

# Preface

Water is the most abundant molecule in cells. Water molecules near membranes affect several biological processes such as transport of drugs and small molecules across the cell, influences formation of membrane rafts, molecular recognition, signal transduction and so on. In the past decade, with a major advancement of computer simulations and experimental techniques, water near bio and soft interfaces are found to have distinct properties with slow relaxations compared to that of the bulk water and these water molecules are termed as biological water. However, dynamics of biological water from membrane experiments remain fragmentary due to the fluidity of membranes at physiological temperature and inaccessible atomistic trajectories. Moreover, the influence of water on global dynamics of membrane or protein are still debated. Thus, the current thesis proceeds to investigate hydration water dynamics near lipid membranes using all atom molecular dynamics simulations.

Capturing structure and dynamics of both lipids and water near membranes using simulations as in experiments is a challenging task till date. Thus, we aim to find most compatible water model and lipid force-field to understand the dynamics of hydration layers using all atom molecular dynamics simulations. Dimyristoylphosphatidylcholine (DMPC) lipid bilayers have been investigated at fluid phase where water residing continuously within  $\pm 3$  Å away from the interface are identified as interfacial water (IW). These IW are hydrogen bonded to different head-group moieties of lipid membranes and are referred to as chemically confined IW. Our investigations show that TIP4P/2005 water model in combination with Berger lipid force field is most suitable to study hydration dynamics near a fluid lipid membrane. IW hydrogen bonded solely among themselves and to carbonyl, phosphate and glycerol head groups of lipids are identified as IW-IW, IW-CO, IW-PO and IW-Glyc respectively. The mean square displacements and the re-orientational auto-correlation functions are slowest for the IW-CO since these are buried deep in the hydrophobic core among all interfacial water. The intermittent hydrogen bond auto-correlation functions of IW show eventual power law behavior of  $t^{-3/2}$  indicating translational diffusion dictated dynamics during hydrogen bond breaking and formation irrespective of the nature of chemical confinement. Employing reactive flux analysis, IW-Glyc is found to exhibit highest Gibbs energy of activation of hydrogen bond breakage due to its proximity to the hydrophobic core regime. Our calculations show that there are hydrogen bonded network between IW molecules which remain continuously intact among themselves and concertedly with lipid moieties. These network help in water mediated lipid-lipid associations.

To find out the physical sources of universal slow relaxations of hydration layers and length-scale of the spatially heterogeneous dynamics, well established formalisms of glass dynamics have been employed on the IW and the membrane. Two time-scales for the ballistic motions and hopping transitions are obtained from the self intermediate scattering functions of the IW molecules with an additional long relaxation time scale which disappears for bulk water. Employing block analysis approach, the length-scale of dynamical heterogeneities of IW is captured which is comparable to the wavelength of the weak undulations of the membrane. The analysis provides a measure towards spatio-temporal scale of dynamical heterogeneity of confined water near membranes. To gain access in membrane dynamics and its functionality towards various biological processes, investigations are carried out on coupling between hydration layer and bilayer dynamics. A gradient in retardation in translational mean square displacements is found to operate coherently for both IW and lipid components across the bilayer normal from the inner core towards the outermost region of a bilayer. The IW molecules exhibit Fickian but intermittent dynamics due to vibrations in the local cages followed by translational jumps with eventual diffusion. Regional dynamics of N lipid heads and IW

located near N heads of DMPC are found to have strongest correlations in fast and slow relaxations times obtained from self intermediate scattering functions.

In summary, the thesis provides insights on the choice of force fields to apprehend physical laws of water relaxations near membranes. Role of water in membrane associations enables to gain deeper insights on thermodynamic stability of soft interfaces. The current study opens up a possible correlation between heterogeneous length scale and membrane curvature for rippled membranes in future. Our results indicate that hydration water dynamics can act as a sensitive reflector of regional membrane dynamics. These will be useful to understand membrane functions such as molecular recognition, binding and domain formation and can contribute to control drug delivery and mimic cryo-preservation techniques for biomedical applications in future.