in the grooves of DNA are partly dictated by the gain in the stabilization energy owing to the interaction with the charged groups of DNA and partly by the loss of entropy because of confinement. These two factors lead to a change in the preference of arrangement to lower energy states which is the 4-coordinated low-density state. Thus, the dynamical (L–L) transition is expected to occur at higher temperature which is also found by computer simulations presented here.

Models and simulation details

Bulk water

A series of 11 simulations at different temperatures starting from 300 K to 230 K has been carried out in isobaric–isothermal ensembles (NPT). The TIP5P water model is used, which has been examined to reproduce the low temperature properties of water excellently. A system of 512 water molecules is first equilibrated for ~1 nanoseconds at 300 K and ~15 ns at 230 K and then the trajectory is saved for several nanoseconds for the analysis. Both equilibration and the subsequent run have been carried out in NPT ensemble. The long range electrostatic interactions are calculated using Ewald summation. The density profile of water has also been reproduced successfully.

DNA hydration layer

The system we studied consists of a Dickerson dodecamer DNA duplex (CGCGAATTCGCG)62 solvated using the LEAP module of the AMBER61 software in a TIP5P water box. The box dimensions were chosen in order to ensure a 10 Å thick solvation shell around the DNA structure. In addition, some water molecules were replaced by Na+ counterions to neutralize the negative charge on the phosphate groups of the backbone of the DNA. These procedures resulted in a solvated structure, containing around 8605 atoms which include 758 DNA atoms, 22 counterions, and ~1565 water molecules. The solvated structure is then subjected to 500 ps of steepest descent minimization of the potential energy, followed by 2000 steps of conjugate gradient minimization. During this minimization, the DNA molecule was kept fixed in its starting conformations using harmonic constraints. This allows the water molecules to reorganize to eliminate bad contacts with the DNA molecule. The minimized structure was then subjected to 500 ps of molecular dynamics (MD), using a 2 fs time step for integration. Subsequently, MD was performed under constant pressure–constant temperature conditions (NPT) with temperature regulation achieved using the Berendsen weak coupling method (0.5 ps time constant for heat bath coupling and 0.2 ps pressure relaxation time). This was followed by another 5000 steps of conjugate gradient. The DNA–water system is then simulated at constant pressure \( P = 1 \text{ atm} \), at several constant temperatures \((T = 300, 290, 280, 270, 260, 250, 240, 230, 220) \text{ K}\) with periodic boundary condition for 10 ns (for \( T = 300 \text{ K} \)) to 30 ns (for \( T = 220 \text{ K} \)). This ensures the equilibration of DNA system which has been checked by root mean square displacement (RMSD) of DNA and other relevant properties. Finally for the analysis, we have carried out 30 ns of NPT simulation for each case with 2 fs time step. Statistical errors have been calculated using four independent trajectories.

We have identified the groove water by using the following procedure. We have calculated the radial distribution function \( g(r) \) of water molecules in the system from the major and minor groove atoms. On the basis of this \( g(r) \), a cut-off distance of 3.5 Å (the first minima of \( g(r) \)) from the groove atoms is used for the selection. For bulk water analysis, we have considered those water molecules which are beyond 10 Å from any DNA atoms. We have checked that at 10 Å distance, water indeed regains bulklike behaviour.

Bulk water: results and discussions

Signatures of dynamic transition

There are several signatures of the presence of a dynamical transition in supercooled liquid water. Here we present two dynamical features, namely average translational relaxation time \((\langle \tau_T \rangle)\) and average orientational relaxation time \((\langle \tau_O \rangle)\), which show the presence of a dynamical transition in our system. Average translational relaxation time, \((\langle \tau_T \rangle)\), can be obtained from the fitting of the long-time intermediate scattering function \( F_2(k, t) \) to a stretched exponential function. The self-intermediate scattering function is defined as:

\[
F_2(k, t) = \langle \exp[-i\mathbf{k} \cdot (\mathbf{r}(t) - \mathbf{r}(0))] \rangle = \left( \frac{\sin(|\mathbf{k}| \mathbf{r}(t) - \mathbf{r}(0))}{|\mathbf{k}| \mathbf{r}(t) - \mathbf{r}(0)} \right),
\]

where \( \mathbf{k} \) is the wave vector and \( \mathbf{r}(t) \) is the position of the oxygen atom of the water molecules. The \( |\mathbf{k}| \) value taken here is 2.5 Å⁻¹.

In Figure 1a we have presented the \((\langle \tau_T \rangle)\) at different temperatures. While in the high temperature region it follows Vogel–Fulcher–Tammann (VFT) law, \( \tau_T = \tau_0 \exp[D(T - T_0)/(T - T_0)] \), where \( D \) is a constant measuring fragility and \( T_0 \) is ideal glass transition temperature at which
relaxation time diverges, it follows Arrhenius dependence in the low temperature region. The crossover between these two temperature dependence of \( \langle \tau_T \rangle \) around \( T = 250 \text{ K} \) marks the presence of a dynamical transition. We have also calculated average orientational relaxation time, \( \langle \tau_R \rangle \), by fitting the long-time part of the dipole–dipole time correlation function (TCF) to a stretched exponential. Dipole–dipole TCF calculated is defined as:

\[
C_\mu(t) = \frac{\langle \mu(0) \cdot \mu(t) \rangle}{\langle \mu(0) \cdot \mu(0) \rangle},
\]

(2)

where \( \mu(t) \) is the dipole moment unit vector of the water molecule at time \( t \) and the angular bracket corresponds to the ensemble averaging. In Figure 1(b), we have presented the \( \langle \tau_R \rangle \) at different temperatures. The temperature dependence of \( \langle \tau_R \rangle \) is found to be similar to what is observed for translational dynamics with a crossover around similar temperature. These dynamical signatures confirm the presence of a dynamical transition in the system around \( T = 250 \text{ K} \).

**Growth in non-linear response function**

Appearance of correlated density fluctuations in the system gives rise to transient heterogeneity in the system which can be detected by calculating the non-linear response function, \( \chi_4(t) \). The latter is related to the four-point density correlation function \( G_4 \) by the following relation:

\[
\chi_4(t) = \beta V N^2 \left[ \langle Q^2(t) \rangle - \langle Q(t) \rangle^2 \right],
\]

(5)

where four-point density correlation function \( G_4 \) can be written as:

\[
G_4(r_1, r_2, r_3, r_4, t) = \langle \rho(r_1, 0) \rho(r_2, t) \rho(r_3, 0) \rho(r_4, t) \rangle
- \langle \rho(r_1, 0) \rho(r_2, t) \rangle \times \langle \rho(r_3, 0) \rho(r_4, t) \rangle.
\]

(4)

Thus, \( \chi_4(t) \) is dominated by the range of spatial correlation between the localized particles in the fluid. It can be shown that definition of \( \chi_4(t) \) as given by eq. (3) is equivalent to the following expression.

\[
\chi_4(t) = \frac{\beta V}{N^2} \left[ \langle Q^2(t) \rangle - \langle Q(t) \rangle^2 \right].
\]

