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Solvation Energy: Role of Charged Species and Solvent Molecule

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ABSTRACT

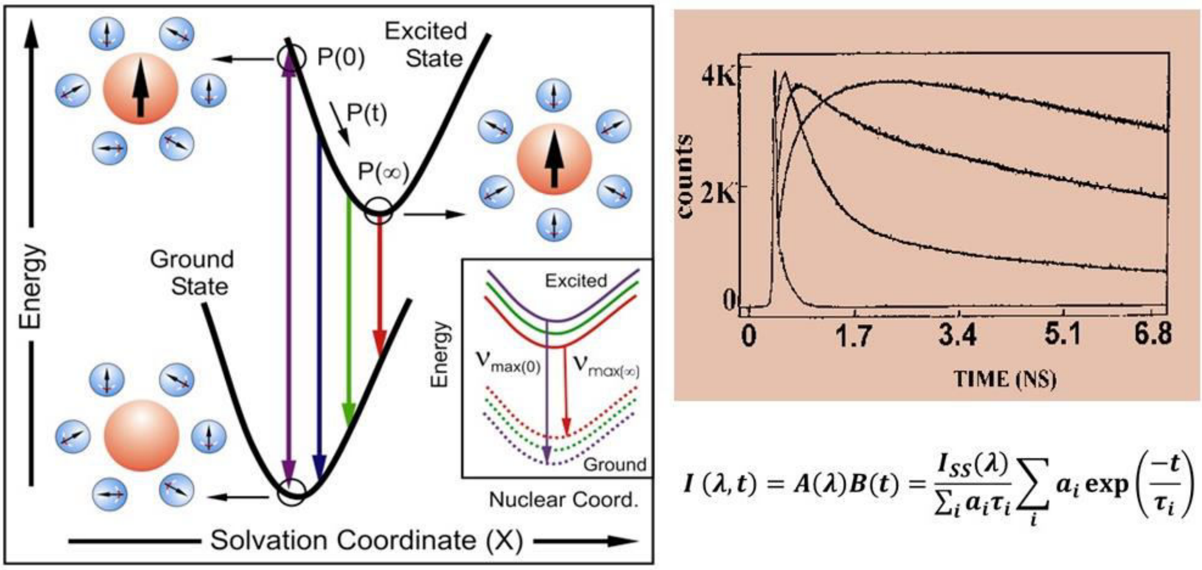
Biological molecules are organized assemblies that hold the structure, dynamics, and function of living organisms. Solvent molecules, particularly water molecules, play a crucial role in surrounding the biological molecules. The stability and functionality of the biological molecule are thermodynamically impacted by changes in the surrounding solvent environment. The most prime factor that contributes to the catalytic activity of proteins, nucleic acids, and vesicles is solvation dynamics, also known as solvation energy. In order to comprehend the role of solvent molecules in the dynamics and operation of biological molecules, we have reviewed the theoretical and experimental findings over the years in this literature. Numerous scientific groups have proposed that the solvation dynamics are influenced by solvent molecules, chain motion, and the charged or polar residues of biological molecules. In this review, we also addressed the roles that polar residues and solvent molecules play in solvation dynamics, especially when it comes to protein molecules.

KEYWORDS: Deuterium isotopic effect; Polar residue; Biological water; Solvation time scale; H-bonding network

1 INTRODUCTION

Although the exact function of water molecules in many molecular features is unknown, water is extremely important for the survival of living things. Proteins, nucleic acids, and vesicles are among the almost all biological building components that cannot operate without water; hydration regulates their structural stability, flexibility, and mode of activity (Frauenfelder et al., 2009; Laage et al., 2017). Particularly, the dynamics of water-protein coupling control a range of protein behaviors, including molecular recognition, the acceleration of enzymatic catalysis, the maintenance of structural integrity, and the facilitation of protein folding. These surface water molecules exist in a glassy amorphous state below the melting point rather than in the physical states of ice and crystal. These water molecules that are intimately associated with biological surfaces such as cell membranes, proteins, or DNA are referred to as "hydrate water" or "biological water" (Ball et al., 2008). These water molecules act diversely from bulk water due to their interactions with polar and charged groups on the biomolecules' surfaces. The involvement of such water molecules on a biological molecular surface is very important since it gives rise to a variety of biological activities in biomolecule (Ruple et al., 1991). Therefore, it is crucial to comprehend the molecular-level dynamic behavior of biological water molecules connected to proteins. Different groups proposed varying thicknesses for the biological water layer, despite the fact that it is impossible to forecast with precision. Conversely, biological water layers are believed to have strongly bound layers with a thickness of 3-5 Å and loosely bound layers that can extend up to 1-2 nm from the biomolecular surface (Bagchi et al., 2008; Zhong et al., 2011).

