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in

Applied Theory On Molecular Systems 2011
(*ATOMS 2011*)

Report No: IIIT/TR/2011/-1



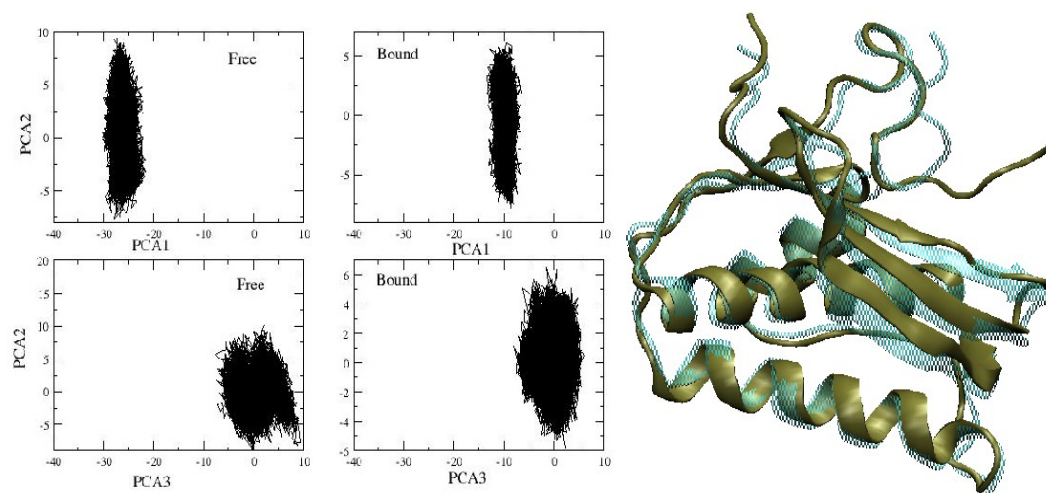
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November 2011

Molecular Dynamics Simulations Reveal Substrate Recognition Mechanism of Ribonuclease H

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Ribonucleases act as biological counter weights by playing a major role in gene expression. Ribonuclease H is one of them which performs the endonucleotic cleavage reaction of the 3'-O-P linkage of RNA strand of DNA/RNA hybrids. These enzymes show specificity towards DNA/RNA hybrids but not pure structures. One of the reason for this differentiation could be mixed A/B-conformation of hybrid compared to pure structures and there might be other reasons. There is a debate concerning the substrate recognition mechanism whether this is because of induced fit type mechanism or conformational rearrangement of monomers in order to come close or may be non bonded interactions which will put the enzyme and substrate together in order to perform the hydrolysis reaction. While the role of metal ions in the reaction has been recognised, the mechanism is not obvious. For differentiating the structural changes, we performed long molecular dynamics (MD) simulations on ribonuclease H enzyme of *B.halodurans* with its substrate and their monomers. The calculations show that the large conformational changes in both the monomers favours the reaction. Since the protein hydrophobic core is very stable, these changes will take place at surface level. The principal component analysis also supports the large conformational changes in protein and hybrid. Apart from these changes, the protein binding increases the plasticity of the hybrids. Overall the calculations show that structural deformations in both hybrid and enzyme brings them close to each other. Free energy calculations have been performed to study the protein-hybrid interactions.



Comparison of the first three principal components of protein in free (cyan) and bound(tan) by projecting each other.