(5)

where \( Q(t) \) is the time-dependent order parameter which measures the localization of particles around a central molecule through a overlap function which is unity inside a region \( a \) and zero otherwise. Figure 2a, displays the non-linear response function, \( \chi_4(t) \), of water molecules (computed with the oxygen atom displacement) for temperatures ranging from 300 K to 230 K (ref. 58). At ambient pressure, the Widom line is located at \( T_{WL} \approx 250 \text{ K} \) for TIP5P water model. For every temperature, the \( \chi_4(t) \) is nearly zero for very short and long time with a maximum value at some intermediate time \( t^* \). Both \( t^* \) and the amplitude of the peak, \( \chi_4(t^*) \), increase sharply while approaching the Widom line. After crossing the Widom line, the value of \( \chi_4(t^*) \) decreases with further decrease in temperature. This suggests that both the spatial correlation between slow moving water molecules and the time at which that correlation is maximum, increase as we approach the Widom line from both the sides. This spatial correlation and \( t^* \) seem to attain the maximum values at the Widom line. We have also calculated another
non-linear response function, the non-Gaussian parameter ($\alpha_T^2(t)$), for the supercooled water and the results are presented in Figure 2b. Both the peak height ($\alpha_T^2(t^*)$), and the time at which the parameter attains, maximum value ($t^*$) increases as Widom line approaches from above similar to $\chi_4(t)$. After crossing the Widom line, $\alpha_T^2(t^*)$ and $t^*$ continue to increase rapidly further unlike $\chi_4(t)$. This surprising difference in the behaviour of these two response functions after crossing the Widom line has not been understood clearly.

Cross-over in fifth neighbour distance distribution: a molecular marker

To understand the molecular origin of the anomalies, we need to identify a microscopic order parameter that shows significant change across the anomalous ($T = 250$ K at ambient pressure) region. The microscopic quantity that undergoes significant change is the coordination number because as water is cooled towards 250 K, 5-coordinated water molecules get replaced by 4-coordinated water to this end, we calculated the distribution and the average of the distances between a central water molecule and its five nearest neighbours, previously also calculated by Chandra and Chowdhuri in the context of correlation of pressure-induced dynamical changes with the changes in hydrogen bond properties of the aqueous solutions. The distribution for the fifth neighbour (the furthest among the five neighbours and the one that leaves the first coordination shell to join the coordination shell of a molecule in the second neighbour list of the central molecule) distance is shown in Figure 3a at different temperatures. The distribution and the average fifth neighbour distance (shown in Figure 3b) show sharp change between 250 and 260 K. Above 260 K, the distribution has a peak around 3.25 Å. Below 240 K, the peak of the distribution shifts to 3.85 Å. The distribution becomes surprisingly flat around 260 K, with a mean value now located at around 3.5 Å. We have also calculated the distribution of the distances of first four neighbours (as shown in Figure 3c) which shows only a gradual squeezing towards a
lower distance with decreasing temperature. These distributions indicate that upon lowering temperature, while the first four neighbours (essential to maintain a tetrahedral geometry) of a water molecule come progressively closer, it is the fifth neighbour that goes out of the first coordination shell (3.5 Å). The temperature at which the peak position of the fifth neighbour distance distribution changes sharply coincides with the region where response functions show anomalous rise (as discussed below). The corresponding free energy surface (with the fifth neighbour distance as an order parameter) is flat, as in a critical phenomenon. Therefore, the number of 5-coordinated water molecules \( N_{5C} \) can serve as a suitable order parameter to study the anomalous behaviour of supercooled water.

**Average coordination number and number of hydrogen bonds**

In search of structural changes associated with observed anomalies, we have studied both the average coordination number and the number of hydrogen bonds formed by water molecules. These two quantities satisfy different criteria. We have taken a cut-off distance of 3.5 Å for coordination number analysis and a cut-off \( < \) HOO of 30° for the hydrogen bond analysis. In Figure 4, we have presented the results of the analysis. At higher temperature while the average coordination number is high, average number of hydrogen bonds is less. With decreasing temperature, average coordination number decreases and becomes \( \sim 4.0 \) in low temperature region. However, average number of hydrogen bonds increases with decreasing temperature and becomes \( \sim 4.0 \) in the low temperature region. We also observe that both the quantities change rapidly near \( T = 250 \) K. The results of this analysis infer that although the number of water molecules decreases progressively from the first coordination shell with decrease in temperature, the arrangement becomes progressively rich towards the tetrahedral geometry. The rates of these structural changes are maximum near the Widom line (\( T = 250 \) K).

**Intermittency and 1/f noise**

We find that water molecules with coordination numbers 4 and 5 are abundantly present at all temperatures. It was shown by Stanley and co-workers\(^{69,70} \) through inherent structure analysis that, in the extended network of liquid water dominated by 4-coordinated species, the 5-coordinated species present should be regarded as normal (i.e. not as an excitation) constituent of water. Additionally, the isochoic differential X-ray experiments have demonstrated that the water molecules can exist in a distinct configuration with five neighbours in the first coordination shell (within 3.5 Å)\(^{71} \). 3- and 6-coordinated species present in the system should be regarded as excitations (not as normal species) of the system as they do not retain their identity in the inherent structure. Simultaneous presence of both 4- and 5-coordinated water molecules in the system suggests the possibility of an exchange between them as a cooperative mechanism of relaxation.

Figure 5 a–c display the temporal variation of the number density of the 4- and 5-coordinated species \( (N_{4C}(t) \) and \( N_{5C}(t)) \) in the system at three different temperatures \( T = 280 \) K, 250 K and 230 K, respectively. Both in the high (\( T = 280 \) K) and low (\( T = 230 \) K) temperature region (away from Widom line), the fluctuations of \( N_{4C}(t) \) and \( N_{5C}(t) \) are random and not correlated, as shown in Figure 5 a and c. However, near the Widom line, \( T = 250 \) K, however, the fluctuations of \( N_{4C}(t) \) and \( N_{5C}(t) \) are slow and surprisingly strongly anti-correlated. This suggests that the anomalies near the Widom line and the divergence-like growth of the response function in supercooled water may originate from the strongly anti-correlated number density fluctuations of 4- and 5-coordinated species.

The plots of the temporal variation of the number density of 4- and 5-coordinated species (Figure 5) also indicate that near the Widom line, the number density of the individual species (4- and 5-coordinated species) fluctuates intermittently in time. The signature of intermittent behaviour can be confirmed by calculating the power spectrum of the fluctuation time correlation function. The power spectrum of the fluctuation of the 5-coordinated species (similarly for the 4-coordinated species) is presented in Figure 6 both for \( T = 300 \) K and 250 K. The linear dependence of the power spectrum for a wide range of frequency region with slope \( \approx -1 \) (in log–log plot) at \( T = 250 \) K confirmed the strong intermittency present in
the fluctuation. Linear dependence of the power spectrum in the low frequency range also indicates the large timescale intermittency in the fluctuations. At $T = 300$ K, the power spectrum shows a linear dependence only at the higher frequency region indicating the presence of small timescale intermittency in the fluctuations. The large timescale intermittency in the fluctuation concurrently induces spatial heterogeneity (as calculated by $\alpha_T^2(t)$, Figure 2b) as well as dynamical heterogeneity (calculated by the function $\chi_4(t)$ as shown in Figure 2a). This intermittency in the fluctuation of the number of species in the system further substantiates the microscopic origin of the Widom line in terms of space and time correlated fluctuations of $N_{5C}(t)$. When one analyses the snapshots of the trajectory visually, the intermittent dynamics is seen as a region where a cluster of 5-coordinated water molecules get converted into 4-coordinated water, whereas the reverse transformation occurs in a nearby region. Such intermittent dynamics has also been observed in the case of hydrogen bond network rearrangement at room temperature and effect of such rearrangement on the dynamical properties of water has been studied extensively.