To uncover the role of water molecules in biological systems, we need to know the dynamics of the time scale that can be measured by solvation dynamics. Following a change in its electronic state, usually as a result of photoexcitation or a chemical reaction, solvent molecules reorganize around a solute species (such as an ion, molecule, or probe molecule) in a time-dependent process known as "solvation dynamics." (Figure 1) The rearrangement of solvent dipoles around a solute may be measured experimentally by producing it abruptly by stimulation with an ultrafast laser pulse. This effect is usually studied using a fluorescent probe molecule, which is slightly polar or non-polar in the ground state but significantly polar in the electrically stimulated state (Figure 1). If the dipole of a fluorescent probe molecule is suddenly oriented in a polar solvent, the solvent dipoles do not respond immediately. Over time, the polar solvent molecules gradually realign and rearrange themselves to equilibrate the new charge distribution of the solute in the excited state. Consequently, the energy of the excited state gradually decreases (Figure 1).



$$I(\lambda,t) = A(\lambda)B(t) = \frac{I_{SS}(\lambda)}{\sum_i a_i \tau_i}\sum_i a_i \exp\left(\frac{-t}{\tau_i}\right)$$

Figure 1: Represents the energy relaxation of an excited probe molecule over time, as well as the fluorescence decays at varied emission wavelengths. The mathematical equation in this figure is used to construct TDFSS

Energy relaxation is shown by a continuous red shift in the emission spectra. This phenomenon is recognized as time-dependent fluorescence stokes shift (TDFSS). The fluorescence decay shows noticeable wavelength dependence in the phenomenon of solvation dynamics. The main source of emission at the short emission wavelength (blue end of the spectrum) is the high-energy un-solvated species. Very long wavelengths (red end emission spectrum) are where emission from low energy solvated species is most prevalent. The fluorescence transients' display marked dependence on emission wavelength. At blue wavelengths, decay is observed, whereas at red wavelengths, a rise precedes decay. The rise at a red wavelength is a direct sign of solvation dynamics. This gradual variation in solvation is recorded by the decay of the normalized solvation correlation function, C (t), which is defined as

$$C(t) = \frac{E(t) - E(\infty)}{E(0) - E(\infty)} = \frac{\nu(t) - \nu(\infty)}{\nu(0) - \nu(\infty)} \qquad \textbf{Eq. 1}$$

Where:

ν(0), ν(t) and ν(∞) are the observed emission frequencies at time 0, t, and ∞ respectively.

and

E(0) is the energy immediately after the excitation (at t = 0)

E(∞) is the energy at equilibrium condition (at t = ∞)

E(t) is the time dependent energy of the probe in the non-equilibrium solvent arrangement

Time dependent energy E(t) of the probe is calculated by the equation -

$$E(t) = -\frac{1}{2}\int drE_0\,(r)P(r,t) \qquad \textbf{Eq. 2}$$

where E_0 is the electric field that is dependent on the environment of the probe molecule and p(r, t) is the polarization that is dependent on time and position.

Ion solution in a dipolar liquid happens quickly than dielectric relaxation. But according to Bagchi et al. (1984), the solvation time constant (τ_L^d) of a dipole is marginally more than that of an ion (τ_L).

$$\tau_L = \left(\frac{\varepsilon_\infty}{\varepsilon_0}\right)\tau_D \qquad \textbf{Eq. 3}$$

$$\tau_L^d = \left(\frac{2\epsilon_\infty+\epsilon_c}{2\varepsilon_0+\epsilon_c}\right)\tau_D \qquad \textbf{Eq. 4}$$

Here, ε_c is the dielectric constant of the molecular cavity, τ_D is the Debye relaxation period, and ε_0 and ε_∞ are the solvent's static and infinite frequency dielectric constants, respectively. For hydration water, the intricate solvation in the bulk becomes much more intricate. Apart from the extensive range of time scales, the coupling between polar residue and water movements plays a significant effect and should yet be properly quantified.

The solvent correlation function C (t) can be express in another form as,

$$C(t) = \frac{\nu(t) - \nu(\infty)}{\nu(0) - \nu(\infty)} = \sum_{\mathrm{i}} \mathrm{a_i} \mathrm{e}^{-\mathrm{t}/\tau_\mathrm{i}} \qquad \textbf{Eq. 5}$$

Thus, the emission energy lowering with time as narrated by,

$$\nu(t) = \nu(\infty) + [\nu(0) - \nu(\infty)] \sum_{\mathrm{i}} \mathrm{a_i} \mathrm{e}^{-\mathrm{t}/\tau_\mathrm{i}} \qquad \textbf{Eq. 6}$$

The solvation dynamics, or solvation energy, have been revealed by using a variety of theoretical and experimental methodologies; new discoveries are being made, particularly in protein molecules (Mukherjee et al., 2017; Dahanayake et al., 2018). Surprisingly, though, the results of theoretical simulation and experiment showed more or less the same butsometimes significant differences at the surface of biomolecules, particularly protein molecules, with reference to the time scale of slow water dynamics employing different experimental techniques. The following long-standing, contentious issues in solvation energy fields are brought up by divergent questions: (i) Why do various experiments yield different results? (ii) What are the specific roots of the multiple time constants that appear to span from a few picoseconds to a few femtoseconds? (iii) What are the prime features in the control of slow solvation dynamics in the biomolecules, water, polar residue of biomolecules, or coupled motion of water and polar residue?

