Molecular dynamics study of a protein-water interface – the role of bound water

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ABSTRACT

We have calculated the reorientational time correlation function Cμ(t) of water dipoles in the aqueous protein (1ETN) solutions for various protein concentrations at two different temperatures (300 K and 350 K) using atomistic molecular dynamics simulation studies. The reorientational time correlation function follows an exponentially decaying function of the form $C_{\mu}(t)=Aexp(-t/\tau)$, where **A** represents the percentage of water dipoles reorienting with an average time constant τ. We find that, with increasing protein concentration, the parameter A or the number of freely reorienting dipoles decreases considerably for both temperatures studied and more so at the higher temperature. We infer that this decrease in the number of freely reorientating water molecules may be related to some of the water molecules bound to the protein back bone.

INTRODUCTION

The structure and dynamics of water in the vicinity of biological macromolecules or micellar aggregates in aqueous solutions are reported to be different from the bulk water and plays an important role in the structure, stability and function of these systems. The water molecules in the hydration shell around a protein play an important role in its biological activity, in addition to stabilizing the native state of protein. Therefore, considerable efforts are being made both theoretically and experimentally to understand the dynamics of water molecules at the surface of proteins in aqueous solutions.

We have carried out atomistic molecular dynamics simulations to investigate the reorientational dynamics of water molecules in an aqueous enterotoxin (1ETN) protein solution as a function of protein concentration at two different temperatures (300 K and 350 K).

1ETN is a small protein of 13 amino acid residue (AAR) and has three β turns and three disulphide bridges.

MD simulations on this protein-water system is already reported by S. Balasubramanian et al and they found that the water molecules near the β_2 segment exhibit a faster dynamics than those molecules near the first and third segments and they inferred that the faster dynamics near β_2 turn have biological significance as β_2 is playing a critical role in the receptor binding of the protein.

Instead of studying the water dynamics around the protein-water interface for the three beta turns (β1,β2,β3) individually as carried out by S.Balasubramanian *et al*, we have studied the water reorientational dynamics at the protein-water interface for the whole protein.

We find a considerable reduction in the number of freely reorienting water molecules on increasing the concentration of proteins in these aqueous solutions indicating an increase in the bound water in the protein-water interface.

SIMULATION DETAILS

Atomistic molecular dynamics simulation of 1ETN soaked in water was performed under constant volume and temperature conditions (NVT). The energy minimized co-ordinates were taken as initial configuration for MD simulation.

The protein contained 152 atoms. The three disulphide bonds were built into the model using rigid constants. This configuration was inserted into a well equilibrated large box of water molecules by removing those water molecules which were within $2A^{o}$ from any atom in the protein. The final system contained 1641 water molecules.

Molecular dynamics calculations were performed using the GROMACS program. Temperature control was achieved by modified Berendsen thermostat. The simulation was carried in a cubic box of edge length $10A^{o}$. The initial MD runs were carried out for time steps of 2fs and to duration of 10ps.

The GROMOS force field and potential parameters for protein were employed to treat the interactions, while the SPC interaction model which is consistent with GROMOS force field was used to describe the water molecule. Coulombic interactions were treated using the particle mesh Ewald method.

The molecular dynamics simulations were carried for two different temperatures (300K and 350K) and the rotational correlation of water molecules were calculated for these two temperatures.

In our case, we tag all the water molecules within 10A^{o}, (whereas S.Balasubramanian *et al* tagged water molecules within 5A^{o}) around the protein surface. We have also studied the dynamics for a maximum of three proteins in the system for two different temperatures.

The orientational correlation function for water molecules is defined as

$\mathbf{C_\mu(t) = \langle \mu_i(0).\mu_i(t) \rangle}$

Where $\mu_i(t)$ is the dipole vector of water molecule i, and the angular brackets denotes averaging over initial times.

We averaged the orientational correlation function over the water molecules 10^oA around the protein surface .

We fit the correlation function $C_\mu(t)$ to an exponentially decaying function:

$\mathbf{C_\mu(t) = Aexp(-t/\tau)}$

Results and discussion

Figure 1 and 2 show the reorierntational correlation function of water dipoles for pure water and at the protein-water interface for three different concentrations of protein at 300K and 350 K respectively. The dotted lines are the fits to the MD simulation (reorientational time correlation function) data to an exponential function $Aexp(-t/\tau)$. Where, the parameter A represents the number of water dipoles reorienting with an average time constant τ. Table 1 shows the fit parameters A and τ for pure water and for three different protein concentrations for both temperatures.