**Two-state model for intermittent population fluctuation**

Next, we explain the intermittency by borrowing a model well known in the area of stochastic resonance. We consider the motion of a Brownian particle in a bistable potential where the two minima are HDL and LDL states.

\[ V(x) = -\frac{1}{2}x^2 + \frac{1}{4}x^4. \]  

(6)

Particle is acted upon by a periodic forcing, $A_0 \cos(\omega t)$, and a random force $\eta(t)$. Periodic forcing term appears owing to fluctuation of the total volume of the system as the two states have different specific volumes.

![Figure 5](image1)

*Figure 5.* Temporal variation of the numbers of 4- and 5-coordinated species in the supercooled water at *a*, $T = 300$ K; *b*, $T = 250$ K and *c*, $T = 230$ K. Note the strong anti-correlated fluctuations between $N_{4C}(t)$ and $N_{5C}(t)$ and intermittency in the fluctuations of both the species at $T = 250$ K.

![Figure 6](image2)

*Figure 6.* Power spectrum of the time correlation function of the fluctuations of 5-coordinated species in log–log plot at $T = 300$ K and 250 K. Note the linear dependence over a wide range of frequency with slope $\approx -1$ (1/f noise) at $T = 250$ K which confirms the intermittency in the fluctuations. The dotted line represent a line with slope $= -1$ for comparison.
In the presence of periodic forcing, the effective potential \( V'(x) = V(x) + A_0 \cos(\omega t) \) will be tilted back and forth, thereby raising and lowering successively the potential barriers for the HDL and LDL states, respectively. Now, we can write total volume of the system as,

\[
V(t) = V_0 + \delta V(t) + \frac{1}{2} k_B T \zeta \delta(t),
\]

(7)

where \( \zeta \) is the dissipation coefficient. In the absence of the periodic forcing (i.e. at fixed volume \( V_0 \)) the system will fluctuate around its local minima (LDL and HDL) with the noise induced hopping between the local minima which can be described by Kramer’s theory.

\[
r_k = \frac{1}{2 \pi \zeta} \exp(-\beta E_{act}) = \frac{1}{2 \pi \zeta} \exp\left(-\frac{\beta}{4}\right).
\]

(8)

Here, \( \beta = 1/k_B T \) and \( E_{act} = 1/4 \). Next, we define the probabilities that the system is in either of the local minima as \( n_{HL} = \text{prob(state = HDL/LDL)} \) and they obey the simple relation \( n_{HL} = 1 - n_L \) between them. Now the governing rate equation of the above system is as follows.

\[
\frac{dn_{HL}}{dt} = \frac{dn_L}{dt} = W_L(\delta V(t))n_L - W_H(\delta V(t))n_H
= W_L(\delta V(t)) - [W_H(\delta V(t)) + W_L(\delta V(t))]n_H,
\]

(9)

where \( W_{HL}(\delta V(t)) \) is the volume-dependent transition rate out of HDL or LDL local minima in the presence of periodic forcing. Now the rate equation can be solved to obtain58,

\[
n_{HL}(t) = \frac{1}{g(t)} \left[ n_{HL}(t = 0)g(t = 0) + \int_0^t W_L(\delta V(t'))g(t')dt' \right],
\]

(10)

with

\[
g(t) = \exp\left[\int_0^t (W_H(\delta V(t')) + W_L(\delta V(t')))dt'\right].
\]

(11)

For simplicity, we now assume that the rate constant \( W_{HL}(\delta V(t)) \) can be obtained under the periodic volume fluctuation as \( W_{HL}(\delta V(t)) = r_k \exp(\pm \beta A_0 \cos(\omega t)) \). Analytical and numerical studies reveal that at higher and lower temperature regions, far away from \( T = 250 \) K, the magnitude of total volume fluctuation is less \( (A_0 \text{ is less}) \) and also very fast \( (\omega \text{ is high}) \). In this condition, \( n_{HL}(t) \) oscillates around 0.5 showing the local equilibrium in both the wells. The fluctuation in the number of 4- and 5-coordinated species in the system also fluctuates near their respective equilibrium values in the temperature region away from \( T = 250 \) K.

However, as we approach \( T = 250 \) K, the volume fluctuation becomes larger \( (A_0 \text{ becomes larger}) \) and slow \( (\omega \text{ becomes lower}) \). In this condition, \( n_{HL}(t) \) oscillates intermittently between 0 and 1 (between the two states). Simulation also shows long-lived periodic fluctuation in total volume. As the free energy surface and hence the rate of transition between LDL and HDL forms depends on volume, the present model can explain the intermittency in the number fluctuation of 4- and 5-coordinated species near \( T = 250 \) K (Figure 5b).

We have calculated the temporal fluctuations of \( N_{4C} \) and \( N_{5C} \) using the volume fluctuation (as shown in Figure 7a) as obtained from the simulation at \( T = 250 \) K. In this
case, we have assumed a linear dependence of the rate on volume fluctuation as

\[ W_{LH}^0(\delta V(t)) = W_{LH}^0 + \left( \frac{\partial W_{LH}}{\partial V} \right) \delta V(t). \]

\( W_{LH}^0 \) is obtained as the inverse of the corresponding lifetime at \( T = 250 \) K and \( \left( \frac{\partial W_{LH}}{\partial V} \right) \) is obtained numerically from the slope of the \( W_{LH}^0 \) with variation of the total volume of the system. We find that the calculated temporal fluctuation of \( N_{ac} \) and \( N_{sc} \) (as shown in Figure 7 b) essentially capture the behaviour of the fluctuation calculated from simulation (Figure 5 b). The remaining difference observed between the fluctuations derived from the model and simulation might be because of non-linear dependence of the rate on volume fluctuation.

Species number fluctuations and growth in linear response functions

To further confirm the correlation between the fluctuations in \( N_{sc}(t) \) and the anomalies in linear response functions, in Figure 8, we compare the temperature dependence of \( \langle (\delta N_{sc})^2 \rangle \) with the isothermal compressibility, \( \kappa_T \), the latter is related to the mean-squared volume fluctuation, \( \langle (\delta V)^2 \rangle \), \( \kappa_T \sim \langle (\delta V)^2 \rangle / V \kappa_0 T \) (refs 22, 23). The calculated \( \kappa_T \) exhibits a maximum precisely at the same temperature where \( \langle (\delta N_{sc})^2 \rangle \) exhibits a sharp maximum, at \( T = 250 \) K. Moreover, with proper scaling, the values of the two overlap (within the standard deviations) with each other at each temperature over the entire temperature range. In the same figure, we have plotted the experimental values of the \( \kappa_T \) which shows that the present hypothesis \( \langle (\delta N_{sc})^2 \rangle \) is responsible for the anomalous rise is in agreement with all the data.

