ABSTRACT

The primary objective of this thesis has been to investigate the microscopic details of the heterogeneously correlated structural and dynamical properties of a protein{DNA complex and its hydration water using atomistic molecular dynamics (MD) simulation method. In pursuit of this goal, calculations have been carried out with the protein{DNA complex formed between the _-helical N-terminal domain (NTD) of the _-repressor protein and its corresponding operator DNA in aqueous media. The thesis consists of six chapters.

Chapter 1 provides a concise overview of the recent status of research in this area and the methodologies employed in the thesis. In Chapter 2, we have examined the microscopic conformational and dynamical properties of the protein and the DNA molecules in their complexed state. It is found that increased structural ordering of the sugar rings of the DNA that are involved in binding with the protein domains are associated with modified ring puckering. Further, it is demonstrated that the non-uniform ordering of the lysine residues side chains in the consensus sequence leads to deferential behavior of the two homodimer protein monomers, P1 and P2. Efforts have been made to explore the locally heterogeneous exibilities of the protein and the DNA residues that are involved in direct binding and the microscopic structure and ordering of water around those in Chapter3. Importantly, the calculation revealed concurrent existence of highly ordered doublycoordinated and randomly ordered triply-coordinated water molecules at the interface of the complex. Such doubly-coordinated ordered water molecules are expected to play a crucial role in bringing the protein and the DNA components closer to form the complex. The inuence of the heterogeneous edibility of the complex on the microscopic dynamics of interfacial water molecules has been probed in Chapter 4. Increasingly restricted dynamics of water around the protein and the DNA components in the complexed state have been observed. The effect has been found to be more around the protein and the DNA residues which are in direct contact in the complexed state as compared to those that are not. Importantly, heterogeneously restricted water motions around the complex are found to be correlated with the relaxation time scale of hydrogen bonds. In Chapter 5, the efforects of complex formation on the low-frequency vibrational-density-of-states (VDOS) of water around the binding and non-binding residues of the protein and DNA molecules have been investigated. Enhanced back scattering due to increased caging effects of the interfacial water molecules has been observed. Due to increased confinement, such back scattering of water increases further in the complexed state, the effect being higher around the protein and the DNA residues that are in direct contact as compared to those that are not. The overall conclusion based on the results presented in the thesis have been highlighted in Chapter 6.

Keywords: Molecular dynamics simulation, Protein-DNA complex, Confined water, Hydrogen bond