Invited: CBIO-I-01

Correlated conformational features and hydration dynamics of protein-DNA complexes

Sanjoy Bandyopadhyay
Molecular Modeling Laboratory, Department of Chemistry, Indian Institute of Technology, Kharagpur 721302, India

Biomolecular recognition in a cellular environment is a necessary step for any biological process. As proteins are present in great variety in living systems, one of the components in such recognition is almost always a protein[1]. For example, single-stranded DNA binding (SSB) proteins bind with single-stranded DNA (ss-DNA) oligomers that are generated as intermediates during DNA metabolic processes. The primary function of an SSB protein is to protect the ss-DNA from being degraded so that other enzymes can effectively act on it. The important issues are how a protein recognizes the target, and the role played by water in mediating the interaction between them and thereby controlling the structure, stability, and dynamics of the complex formed.

Attempts have been made in our laboratory to address some of the issues as mentioned above by performing molecular dynamics (MD) simulations of two DNA binding K homology (KH) domains (KH3 and KH4) of the far upstream element (FUSE) binding protein (FBP) complexed with two ss-DNA oligomers in aqueous medium[2]. In particular, the effects of complexation on the internal motions of the protein domains and the correlated dynamics of the amino acid residue side chains have been explored in detail. In agreement with experiments, KH3 domain has been found to be relatively more flexible in the complexed state. The calculations revealed increased long-range anticorrelated motions among several amino acid residues in the complexed forms. Importantly, it is demonstrated that the effects of the DNA strands on the side chain orientations of the arginine and lysine residues and their ordering and dynamics play critical roles in forming such complexes and their structural stability[3]. Further, we have identified the presence of a highly constrained thin layer of water molecules bridging the DNA oligomers and the protein domains. It is found that the restricted motions of these water molecules originate from more frequent hydrogen bond reformations[4]. We believe that such water molecules play an important role in freezing the conformational oscillations of the ss-DNA oligomers and thereby forming rigid complex structures.

References:

1. D. L. Nelson and M. M. Cox, *Lehninger Principles of Biochemistry* (3rd Ed., Worth: New York, 2000).
2. D. T. Braddock, J. M. Louis, J. L. Baber, D. Levens and G. M. Clore, *Nature*, **415**, 1051 (2002).
3. K. Chakraborty and S. Bandyopadhyay, *J. Phys. Chem. B*, **119**, 10998 (2015).
4. K. Chakraborty and S. Bandyopadhyay, *J. Chem. Phys.*, **143**, 045106 (2015).