Anomalous lifetime dynamics

We next discuss the lifetime dynamics of the different species. The lifetime correlation function \( S_{L}(t) \) \((i = 4, 5)\) of 4- and 5-coordinated water molecules is defined as follows.

\[ S_{Li}(t) = \frac{\langle n_i(0)n_i(t) \rangle}{\langle n_i(0) \rangle}, \tag{12} \]

where \( n_i(t) \) is considered to be unity if a water molecule is continuously found in a state of coordination number \( i \) for the time interval 0 to \( t \), and otherwise zero. This function provides information about the probability that a particular water molecule remains in a particular state of coordination for a time interval 0 to \( t \). Figure 9 a and b displays the decay of the correlation function of 4- and 5-coordinated species, respectively, at different temperatures. For the 4-coordinated species, the decay of the lifetime correlation function \( S_{L4}(t) \) slows down upon cooling across the Widom line. This is similar to features observed in the dynamics (such as \( F_{S}(k, i) \)) of supercooled water. On the other hand, the decay of \( S_{L5}(t) \) remains fast over the entire temperature range and shows no dramatic change on crossing the Widom line. We have also calculated the average lifetime by fitting of the correlation functions. The result is displayed in Figure 10. This indicates that the barrier height for the 4-coordinated species becomes higher after crossing the Widom line, but the same for 5-coordinated species continues to remain low even after crossing the line. This behaviour suggests the important role of 5-coordinated species in the dynamics of supercooled water.

We have also calculated the distribution of lifetimes of the 4- and 5-coordinated species at \( T = 250 \) K. Figure 11 a and b displays the distributions for 5- and 4-coordinated species, respectively. Lifetime distribution for 5-coordinated species is an exponential distribution starting at \( t_0 = 0.2 \) ps with a time constant of 0.08 ps. However, the distribution for 4-coordinated species starts from a value of 0.37 at 0.1 ps and then continues to decrease up to 1.4 ps. After 1.4 ps, the distribution starts increasing up to 2.1 ps and finally decays to zero with a long time tail. We have decomposed the distribution as the sum of two different distributions and shown in Figure 11 c. The decomposed short-time distribution takes care of the initial decay of the total distribution. This part describes the lifetime distribution of the relatively short-lived 4-coordinated species which are present as immediate neighbours to a 5-coordinated species making the inter-conversion between 4- and 5-coordinated species.
Figure 9. Decay of the lifetime correlation function, $S_i(t)$, in log–log plot for (a) 4-coordinated ($S_{4i}(t)$) and (b) 5-coordinated ($S_{5i}(t)$) water molecules. Note the slowdown of the decay for $S_{4i}(t)$ after crossing the Widom line and relatively unchanged decay pattern for $S_{5i}(t)$ over the entire temperature range.

Figure 10. Temperature dependence of the lifetimes of 4- and 5-coordinated species. Lifetime has been obtained from the fitting of the corresponding lifetime correlation function (as shown in Figure 9).

faster. However, another part of the distribution which has the long time tail describes the lifetime distribution of the 4-coordinated species which are not immediate neighbours to a 5-coordinated species.

Now, one can consider the following equation for 4- and 5-coordinated species as the system is in equilibrium.

$$\frac{\langle N_{5c}(t) \rangle}{\langle N_{4c}(t) \rangle} = \frac{k_{4\rightarrow5}}{k_{5\rightarrow4}} \exp\left(-\frac{\Delta G}{k_B T}\right).$$

Here $k_{A \rightarrow B}$ represents the rate at which species A transforms to species B and $\Delta G$ is the free energy difference between species A and species B. Now as we lower the temperature $k_{5\rightarrow4}$ remains same but $k_{4\rightarrow5}$ slows down. According to the above relation, $\Delta G$ also increases with lowering of temperature. This infers that the free energy diagram between 4- and 5-coordinated species is governed by the following equation.

$$\Delta G = a(T - T_C)x^2 + Bx^3 + Cx^4.$$  \hspace{1cm} (14)

Here $x = (\langle N_{4c}\rangle - \langle N_{5c}\rangle).$ However, the activation energy for the transformation from 5- to 4-coordinated species remains almost the same in the whole temperature range as lifetime distribution does not change significantly.

**Time correlation functions of number density fluctuations: emergence of slow decay**

Next, we have studied the self- and cross-correlation of the number fluctuation of the 4- and 5-coordinated species in time. The self-correlation function $C_i(t)$ ($i = 4, 5$) is defined as follows.

$$C_i(t) = \frac{\langle \delta N_i(0) \delta N_i(t) \rangle}{\langle \delta N_i(0) \delta N_i(0) \rangle}.$$  \hspace{1cm} (15)

Similarly, we define the cross-correlation function $C_{4,5}(t)$ as follows.

$$C_{4,5}(t) = \frac{\langle \delta N_{4c}(0) \delta N_{5c}(t) \rangle}{\langle \delta N_{4c}(0) \delta N_{5c}(0) \rangle}.$$  \hspace{1cm} (16)

Figure 12a–c displays the decay of the number fluctuation of the time correlation function in the log–log plot for 4-coordinated species, 5-coordinated species and between both of them. The decay of the self-fluctuation time correlation function of both the species (as shown in Figures 12a and b) becomes slowest at $T = 250$ K (Widom line). A step-like feature also develops (such as glassy relaxation) in the relaxation pattern as the Widom line is approached from above and continues to be present.
Figure 11. Distribution of the lifetimes of $a$, 5-coordinated and $b$, 4-coordinated species in supercooled water at $T = 250$ K. Note the maximum at intermediate time and long time tail in the latter. $c$, Decomposition of the 4-coordinated lifetime distribution to short and long time part.

Figure 12. Decay of fluctuation time correlation function. $a$, $C_4(t)$; $b$, $C_5(t)$ and $c$, $C_{4,5}(t)$ in log–log plot. Note the negative cross-correlation ($C_{4,5}(t)$) between the fluctuations of 4- and 5-coordinated water molecules. Note also the slowest decay of all the correlation functions at $T = 250$ K and also the emergence of step-like feature near the Widom line.

DNA hydration layer: results and discussions

Mean-square fluctuation of DNA and translational diffusivity of water

We first report the calculated mean-square atomic fluctuation (which measures the variance of the position of atoms at equilibrium) $\langle X^2 \rangle$ of the DNA atoms starting from 300 K down to 220 K in order to characterize the macromolecular ‘glass’ transition temperature ($T_{DNA}$). Left panel of Figure 13 displays the same. We find that the mean-square fluctuation (MSF) of DNA slows down dramatically around 247 K and continues to remain slow for the lower temperatures. The onset of the change in slope (near $T_{DNA} \approx 247$ K) of MSF indicates a macromolecular dynamic transition. Right panel of Figure 13 shows temperature dependence of the diffusivity (obtained from the slope of the mean-square displacement of water molecules at long time) for all the water molecules in the system. It shows a cross-over around the same temperature ($T_L \approx 247$ K) from a high-temperature power law form to a low-temperature Arrhenius form.$^{75}$ From the power law fit to the high-temperature region, we get a glass transition temperature of 231 K which is in agreement with the earlier simulation study by Stanley and co-workers.$^{55}$