From the Table 1, it is seen that the parameter A decreases with increasing protein concentration to about 30% at 300 K and about 60 % at 350 K. The correlation time τ is about 1-2 ps which corresponds to the reorientation correlation time associated with the free reorientation of water dipoles in the system. The decrease in A indicates a decrease in the number of freely reorienting water molecules on the addition of proteins in the system. We infer that the decrease in free reorientation of water molecules may be related to an increase in the bound water in the system.

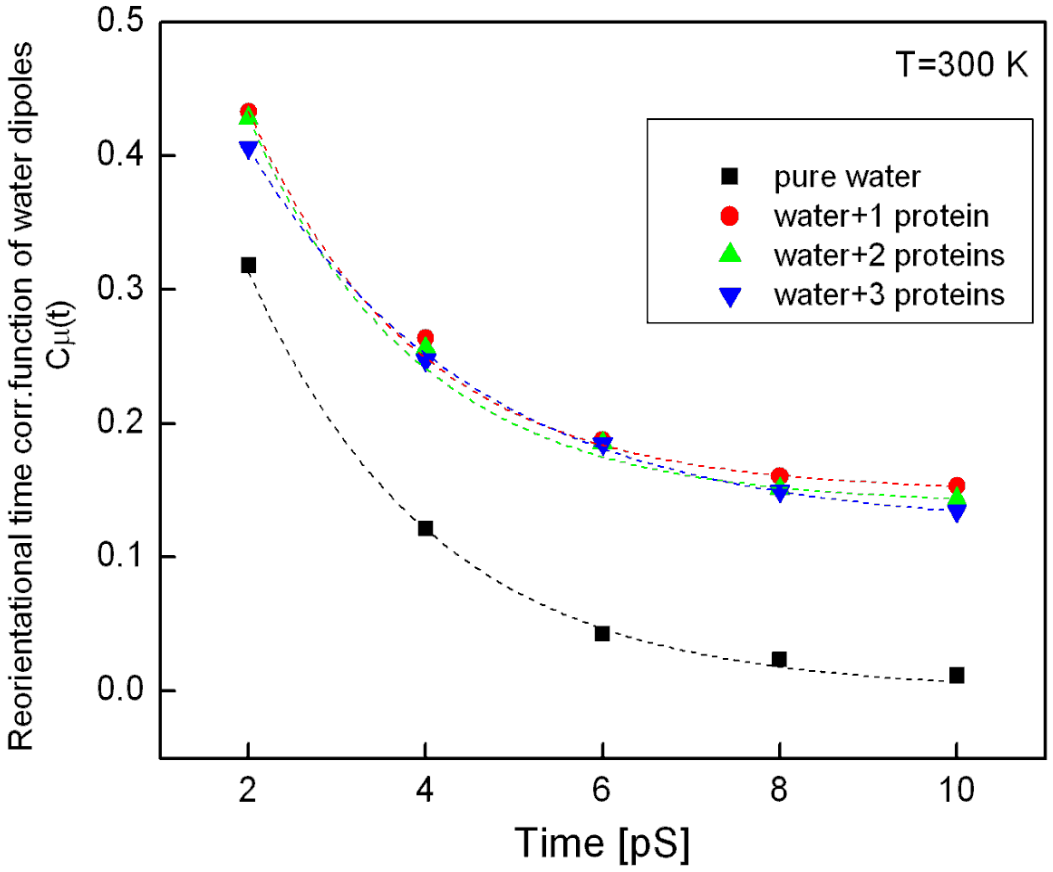

Figure 1. Reorientational time correlation function of the water dipole, $C_{\mu}(t)$ for water molecules for pure water and at the 1ETN protein –water interface for the whole protein for different concentrations at 300 K. The dotted lines are the fits to the exponential function $Aexp(-t/\tau)$.