In this review article, the main aim is to find out the role of the solvent molecule and the root of the time scale in solvation dynamics. The time scale of solvent action in bulk water, micelles, reverse micelles, microemulsions, proteins, and DNAs is reported using various experimental and theoretical studies. Overall, both the experimental and theoretical studies emphasize similar timescales of solvation response; modest differences may arise depending upon experimental resolution and simulation timescale. In all the systems, especially protein, bulk solvent-like molecules, the orientation of solvent molecules, the retention time in the hydration layer, the perturbed hydration layer by charged groups, and the dynamic motion of the chain along with solvent molecules impart different time-scale solvation dynamics. Thus, the perturbed structure of the solvent network may be the prime origin of slow solvation. We believe that this review provides a comprehensive foundation for understanding the role of solvents in solvation dynamics and offers new insights into this field.

2 SOLVATION IN BULK WATER

The dynamics of a probe molecule in a bulk water system were investigated using both theoretical and experimental methods. Although they typically produce results that are similar, there are occasionally minor variations in time and space scales. Experimental methods often include Time-Resolved Fluorescence Spectroscopy, Fluorescence Up-Conversion, Time-Resolved Infrared (TRIR) Spectroscopy, and Terahertz (THz) Spectroscopy. A long-time component of 10-100 ps is caused by bulk solvent reorganization; an intermediate component of 1 to 10 ps is caused by diffusive reorientation of solvent molecules; and an ultrafast component ranging from sub-ps to a few ps is caused by inertial motions (librations, hindered rotations) and initial rearrangement of the solvation shell. A probe such as coumarin-153, for instance, usually exhibits a dominating rapid component (~100 fs) and a slower one (~1-2 ps) in its solvation dynamics in water (Glasbeek & Zhang, 2004). The solvation time scale can be determined from the trajectory data of the MD simulation's solvation response function or solvation time correlation function (STCF). Similar to experimental methods, three distinct time scales of 0.5–1 fs, 0.1–1 ps, and 10–100 ps were detected, depending on the simulation time scale duration (Choudhury et al., 2007). Nevertheless, depending on resolution, both MD simulation and experimental methods have certain drawbacks (Table 1).

Table 1: Comparison of solvation time scale in experimental and simulation studies

Process	Time Scale (Experiment)	Time Scale (MD Simulation)	Remark
Inertial response	~100 fs	~100 fs – 1 ps	Visible in both; depends on resolution
Solvent shell rearrangement	~1–10 ps	~1–10 ps	Good agreement
Bulk solvent relaxation	10–100+ ps	10–100+ ps	Needs longer simulation times
Hydrogen bond dynamics (*e.g.,* in water)	0.1–1 ps	~0.2–1 ps	MD gives atomic-level insight

3 SOLVATION DYNAMICS IN BINARY SOLVENTS

A binary solvent blend exhibits a to some extent different solvation trend than pure solvents. Here the solvation time scale rely on a number of factors, including the environment of the solvents, the solute (or probe molecule), and the precise interactions (e.g., hydrogen bonding, polarity, viscosity). However, the general patterns and time scale found in the experiment and simulation are reasonably similar; three diverse time scales are mainly observed: (i) an ultrafast component in the order of 100 fs to 2 ps, which is caused by inertial motions and fast local solvent rearrangements nearby the solute; (ii) an intermediary component of around 2 to 10 ps, which is caused by diffusive reorientation of solvent molecules, which may be regulated by solvent viscosity and polarity mismatches; and (iii) a sluggish time scale of 10 ps to more than 100 ps, which is caused by long-range solvent structural reorganization, mainly in highly viscous or structured binary mixtures. Higher viscosity, a change in the hydrogen bonding network compared to a pure solvent, the composition of the binary solvent, and solvent-solvent interaction—which can result in microheterogeneity or preferential solvation—all affect the slightly longer time scale of solvation dynamics seen in a binary solution.

Mahanta et al. (2018) studied the dynamics of water molecules in a water-1,2-dimethoxyethane (DME) mixture by spectroscopic techniques using coumarin 500 probes and molecular dynamics simulation. It was observed that the average solvation time scale from ~0.25 ns decreases slightly up to 0.6 mole fraction of water, then abruptly. The large percentage of DME water molecules that are restricted and have strong hydrogen bonds with DME molecules might be the cause of this. According to MD simulation results, the solvation process is slowed down at lower water fractions because water molecules are clustered due to polar-polar interaction rather than being confined by hydrogen bonding with DME. However, because there were more DME-free water molecules accessible in the solution, the solvation phenomenon accelerated at a high mole fraction of water. Zhang et al. (2013) used a C153 probe in conjunction with spectroscopic methods to describe the solvation response function and the dielectric relaxation of a binary solution mixture [([Im41][BF$_4$]) + water] within the time scale of 80 fs to 20 ns. The average relaxation time rises as the composition of ionic liquids increases, and they discovered four distinct dielectric time scales (~1 ps, ~10 ps, ~70 ps, and ~300 ps) in all binary combination compositions. With the exception of composition (χI_L = 0.05), the solvation response function in pristine ionic liquids and binary mixes has a very fast component in the sub-picosecond time scale and a widely dispersed slow time scale in the upper picosecond time scale, which is akin to the dielectric time scale. The viscosity of the binary solution has a linear correlation with both the average and long-term solvation time scales.