Intermediate scattering function

We next discuss the self-intermediate scattering function (ISF) of the oxygen atoms of the water molecules in the grooves of DNA for a set of temperatures starting from 300 to 220 K. The self intermediate scattering function is defined by eq. (1). The translational relaxation time ($\tau_T$) after crossing. The cross-fluctuation time correlation function (Figure 12 $c$) between 4- and 5-coordinated species is negative and the decay pattern is similar to the self-fluctuation time correlation function. This negative cross-correlation indicates the anticorrelation between the numbers of 4- and 5-coordinated species, as discussed earlier. The slowest decay near the Widom line ($T = 250$ K) suggests the appearance of strong anticorrelation which is correlated over a long time. The appearance of step-like feature in the relaxation pattern of self- and cross-fluctuation time correlation function of the species is an indication of the crossing of Widom line for the supercooled water.
Mean-square fluctuation of DNA duplex (left panel) and diffusivity (right panel) of the oxygen atoms of all the water in the system. In the left (DNA) panel, MSF of DNA shows a dynamic transition at $T \approx 247$ K. We have fitted two straight lines (one using $T = 300$–250 K data and other using $T = 240$–220 K data) to show the transition. In the right (water) panel, water shows dynamical cross-over around same temperature from a high-temperature power law (fitted using $T = 300$–250 K data) behaviour (cyan) to a low-temperature Arrhenius (fitted using $T = 240$–220 K data) behaviour (red). The cross-over temperatures for bulk water and major groove water are found to be $T \approx 247$ K and $T_{GL} \approx 255$ K, respectively. The dynamical transitions are of fragile-to-strong type, although the fragility of major groove water is smaller of the two.

The minor groove water molecules however show a remarkably different translational dynamics. Minor groove water does not show any signature of a fragile liquid in the studied temperature range. Instead, temperature dependence of translational relaxation time for minor groove water fits well into two Arrhenius forms of different slopes with a cross-over temperature around $T_{GL} \approx 255$ K (same as major groove water). This can be understood in the context of difference in the structure of hydration layer in the grooves of DNA. Hydration in the minor groove is more extensive, regular with a zig–zag spine of the first and second shells of hydration whereas hydration in major groove is restricted to a single layer of water molecules. Water molecules in minor groove are thus more structured in comparison with major groove water which results in a strong liquid type of behaviour for water molecules in minor groove even in the high-temperature region. This explains why in contrast to bulk and major groove water, minor groove water shows a strong-to-strong type of dynamical transition.

Orientational dynamics

We next analyse orientational (dipole–dipole) time correlation function (TCF) (defined by eq. (2)) of water molecules in different regions of aqueous DNA. Figure 15a is obtained by fitting the two-step relaxation of ISF at different temperatures using relaxing cage model (RCM). The fitting equation used here is given by

$$F_S(k, t) = (1 - A(k)) \exp \left[ -\left( \frac{t}{\tau_S} \right)^2 \right] + A(k) \exp \left[ -\left( \frac{t}{\tau_T} \right)^\beta \right].$$

Here $A(k)$ is the Debye–Waller factor and $\beta$ is the stretched exponent.

Figure 14a shows ISF of oxygen atom for the water molecules in bulk, major groove and minor groove at 300 and 260 K. It is evident from both the figures that water molecules in the major and the minor grooves tend to behave like a liquid at a temperature lower than the bulk. The behaviour is more prominent for water molecules in the minor groove. This can be ascribed to the fact that translational motion of water molecules in the minor groove is more constrained owing to the more ordered structure in the minor groove than water molecules in the major groove of DNA. Water molecules in the major groove are, in turn, translationally more constrained than bulk water. Figure 14b shows the temperature dependence of $\tau_T$ for water molecules in bulk, major and minor grooves. For both bulk and major groove water, the temperature dependence at high-temperature region can be fitted to the VFT law. In reality, however, the divergence is avoided as below a certain characteristic temperature, the functional dependence of relaxation time switches over to an Arrhenius form which indicates a strong liquid.
Figure 14. \(a\), Intermediate scattering functions \(\langle F_S(k, t) \rangle\) of the oxygen atoms of water molecules in bulk, major and minor grooves of DNA duplex at two different temperatures, \(T = 300\) K (left panel) and \(T = 260\) K (right panel) for \(|k| = 2.5\) Å\(^{-1}\). 

\(b\), Translational relaxation time \(\tau_T\) for bulk (left panel), major groove (middle panel) and minor groove (right panel) water. Bulk and major groove water show dynamical cross-over between high-temperature VFT behaviour (cyan) and low-temperature Arrhenius behaviour (red). Minor groove water shows a transition between two Arrhenius behaviours. For bulk water, VFT fitting has been done using \(T = 300–250\) K data, and Arrhenius fitting has been done using \(T = 240–220\) K data. For major groove water, VFT fitting has been done using \(T = 300–260\) K data, and Arrhenius fitting has been done using \(T = 250–220\) K data. For minor groove water, two Arrhenius fittings have been done using \(T = 300–260\) K data and \(T = 250–220\) K data. 

Table displays \(C_\mu(t)\) for water molecules in bulk, major and minor grooves at 300 and 260 K, respectively. Similar to the translational motion, rotation of the minor groove water molecules is found to be the most constrained. Figure 15\(b\) shows the temperature dependence of orientational relaxation time \(\tau_R\) as obtained from stretched exponential fitting at long time of dipole–dipole TCF for bulk, major and minor groove water. Bulk water shows a fragile-to-strong transition around the same temperature \(T_L \approx 247\) K as observed for translational relaxation time. However, unlike translational relaxation, orientational relaxation shows a transition between two Arrhenius forms of different slopes with a cross-over temperature \(T_{GL} \approx 255\) K for both major and minor groove water. Strong-to-strong transition observed in the minor groove (both translational and orientational dynamics) can be attributed to the effect of confinement in the minor groove (higher depth and lower width). It is known that a confined liquid is comparatively less fragile than in the bulk and this eventually gives rise to Arrhenius temperature.
Figure 15. a, Dipole–dipole time correlation functions ($C_\mu(t)$) of water molecules in bulk, major groove and minor groove of DNA duplex at two different temperatures, $T = 300$ K (left panel) and $T = 260$ K (right panel). b, Rotational relaxation time ($\tau_R$) for bulk (left panel), major groove (middle panel), and minor groove (right panel) water. Bulk water shows a cross-over between high temperature VFT behaviour (cyan) and low temperature Arrhenius behaviour (red). Major groove and minor groove water show transition between two Arrhenius behaviours. For bulk water, VFT fitting has been done using $T = 300–250$ K data, and Arrhenius fitting has been done using $T = 240–220$ K data. For major and minor groove waters, two Arrhenius fittings have been done using $T = 300–260$ K data and $T = 250–220$ K data in each case.  

dependence of the relaxation times (signature of strong liquids) even at the higher temperature region. The reason for the different behaviour of major groove water is thus probably because rotation probes local environment more faithfully than translation.