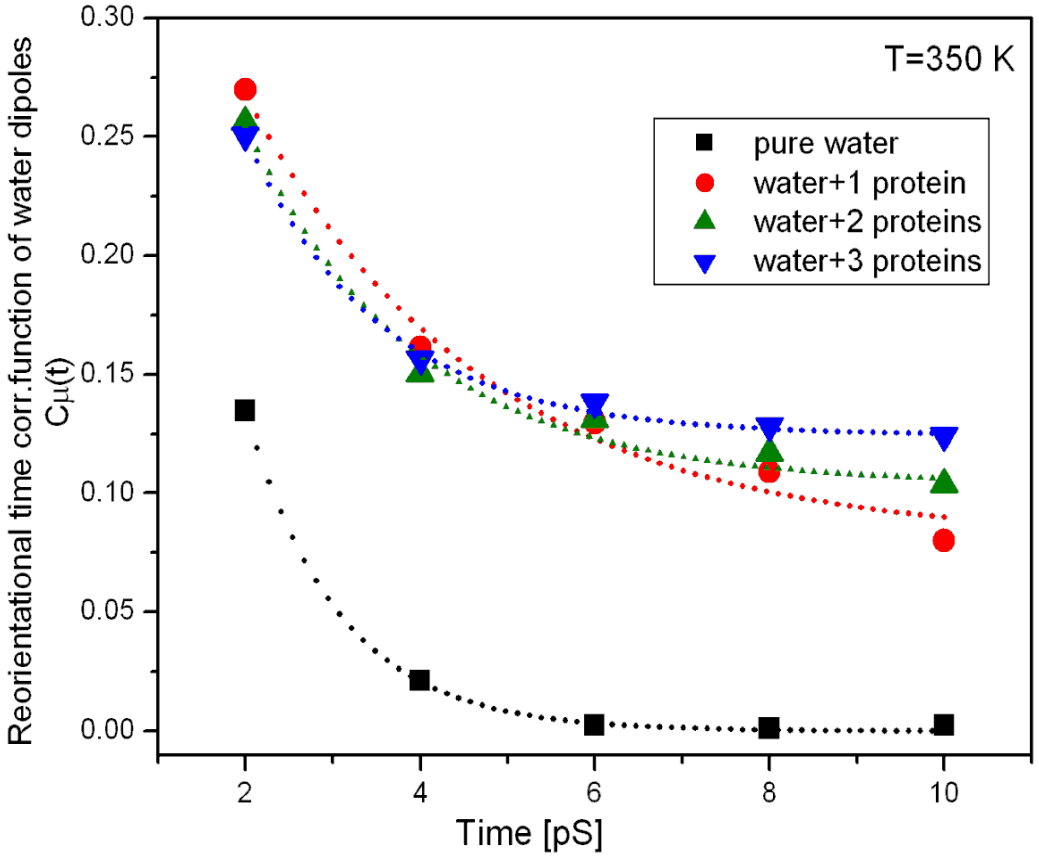

Figure 2. Reorientational time correlation function of the water dipole , $C_{\mu}(t)$ for water molecules for pure water and at the 1ETN protein –water interface for the whole protein for different concentrations at 350 K. The dotted lines are the fits to the exponential function $Aexp(-t/\tau)$.

Temperature	Sample	Fit Parameters	
		A	Reorientational correlation time τ (ps)
300K	Pure Water	0.9941	1.95
	Water + 1Protein	0.8089	1.91
	Water + 2Proteins	0.8180	1.91
	Water + 3Proteins	0.6221	2.55
350K	Pure Water	0.9976	0.93
	Water + 1Protein	0.4484	2.43
	Water + 2Proteins	0.3245	2.89
	Water + 3Proteins	0.3646	1.91

CONCLUSIONS

We have carried out molecular dynamics simulation studies on water dynamics near protein-water interface for two different temperatures 300 K and 350 K. we have fitted the time correlation function to an exponentially decaying function $Aexp(-t/\tau)$. We find the parameter A which is a measure of the number of water dipoles reorienting with an average time constant 1-2 PS decreases considerably. We infer that this decrease in the number of water molecules reorienting freely may be related to some of the water molecules bound to the protein backbone.

REFERENCES

1)S. Balasubramaniam, et al. *Dynamics of water at the interface of a small protein , enterotoxin".* Current Science, 1571-1678,85,2003.

2) D. Vijayaraghavan et al. *Magnetic susceptibility studies on a lyotropic liquid crystal system – the role of bound water.* Mol.Cryst.Liq.Cryst. 15-20, 478,2007.