4 SOLVATION DYNAMICS IN MICRO-EMULSIONS, REVERSE MICELLES, ANDMICELLES

Experimental and theoretical/simulation approaches have been used to study solvation dynamics in micelles, reverse micelles, and microemulsions due to their complex environments, which mimic biological systems. These systems feature heterogeneous and confined environments that significantly influence the dynamics of solvent relaxation around solutes (probes). All systems exhibit multi-component dynamics, with ultrafast components ranging from sub-picoseconds to greater than hundred ps. Bound water that interacts strongly with the polar head group of the surfactant molecule or trapped water molecules whose mobility is limited or constrained might cause long-time-scale dynamics that differ dramatically from the pure solvent.

Recently, Crowder et al. (2023), using MD simulation, determined the water dynamics interior a reverse micelle made of AOT surfactant [sodium bis (2-ethylhexyl) sulfosuccinate] dispersed within isooctane solvent. By altering the composition, the proportion of water to AOT molecules (W_0) changed from 5 to 20. Water molecules' mobility is extremely constrained at low W_0 values and progressively shifts toward bulk water-like motion as W_0 grows (Crowder et al., 2023). They get to the conclusion that the water-water interaction and hydrogen bonding network reduce rotational flexibility because water molecules are confined in reverse micelles with small W_0 sharpness. Similar observations were reported in BHDC (benzyl hexadecyl dimethyl ammonium chloride) cationic RMs (reverse micelles) with W_0 5 and 10 from MD simulation. Water molecules in RMs with $W_0 = 5$ are more confined, strongly coupled, and localized with ionic head group surfactants at the interior portion of the RM, according to density profile data (Agazzi et al., 2014). With a W_0 increase, the average rotational time constant and sporadic hydrogen bond durations for water molecules moved in the direction of bulk-like water (Table 2).

Table 2: Calculated Average Reorientational Times (τ_{rot}) and Intermittent Hydrogen Bond Lifetimes (τ_{HB}) for Water Molecules in W_0=5, W_0= 10, and Bulk water.

System W_0= [water]/[surfactant]	τ_{rot}(ps)	τ_{HB}(ps)
W_0 =5 (RMs)	~43	~53
W_0= 10 (RMs)	~23	~24
Bulk water	~3	~5

Mixed micelles composed of TX-100 and cationic gemini surfactants with varying composition and chain length were recently reported by the Saha group (Kumari & Saha, 2016). They revealed that the microviscosity around C153 decreases as the amount of gemini surfactant increases. The Gemini surfactant showed a favorable correlation with the rotational relaxation and solvation dynamics of C153 (Kumari & Saha, 2016). Two solvation time scales were identified in all micelle systems, with open water providing fast solvation and bound water causing slow solvation. The time scale of dynamics in a pure TX-100 micellar system is 1.16 ns (0.73) and 4.11 ns (0.27), which is significantly sluggish than that of a bulk water system. The time scale of solvation dynamics changes to 0.57 ns (0.63) and 0.82 ns (0.37) when 0.4 percent X12-3-12 Gemini surfactant is added (Kumari & Saha, 2016). Faster dynamics as a consequence of increased H-bonding between water molecules as the stern layer thickness increases, which raises the environment's polarity and microfluidity. The authors conclude that total solvation is caused by a variety of variables, including spacer groups of gemini molecules, polar groups of surfactants, and counterions, in addition to water molecules. The polar regions of a surfactant molecule are attached to the tail of the hydrocarbon, and the spacer group is associated with the tails using a headgroup. This arrangement causes the polymer chain to move very slowly (~ 100 ns) and with limited mobility. Therefore, both water molecules and counterions impart to the dynamics of solvation. Using a C480 probe, Pramanik et al. (2011) demonstrate the solvation dynamics in plain ionic liquid and [bmim][BF_4]/BHDC/benzene RMs at various temperatures and ionic liquid/BHDC molar ratios using spectroscopic methods. At 288 K, the solvation dynamics time constants in a plain ionic liquid are 0.41 ns (0.59) and 1.88 ns (0.41), respectively. This is significantly sluggish than in pure water (Pramanik et al., 2011). Because the viscosity drops from 176 cP to 60 cP at a high temperature of 308K, the solvation time constant becomes faster with components of 0.18 ns (0.61) and 0.76 ns (0.39) (Pramanik et al., 2011). The solvation time scale was faster as the molar ratios of [bmim][BF_4]/BHDC increased, and two components (~0.90 ns and 14 ns) were reported in all RMs. These time constants originate from two distinct ionic liquid environments: RTILs close to and far from the surfactant molecule. The slower translational rotation motion of RTILs around the interface, compared to those isolated from surfactant molecules, greatly restricts their movement. Because RTIL molecules are present in the RMs' interfacial environment, slow solvationis therefore taking place (Pramanik et al., 2011). In soluble micelles, the DCM probe fully recorded the intrinsic solvation dynamics of the micellar interface, as it is totally insoluble in water. Mandal et al. (2002) used this property to report on the water molecule dynamics in TX-100 and CTAB micelles. Three exponential decay components are seen in the micellar environment: an ultrafast component, a slow component, and a long component. The slow and very slow components of the TX-100 micelle are 160 ps (0.1) and 2050 ps(0.6), respectively, whereas the ultrafast component is 2.1 ps (0.3). In CTAB micelle, all three-time scales are much faster than TX-100, and the components are 0.23 ps (0.5), 6.5 ps (0.25), and a very slow component of 350 ps (0.25) (Mandal et al., 2002). According to the structural analysis, a portion of the DCM probe protrudes from the micellar surface of a CTAB micelle, whereas it is fully implanted in a TX-100 micelle. They have concluded that different time scales arise due to the location of the probe, the long component due to the confinement of the water molecule, and the perturbation by the charge and polar head group of the surfactant.