Microscopic characterization: O–O–O angle distribution

To understand how the structure of groove water changes across the dynamical transition, we have calculated the O–O–O angle distribution inside the first coordination shell of a water molecule. Angle distributions at three different temperatures (300, 250 and 230 K) for groove water molecules are displayed in Figure 16. At all the temperatures, the distribution has a two-peak character. While the peak at lower angle is the signature of the presence of interstitial water molecules inside the first coordination shell, higher angle peak characterizes the degree of tetrahedrality present. As it is evident from Figure 16, with decreasing temperature the degree of tetrahedrality increases (at higher angle peak, height increases) with the removal of interstitial water molecules (at lower angle
peak, height decreases) from the first coordination shell. Structural change of this kind (increase in order with decrease in temperature) is responsible for the dynamical transition for groove water molecules.

Bulk water also exhibits a dynamical transition near 250 K. The signatures are, however, weaker in the case of bulk water than what are observed in the grooves. The role of confinement in fostering the transition of tetrahedral water can be understood in the following fashion. In the confined state, water molecules gain in energy but lose entropy (see next section). The tetrahedrally coordinated water is a low entropy state of the system. Confinement thus favours the cross-over/transition to the tetrahedral state.

**Entropy of layer water and Adam–Gibbs correlation**

To understand the origin of the large observed differences between the dynamics of water molecules in the minor groove and in the bulk, we have calculated the entropy of water molecules in the respective regions at two different temperatures (300 and 280 K). We have used 2PT method\(^{11,78}\) to calculate the entropy. In this scheme, the total entropy is decomposed in four parts as \(S = S_{\text{vib}} + S_{\text{Conf}} + S_{\text{rot}} + S_{\text{b-vib}}\). \(S_{\text{b-vib}}\) is negligible compared to other parts and \(S_{\text{rot}}\) has been considered to be constant for each region. To calculate the other two parts of the total entropy, the method requires the translational velocity autocorrelation (VAC) function as input. We have obtained the total density of states (DOS) by taking the Fourier transform of the translational VAC function. Now, one can decompose the total DOS into a solid-like nondiffusive DOS (\(g_S(\omega)\)) and a gas-like diffusive DOS (\(g_g(\omega)\)) using 2PT method. Under the harmonic approximation, the vibrational entropy (\(S_{\text{vib}}\)) can be written as follows.

\[
S_{\text{vib}} = \int_0^\infty d\omega g_S(\omega)W_{S}^{HO}(\omega),
\]

Here \(W_{S}^{HO}(\omega)\) is the well-known weight function for the entropy of a harmonic oscillator. Now, the configurational entropy (\(S_{\text{Conf}}\)) can be written as follows.

\[
S_{\text{Conf}} = \int_0^\infty d\omega g_g(\omega)W_{S}^{HS}(\omega).
\]

Here \(W_{S}^{HS}(\omega)\) is the weight function for the entropy of the hard sphere gas. In both the temperatures, minor groove water molecules have substantially lower entropy than bulk. At 300 K, the difference is \(\sim 60\%\) of the latent heat of fusion of bulk water. Entropy is usually found to be closely correlated with diffusion coefficient and structural relaxation time, in Figure 17, we show the correlation between \(T S_{\text{Conf}}\) and translational diffusivity and show that the Adam–Gibbs relation remains valid for the different regions of DNA. Interestingly, we find that the Adams–Gibbs plot for the two different temperatures collapse on a single curve which can be fitted to a straight line. This seems to indicate that the activation energies for the transfer of water molecules between different regions of aqueous DNA are utmost weakly dependent on temperature above the L–L transition. Dynamics below the L–L transition is too slow to allow a comprehensive study. The present calculation of entropy is semi-quantitatively reliable as the entropy of bulk water is correctly (within 5%) reproduced and also the chemical potential of bulk water and groove water is found to be the same, as expected for systems in equilibriunm.
In a thermodynamic coexistence between two phases, a discontinuous change in entropy signals the presence of latent heat and a first-order phase transition. However, in this study, the large difference in entropy between bulk and minor groove water molecules should be regarded as a signature in the difference in structure between the two phases. Owing to the small number (~120 for major groove and ~80 for minor groove) of water molecules present in the groove region, a detailed quantification of microscopic structural arrangement is difficult to perform.

Correlation between tetrahedral ordering and configurational entropy

We have studied the structure, dynamics and thermodynamics of water molecules in different grooves of poly-AT and poly-GC DNA. We have calculated the O–O–O angle distribution for water molecules in different grooves and quantified the average tetrahedral order parameter, \( \langle t_h \rangle \), for water molecules in the different regions using the relation

\[
\langle t_h \rangle = 1 - \frac{9}{4} \left( \cos(\theta_{\text{OOO}}) + \frac{1}{3} \right)^2
\]

\[
= 1 - \frac{9}{4} \int_{0}^{\pi} \left( \cos(\theta_{\text{OOO}}) + \frac{1}{3} \right)^2 P(\theta_{\text{OOO}}) d\theta_{\text{OOO}}.
\]

Here \( \theta_{\text{OOO}} \) is the O–O–O angle and \( P(\theta_{\text{OOO}}) \) is the distribution. We find the values of \( \langle t_h \rangle \) are 0.41, 0.47, 0.48, 0.52 and 0.57 for bulk water, major groove water of poly-GC, major groove water of poly-AT, minor groove water of poly-G and minor groove water for poly-AT, respectively. Thus tetrahedral ordering in the groove of DNA increases with increasing confinement. We have also calculated entropy and diffusivity of water molecules in the different regions and the Adam–Gibbs relation is found to be valid as shown by the linear fit of the data in Figure 18. We found a correlation between \( \langle t_h \rangle \) and configurational entropy of water in different regions as indicated by the dashed curve in Figure 18. It is clear from the figure that \( \langle t_h \rangle \) increases with decreasing configurational entropy.

**What is the nature of the phase transition at 247 K?**

The divergent-like growth of the response functions, such as specific heat and isothermal compressibility certainly appears to support the conjecture of a phase transition at 247 K at ambient pressure. Owing to the finite size of the system, we cannot truly address the nature of the transition. However, we can still attempt to answer a few questions. First, the presence of intermittency suggests the existence of a weak first-order phase transition. Across this apparent transition, the number of 5-coordinated water molecules change sharply. A separate calculation with SPC/E water shows that the transition of a 4-coordinated water molecule to a 5-coordinated water molecule and vice versa becomes increasingly correlated as temperature is lowered. It is shown in Figure 19 that such an event takes the form of a connected string at low temperatures and 3-coordinated H-bonded water molecules behave as a sink.