5 SOLVATION OF PROTEIN

Protein folding, stability, and function are all significantly impacted by protein solvation. Determining its time scale reveals a number of biological processes, including signal transmission, ligand binding, molecular recognition, and enzyme catalysis. Protein minimizes its free energy by forming hydrogen bonding along with the polar and charged residue, modulating hydrophobic interaction among the nonpolar residue, and electrostatically programming the charged amino acid residue, where solvation plays a pivotal role. Depending on the protein's location, protein solvation can take place a variety of time scales, ranging from ultrafast picosecond components to nanoseconds. Fast solvation may be slowed down by grooves, a hydration cell close to the protein, charged amino acid residues, irregular surface topology, and protein dynamical flexibility or conformational shift.

As previously stated, in the presence of water, namely ‘biological water,’ numerous numbers of theoretical studies had been performed on the molecular length scale to reveal the heterogeneity of the protein hydration shell. MD simulations are commonly used to connect the retention time of a water molecule in a protein hydration shell with the rotational and translational diffusion coefficient (Jana et al., 2008). Trajectory analysis revealed the coexistence of the "free" and "bound" water molecules, which are categorized by the rapid dynamical interchange between them. Understanding the orientation and distribution of water molecules adjacent to the charge and polar amino acids is crucial for comprehending water dynamics since a protein's surface is quite heterogeneous. Qiao et al. (2019) used MD simulation to explore the orientation and dynamics of water molecules in three distinct protein types in order to address this question. Negatively charged, positively charged, and neutral polar amino acid residues orient the water molecule towards themselves, but the extent and distance vary depending upon the types, and water molecules become free beyond 15 Å. The breadth of the hydration shell around the protein may be considered armstrong; a thicker hydration layer is found in proteins having a net charge. Furthermore, they noticed that from polar amino acid residue to charged amino acid residue (positively charged residue about 94% and negatively charged residue approximately 98%), the orientation of the nearest water dipoles towards a certain direction increases. The residence time of a water molecule next to an amino acid atom rises in the following directions, similar to the orientation of water dipoles: charged nitrogen (N+) and oxygen (O-) atoms, polar N and O atoms, and nonpolar carbon atoms. The two solvation time scales (~0.8 ps and 38 ps) in the subtilisin Carlsberg protein may be explained by the residence time; the slow component comes from a stronger and more rigid water structure, while the ultrafast time scale results from weak interaction with amino acids at the surface (Pal et al., 2002). As a result, the simulation shows how amino acid residues affect dynamics on within the angstrom-length scale.

The Bagchi group attempts to uncover the cause of varying solvation time scales in three distinct protein-water model—myoglobin, lysozyme, and sweet protein monellin, using atomistic simulation techniques (Mondal et al., 2017). They employed two distinct methods: (i) freezing the entire protein motion to remove the inherent fluctuation of the amino acid chain, and (ii) mutation of the amino acid of interest within 7-10 Å to investigate the function of surrounding amino acids (charged or nonpolar). The time-dependent total solvation energy arises from the sum of the protein core, side chain, ions, and water. A much faster average solvation time was noted when the charged amino acid around the tryptophan amino acid was mutated to a nonpolar amino acid, particularly for lysozyme and myoglobin. This faster solvation is in charge of amino acid removal due to elevation of weightage and faster time scale (~20-80 ps). After all, in the event of W3 in monellin, the opposite outcome was noted. This data unequivocally shows that the charge residue—which results from a strong hydrogen bond with the nearby protein hydration layer—plays an important role. Protein side chain motion completely stops when the protein is frozen, the solvation time period of ~20-80 ps remains present, and the weightage of the solvation time scale above 100 ps drastically decreases (in certain cases, it is only slightly present). These findings suggest that the ultraslow time feature arise from the coupled motion of water and amino acid side chains (Mondal et al., 2017).

The DNA polymerase IV (Dop4) enzyme does not contain tryptophan amino acid residue, an ideal system to map the water dynamics in different regions by point mutation. Qin et al. (2016) studied the solvation dynamics at 9 different locations by point mutation to tryptophan amino acid residue using femtosecond up-conversion spectroscopy. Generally, it was noticed that there are two long solvation components for buried tryptophan or three components for exposed tryptophan (300 fs, 10 ps, and 100 ps) and four anisotropy decay components (~ 70 fs for ultrafast internal switching, ~10 and 150 ps due to local wobbling motion, and ~20 ns for tumbling motion) for all regions (Qin et al., 2016). The solvation and chain dynamics map are highly heterogeneous; they depend upon the location of the tryptophan amino acid mutation. MD simulation of water molecules within 10 Å exhibits that in buried tryptophan, only inner-layer hydration cell water molecules within a 7 Å radius contribute to the solvation, but for exposed tryptophan water molecules beyond 7 Å, bulk-like water contributes to ultrafast solvation. Temperature-dependent two-picosecond solvation time scales and two intermediate protein side chain dynamics were linearly correlated in all nine mutants. It clearly manifested that inner hydration layer hydration dynamics and protein side chain dynamics are intrinsically coupled with the same activation energy barrier and should be from the same origin (Qin et al., 2016). Thus, the Zhong group proposed that slow water dynamics arise from the coupled motion of water and protein chains. Jumper et al. (2016) used pump–probe spectroscopy to study the solvation dynamics of a light-harvesting protein, cryptophyte algae, in four different states using rhodamine dye. Tuning the impulsive excitation pulse that oscillates with the excited rhodamine dye potential energy surface allows building a solvent correlation function. In all for the state, a 97% weighted average of solvation arises on a few pico-second time scales; only a small contribution arises in nanosecond time, indicating that protein reorientation (nanosecond time scale) does not impart remarkably (Jumper et al., 2016). Two-time components, one component (~22-62 fs) and the other (~0.3-9.2 ps), arise depending upon the protein structure. The relative weight of the fast components dominates in protein containing close structure (PC630 and PC645), whereas long picosecond components are more in protein having open structure (PC577 and PC612), although the slow time component is a few times faster in close structure. They have proposed that in the excited state of the probe molecule, three different phenomena furnish over three-time scales: bulk water, “biological water,” and protein reorientation. Thus the “biological water” that is the sphere of the hydration shells bound to the protein surface imparts picosecond-time solvation. Dynamic and hydration shell structures that are crucial for the function of a protein can also be evaluated with the help of a dielectric spectrometer. Using a dielectric spectrometer with frequencies ranging from MHz to THz, Charkhesht et al. (2018) evaluate the dielectric response of bovine serum albumin (BSA) protein in aqueous solution. Three relaxation time constants (~8 ps, 38 ps, and 360 ps) for the dielectric loss spectrum reveal three different types of water environments around BSA. One short relaxation time constant (~8 ps) arises from bulk water, and the other two long time constants (~38 ps and 360 ps) arise from “biological water” that is loosely bound and tightly bound, respectively. MD simulation of water molecules in BSA found a densely packed water layer with two relaxation time constants: ~380 ps for water molecules tightly bound within the hydration layer and 45 ps for weakly bound water molecules (Charkhesht et al., 2018). Experimental and simulation results in BSA protein clearly manifested that the presence of “biological water” is the primary contributor to the slow dielectric response.

6 SOLVATION OF DNA

Solvation of DNA, like that of proteins, is essential for molecular function, stability, and structural integrity. A DNA biopolymer with a high surface charge draws in a hydration cell composed of ions and water molecules. According to MD modeling, the hydration shell around the DNA surface and groove constantly exchanges and reorganizes water molecules; the timeframe ranges from a few picoseconds to nanoseconds, which is noticeably slower than bulk water. The most notable distinction between DNA solvation and other systems is the presence of a power law-dependent nanosecond or even microsecond solvation component, which can be caused by buffer solution ions and counterions. In a probe that is intercalated to DNA, this characteristic is quite prevalent (Andreatta et al., 2005). Mukherjee et al. (2018) used a variety of theoretical techniques, including simulation and analytical data, in 38 base pair DNA to deduce the origins of the power law-dependent, extremely long solvation time scale. It was observed that diverse experimental methods provided different time scales of solvent relaxation. Three distinct time scales of solvation are concluded after a summary of all the findings: (i) a component for bound water to DNA molecules that is > 100 ps; (ii) bulk water-like energy relaxation durations of about 250 fs and 1 ps; and (iii) a far slower component of the nanosecond time scale. When they applied the Oosawa model in combination with the continuous time random walk technique developed by Scher, Montroll, and Lax, power law-dependent slow solvation was obtained by the joint effect of counterions. Using MD modeling, Dickenson's-dodecamer B-DNA showed a time scale of ~1 ns for base pair opening and ~10-35 ns for positive charged counterion dissociation to the minor groove; this might be another source of long-term slow solvation (Pérez et al., 2007). Sardana et al. (2019) employed a DAPI probe that binds the minor groove to investigate the solvation dynamics in Dickerson-Drew DNA using both theoretical and experimental methods. According to time-resolved fluorescence stock shift (TRFSS) data, approximately 80% of solvation is achieved in 100 ps, and approximately 68% of solvation is finished in 10 ps. The remaining solvation, however, is power law dependent and takes a long time (~4 ns) to finish (Sardana et al., 2019). The solvation time-correlated function (TCF) is saturated at a time scale of about 3 ns, as demonstrated by MD simulation up to 200 ns trajectory using the AMBER-1473 puls*parmbsco0* force field and in the existence of water molecules, Na^+, and Cl^- ions. They have also found a widespread distribution of water molecule resident time from ~6 ps to ~3.5 ns around the DAPI probe. The first layer of hydration had around 14 water molecules with a resident time of more than 1 ns. However, compared to extended solvation components, the dynamics of ions were discovered to be substantially quicker (< 150 ps). The decomposition of TCF data shows that the contribution of Na^+ and Cl^- ions is negligible, but linked DNA-water motion close to the groove gives higher weight to total solvation, mainly to the longer time scale. They thus draw the conclusion that the power law-dependent slow solvation in the Dickerson-Drew DNA groove is determined by coupled DNA-water dynamics.