Propagating jump events can have an interesting resemblance with the excitation energy transfer between molecules observed in many chemical and biological systems. If we consider 5-coordinated species as excitations then it can relax either by transferring the extra water molecule to the 4-coordinated water molecule in the 2nd hydration layer and making it 5-coordinated (this step is similar to the jump of excitation to other molecule by Förster mechanism) or by transferring to 3-coordinated species (traps) from which further excitation transfer is not possible (this step is similar to the fluorescence quenching). Unlike the molecular relaxation, the 5-coordinated species cannot relax by a mechanism similar to fluorescence (radiative decay), particularly at low temperature. The quenching of propagating jump event can be described as (shown in Figure 19)

\[
N_5 + N_3 + N_4 \rightarrow (N_5 - 1) + (N_3 - 1) + (N_4 + 2).
\]

We simplify the description further by treating \( N_4 \) as bulk matter. Then the corresponding rate equation is as follows.

\[
\frac{dN_4}{dt} = kN_3 \frac{N_5}{V}.
\]

**Figure 18.** Correlations between diffusion coefficient, configurational entropy and tetrahedral order parameter \( \langle t_h \rangle \). Note that left side of the y-axis represents logarithm of diffusivity and right side of the y-axis represents \( \langle t_h \rangle \). The straight line fitting of the data validates the Adam–Gibbs relation.
Figure 19. a. Schematic representation of the mechanism of propagation and death of the string-like motion in supercooled liquid water. The numbers indicated here are the coordination states of the water molecules. The arrow indicates the transfer of water molecules during the H-bond breaking events. For clarity, we have not shown all other water molecules inside the coordination sphere.

b. Histogram of the distribution of correlation lengths in terms of number of water molecules (n) involved in sequential H-bond breaking events at three different temperatures (300, 273 and 250 K)\(^74\). The relaxation of 5-coordinated water molecules can be modelled as reaction–diffusion phenomena, usually used to study the dynamics of fluorescence quenching and diffusion controlled charge transfer reactions in solution\(^81\).

At low temperature, concentrations of 5- and 3-coordinated species are quite low compared to the 4-coordinated species, so one can neglect the self-interaction between 5–5 and 3–3-coordinated species. We consider that the two particles (3-coordinated and 5-coordinated) execute Brownian motion independently of each other with diffusion coefficients \(D_3\) and \(D_5\). Following Smoluchowski approach to the diffusion controlled reactions, we consider a sink at the centre of a sphere of radius \(R_0 = 3.5\ \text{Å}\) (1st peak of \(g(r)\) of water) and an absorbing boundary at the surface of the sphere (reaction surface), then the rate of quenching can be given by the well-known Smoluchowski relation.

\[
k = 4\pi D_{35} R_0 C \left(1 + \frac{R_0}{(\pi D_{35} t)^{1/2}}\right),
\]

where \(D_{35}\) is the mutual diffusion constant given by \(D_3 + D_5\). \(C\) is the concentration of 5-coordinated water molecules. Note that the above rate expression for quenching is for a single sink (3-coordinated water molecule) only.

As the temperature \(T\) of the system is lowered, the concentration of 3-coordinated water molecules decreases (sharply). At the same time, the rigidity of the H-bond network increases and \(D_{35}\) decreases. Both the factors lead to the decrease in the rate of annihilation of excitations or increase in the survival time of a 5-coordinated water molecule, leading to the prediction of a strong temperature dependence of the relaxation time of deeply supercooled water.

In the above discussion, we have neglected the interaction between the 5-coordinated and 3-coordinated species. At low \(T\), when the H-bonded network is rigid, the defects can interact with each other. If we assume that there is a long range (such as Coulombic) interaction between diffusing 3-coordinated and 5-coordinated species (defects), then the probability of finding the 3-coordinated and 5-coordinated species at a separation \(R\) at any time \(t\) can be described by the Smoluchowski equation.

\[
\frac{\partial P(R, t)}{\partial t} = D_{35} \nabla^2[P + \beta V(R)]P,
\]

where \(V(R)\) is the interaction potential between 3-coordinated and 5-coordinated defects. We assume that it can be approximated as \(-A/R\). To get the time-dependent survival probability, one can solve the above equation with appropriate initial and boundary conditions. The interaction between defects can play an important role for relaxation, however, the exact nature of the interaction or the form of potential is still not known.

Note that 4-coordinated water molecules in an ice-like structure is the lowest energy configuration at temperatures below the freezing/melting temperature of 273 K at ambient pressure. However, this ideal structure is separated from disordered water by a large barrier. What we observe here is a muted transition between low density water which comprises mostly 4-coordinated water molecules and high density water which has a significant number of 5-coordinated water molecules. This L–L transition is believed to have a critical temperature (for TIP5P water model) at a higher than ambient pressure. It has been conjectured that the effects we observe is a consequence of crossing the Widom line. A physical explanation, not too different from this is forwarded here in terms

The relaxation of 5-coordinated water molecules can be modelled as reaction–diffusion phenomena, usually used to study the dynamics of fluorescence quenching and diffusion controlled charge transfer reactions in solution\(^81\).
of frustration, discussed by Kivelson and coworkers to explain rapidly growing timescales in supercooled liquids as temperature is lowered. Here, the cause of frustration is the existence of 5-coordinated water molecules which are difficult to destroy as they are locally conserved. However, we still do not have a quantitative theory for the role of the 5-coordinated water molecules.

**Reverse micelles: frustration effects owing to surface interactions**

In a reverse micelle (RM), water is confined within a small, nearly spherical, cavity and walls are formed by charged groups. The charged groups on the surface undergo strong interactions with the nearest neighboring water molecules. A popular example is given by sodium dodecyl sulphate (SDS), where the negatively charged sulphonate groups in the surface form strong hydrogen bonds with the water molecules. Dynamics in RMs has drawn tremendous attention in recent times as it represents a nano-confined system where water dynamics gets significantly modified.

Water in confinement exhibits slow as well as fast dynamics. The slow dynamics has been reported to have time constants 2–3 orders of magnitude larger than that in the bulk. Paradoxically, the fast dynamics has been found faster than the bulk, with time constants smaller by as much as a factor of 3. The origin of both fast and slow components are the subjects of significant interest.

Recently, we have proposed a simple analysis based on the one-dimensional Ising model to illustrate the dynamical behaviour of water in confined systems. Our model is especially applicable to RMs. We discuss here this modified finite length one-dimensional Ising model and use it to study the propagation and the annihilation of dynamical correlations in finite systems and to understand the intriguing shortening of the orientational relaxation time that has been reported for small-sized RMs. This model has been designed to mimic the frustration scenario present in RMs, which arises owing to the strongly hydrogen-bonded surface water molecules.

The main motivation behind this model is that in confined systems, such as RMs, the water molecules that are located diametrically opposite to each other are orientated opposite to each other. Thus the opposite correlations induced by spatially opposite surface groups propagate inside and are expected to annihilate each other at the centre.

Effects of correlations on orientational relaxation can be modelled in a very simple way by using the ferromagnetic interaction in a one-dimensional Ising chain with two terminal spins fixed in opposite directions, one as up (i.e. ‘+1’) and the other at the opposite side as down (i.e. ‘−1’) (see Figure 20). The inhomogeneity created by the fixed spins at surface will propagate through the nearest neighbour interaction and naturally decrease as one moves away from the terminal towards the centre. The two opposite polarizations will cancel each other exactly at the centre. So the central spin will behave similar to a free spin and can relax faster than the bulk.

We have carried out both analytical and numerical calculations of our new model by using Glauber master equation for various number of spin systems.