7 DEUTERIUM ISOTOPE EFFECT ON SOLVATION DYNAMICS

There is a continuing argument about whether the polar or charged residue of the system, the water molecule, or the coupled effect together plays a principal role in the slow solvation dynamics. The existence of highly structured bound water molecules surrounding the biomolecule was demonstrated by a variety of theoretical investigations (Laage et al., 2017; Bagchi et al., 2005). Some groups, however, disagree with this hypothesis and propose that the water molecule has a limited role in slow dynamics (Nilsson et al., 2005; Rodriguez et al., 2008). Rossky and Bagchi group, on the other hand, defy this advice and demonstrate that a hydrogen bonding network is crucial for slow solvation (Bagchi et al., 2005; Pizzitutti et al., 2007). Using femtosecond up-conversion spectroscopy and MD modeling, Li et al. (2007) showed that in apomyoglobin, the slow solvation was restored when both protein and water molecules were present; hence, the slow dynamics were the result of linked dynamics between the two molecules. Examining the deuterium isotope effect, in which a deuterium atom replaces a hydrogen atom, is one method to determine whether polar charged residues or water molecules are primarily in control of slow solvation. If water molecules act a minor role in slow solvation, there is no significant change in the time scale upon replacing hydrogen by a deuterium atom. Slow solvation and time constant may be increases of around 30% resulting from the stronger and heavier deuterium atom, which slows down hydrogen bond dynamics and solvent relaxation time, a clear manifestation of the role of the water molecule. Using femtosecond up-conversion spectroscopy at various excitation wavelengths, the function of the water molecule in slow solvation dynamics has been scrutinize in [pmim][BF4] – RTIL/TX-100/benzene microemulsion (Sasmal et al., 2010). The average solvation time increased in microemulsion systems all excitation wavelengths when D_2O was substituted for water. The two additional slow components (~ 250 ps and 2200 ps holding H_2O microemulsion and ~ 500 ps and 3800 ps holding D_2O microemulsion, at excitation wavelength 375 nm) show a persistent deuterium isotopic impact (Table 3), but the ultrafast component of solvation remains mostly unchanged when water is replaced with D_2O. While water molecules are more free in the microemulsion's core, they are bound in the palisade layer of TX-100 and form powerful hydrogen bonds with the charged groups of the

TX-100 molecule. C480 has been employed in a way that distributes it throughout the whole microemulsion. The palisade layer of TX-100 provides the water molecule's dynamics at the blue end excitation wavelength (λex = 375 nm), whereas the core area of the microemulsion is primarily responsible for the dynamics at the red end excitation wavelength (λex = 435 nm). It should be mentioned, too, that two sluggish components and a notable shift in average solvation duration were seen in both regions. This experiment suggested that water molecules take part in major function in the dynamics other than charge/polar residue in microemulsion. Similarly, solvation dynamics of C153 encapsulated into trimethyl β-cyclodextrin (TMB) and dimethyl β-cyclodextrin (DMB) reveal a substantial deuterium isotopic impact. TMB in D_2O and DMB in D_2O were found to have average solvation times that increase by approximately 1.5 and 1.7 times, respectively (Sasmal et al., 2009). Using the C153 probe with an excitation wavelength of 405, Das et al. (2011a) investigated the deuterium isotopic impact to comprehend the function of the water molecule in the lysozyme protein. There is no red edge emission shift when the excitation wavelength is changed because the probe molecule is attached to a particular hydrophobic pocket of the lysozyme protein. According to a report, the H_2O solvent's slow solvation time constant (~105 ps) is significantly faster than that of D_2O (410 ps) (Das et al., 2011a). The C153 probe is a well-known binder to human serum albumin (HSA) protein, whose structure slightly changed in D_2O solvent. The placement of the C153 probe is approximately 21 Å from the single tryptophan amino acid residue in both solvents, according to fluorescence resonance energy transfer (FRET) (Das et al., 2011b). It is therefore a useful system for researching the slow solvent's genesis. The solvent correlation function C(t) is biexponentially fitted in both systems (Das et al., 2011b). The components found in the D_2O solvent are 4 ps (0.41) and 950 ps (0.59), which is significantly different from the components found in the H_2O system, which are 7 ps (0.30) and 350 ps (0.70) (Das et al., 2011b). Thus, the Bhattacharyya group hypothesizes that water has a significant impact on solvation dynamics, particularly slow solvation, based on the aforementioned findings (Sasmal et al., 2010; Sasmal et al., 2009; Das et al., 2011a, b).

Table 3: Solvation parameter of different system at different excitation wavelength.

System	Excitation wavelength (λex)	Solvation time scale (ps) [τ_i (a_i)]	Average solvation time scale [τ_t (ps)]	Reference
Microemulsion with 5 wt % water	375	2 (0.10), 250 (0.13), 2200 (0.77)	1725	Sasmal et al. (2010)
	405	<0.3 (0.03), 2 (0.04), 250 (0.35), 2200 (0.58)	1360	
	435	< 0.3 (0.65), 2 (0.07), 250 (0.12), 500 (0.16)	120	
Microemulsion with 5 wt % Deuterium di-oxide	375	3 (0.08), 500 (0.17), 3800 (0.75)	2940	Sasmal et al. (2010)
	405	<0.3 (0.01), 3 (0.04), 500 (0.43), 3500 (0.52)	2040	
	435	<0.3 (0.51), 3 (0.12), 300 (0.21), 800 (0.16)	180	
Lysozyme in H_2O	405	<0.3 (0.22), 2 (0.29), 150 (0.49)	74	Das et al. (2011a)
Lysozyme in D_2O		<0.3 (0.34), 3 (0.33), 416 (0.33)	138	
HSA in H_2O	405	7 (0.3), 350 (0.7)	247	Das et al. (2011b)
HSA in D_2O		4 (0.41), 950 (0.59)	562	

8 CONCLUSION

Solvation dynamics take part in an essential function in understanding the activities of biological systems, predominantly inside the hydration layer of biomolecular assemblies such as micelles, reverse micelles, microemulsions, nucleic acids, and proteins. To understand the origin of such dynamics, one needs to shed light on solvent residence time, solvation time scale, and the perturbed structure of the hydration layer by the surrounding region. Ultrafast solvation time scale

(~100-200 fs) in pure bulk water arises owing to the highly mobile hydrogen bonding network. Although, in many biomolecular assemblies, solvation dynamics is much more complex, as the system is highly heterogeneous and varies from region to region. Near the surface of a biological assembly or inside an enclosed area, the time scale of dynamics slows down and elongates into a few picoseconds or indeed sometime in the nanosecond range. These slow dynamics originated owing to confined water motion, perturbation of hydrogen bonding by polar and charged residue, and coupling with slower chain motion. Many experimental and theoretical studies indicate that slower solvation arises due to charged and polar residue and coupled chain-water motion, chain dynamics and charge or polar residues. However, the deuterium isotopic effect somehow contradicts the above statement. Marked changes in the solvation time scale by replacing H_2O to D_2Oin different systems suggested that only the water molecule plays a prime role in slow solvation dynamics. Although the origin of slow solvation is still an ambiguous question, one cannot rule out the role of the perturbed hydration layer and coupled polymer chain–water motion in biological organized assembly.

The solvation layer generally spread up to 6-10 Å from the biomolecular surface, dynamically and structurally completely different than the bulk solvent. It provides a dynamic interface between the biomolecules and the neighboring solvent network. Slower translational and restricted movement was observed in this region compared to the bulk solvent. This solvation layer arbitrates fundamental biological action such as ligand binding and catalytic action by changing regional dielectric environment, folding, and thermodynamic environmental change. In addition, the solvation layer is influenced by the polarity, topography, and conformational change of biomolecules, structuring a heterogeneous solvation landscape. The retention time of the solvent molecule in the layer plays a crucial role, especially on the biomolecular surface prior to exchange with bulk solvent. For water, residence times are much longer, differing from 10 to 100 ps near the biomolecular surface. This elevated residence time is ascribed to strong interaction with the hydration layer (electrostatic or hydrogen bonding). Prolonged residence times suggested a more rigid or "bound" solvent molecule population that may affect the solvation time scale.

In summary, in all biological systems, solvation energies vary significantly from bulk solvent owing to the existence of a structured solvent layer. The time scale ranges from sub-picoseconds to picoseconds, even longer in a few systems, indicating stronger solvent-biomolecular interaction. Deciphering the time scales and genesis is essential to comprehending the fully functioning picture of these systems at the molecular level.

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The author declares that they have no competing financial interest.

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