**Theoretical formulation**

The Glauber master equation for one-dimensional array of spin is given by:

\[
\frac{d}{dt} p(\sigma_1, \sigma_2, ..., \sigma_N, t) = -\sum_j w_j(\sigma_{j-1}, \sigma_j, \sigma_{j+1}) p(\sigma_1, \sigma_2, ..., \sigma_{j-1}, \sigma_{j+1}, t) + \sum_j w_j(\sigma_{j-1}, -\sigma_j, \sigma_{j+1}) p(\sigma_1, \sigma_2, ..., -\sigma_{j-1}, \sigma_{j+1}, t)
\]

and the transition probability \(w_j(\sigma_{j-1}, \sigma_j, \sigma_{j+1})\) is given by

\[
w_j(\sigma_{j-1}, \sigma_j, \sigma_{j+1}) = \frac{1}{2} \alpha \left[1 - \frac{1}{2} \sigma_j (\sigma_{j-1} + \sigma_{j+1})\right].
\]

One can define a stochastic variable for average spin value as

\[
q_j(t) = \langle \sigma_j(t) \rangle = \sum_{\{\sigma\}} \sigma_j(t) p(\sigma_1, \sigma_2, ..., \sigma_N, t).
\]

By using the value of \(w_j(\sigma_{j-1}, \sigma_j, \sigma_{j+1})\) and \(q_j(t)\), one can find the following equation of motion for the \(k\)-th spin

\[
\frac{dq_k(t)}{dt} = -\alpha q_k(t) + \frac{\alpha^2}{2} (q_{k-1}(t) + q_{k+1}(t)).
\]

This equation of motion can be solved for short chains, and numerically for large system size. We have obtained the analytical solutions for \(N = 3, 4\) and \(5\) spins systems. The time dependence of various spins in these systems is given as follows.
For $N=3$ system with terminal spin fixed, the central spin will decay as

$$q_2(t) = q_2(0) \exp(-\alpha t).$$

(29)

Thus, the decay of the central spin follows the dynamics in the non-interacting limit. This gives a nice and simple example of the destructive interference owing to the interaction with the surface.

In case of $N=4$ system, the same treatment leads to the following solution.

$$q_2(t) = \frac{\gamma}{\gamma + 2} \frac{1}{2} q_{23}^-(0) \exp(-\alpha \lambda^+_4 t)$$

$$+ \frac{1}{2} \left[ q_{23}^-(0) - \frac{2\gamma}{\gamma + 2} \right] \exp(-\alpha \lambda^-_4 t),$$

(30)

$$q_3(t) = -\frac{\gamma}{\gamma + 2} + \frac{1}{2} q_{23}^+(0) \exp(-\alpha \lambda^-_4 t)$$

$$- \frac{1}{2} \left[ q_{23}^+(0) - \frac{2\gamma}{\gamma + 2} \right] \exp(-\alpha \lambda^+_4 t),$$

(31)

where

$$q_{23}^-(0) = q_2(0) \pm q_3(0)$$

(32)

and

$$\lambda^\pm_4 = \left\{ 1 \pm \frac{\gamma}{2} \right\}.$$  

(33)

It is clear from eqs (30) and (31) that the decay pattern of $q_2(t)$ and $q_3(t)$ have two time constants, one is smaller (the decay is faster) and the other is larger (the decay is slower) than the time constant for the non-interacting limit.

At high temperature or low $J$, limit $\gamma \to 0$, thus $q_2(t)$ and $q_3(t)$ decay with only one time constant, i.e. $1/\alpha$. However, the timescales differ by as much as a factor of 3 in the strong coupling limit ($\gamma = 1$).

We could also solve the system of equations of motion for the $N=5$ system and the solution is as follows.

$$q_2(t) = \frac{\gamma}{2} + q_{24}^-(0) \exp(-\alpha \lambda^+_4 t)$$

$$+ \frac{1}{2} q_{24}^-(0) - \frac{1}{2} q_3(0) \exp(-\alpha \lambda^-_4 t)$$

$$+ \frac{1}{4} q_{24}^+(0) + \frac{1}{2} q_4(0) \exp(-\alpha \lambda^+_4 t),$$

(34)

Numerical results and discussions

For larger number of spins, we have solved Glauber equation of motion (eq. (28)) at temperature $T = 1.0 J/ k_B T$, with time step $dt = 1 \times 10^{-3}$ ($\alpha = 1$ sets the timescale), with the terminal spins fixed in the opposite directions for several system sizes.

The opposite polarizations created by the two-terminal fixed spins propagate from surface to the centre and cancel each other at the centre (see Figure 21). Therefore, the
central spin can exhibit a behaviour which is different from the bulk which can be described either by imposing periodic boundary condition, or by taking the central spin in a very large system ($N$ very large).

In the case of small size RMs, the central spin exhibits an initial decay rate faster than the bulk generated with periodic boundary condition. The central spin decay pattern also exhibits a cross-over from overall faster decay to bulk-like behaviour with increase in system size, as shown in Figure 22. For small chains (such as $N = 5$), we have found that the central spin indeed has two decay constants (eq. (35)), and an overall faster decay rate than the bulk, as shown in Figure 22.

Note that the decay of spins in the non-interacting limit (given by rate $\alpha$) is considerably faster than that of the interacting limit. This is the reason for the faster decay of the central spin for small chains.

The frustration behaviour in RMs can be explained in a more general way, in terms of a quasi-two-dimensional model. We have designed a new model by partly following Shore–Zwanzig model of interaction among spins. Instead of working with a two-dimensional (2D) square lattice, we have designed this new model that consists of several concentric rings having unit inter-ring spacing with constant spin density for every ring (see Figure 23). The spins on the outermost ring (layer) are kept fixed in such a way that the two-terminal spins along a diameter are oriented exactly opposite to each other (see Figure 23). Other spins are free to move in an $xy$ plane. These fixed spins will create inhomogeneity (frustration) in the system and thus the opposite polarization will propagate from the terminal ring towards the centre.

We define a spin–spin time correlation function by averaging over all the spins in a given ring by

$$C_i(t) = \frac{1}{N} \sum_{j \neq i} \langle \sigma_j(0) \sigma_j(t) \rangle,$$

where $N$ is the total number of spins in $i$th ring.

The spin–spin orientational function defined as eq. (39), shows an interesting behaviour especially in the short-time window (Figure 24). As depicted in Figure 24, the overall decay pattern for the ring adjacent to the fixed one is slower than the other, and it becomes faster as one moves towards the centre. The central region exhibits a bit slower decay at shorter times but faster in the longer times.
Therefore, this model also established the fact of annihilation of opposite polarizations propagated from surface to the centre.

Conclusions

We have discussed the fascinating problem of anomalous static and dynamic properties of water in the bulk, in RM s and in the DNA hydration layer. Although, the simulation results in bulk water are in close agreement with experimental ones, we hardly have any experimental result for the DNA hydration water except that the tetrahedral nature of water coordination in the ‘spine of hydration’ along the AT minor grooves are well known from X-ray studies. Water within RM s also pose several intriguing problems.

Although a complete theoretical understanding of the anomalous behaviour of low-temperature water is yet not fully understood, we have demonstrated here a critical role of 5-coordinated water molecules. It will be interesting to study the importance of this 5-coordinated water molecule in confined water. We are yet to study this problem in detail for water within RM or even when the confining surface is structureless. In the minor groove of DNA, relative importance of the 5-coordinated water molecules decreases substantially, because of the interactions with the polar groups. In the entropy–enthalpy balance, stabilization by interaction energy favours 4-coordinated structures.

To study the effects of confinement, we have introduced two different lattice models that are shown to exhibit interesting dynamics, some of which are in agreement with experimental results.


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