Theoretical Study of Protein Flexibility During Molecular Docking

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Understanding the protein interaction has huge capability to improve drug development process. Flexibility of the protein plays important key role to generate active binding sites and orientation for favorable docking over a wide rage of energy. In the present study, we have studied the variation of flexibility of protein and its influeance during the molecular docking. The vibrational density of states of protein in the range from 2.3 to 10.3 nm is studied with the help of molecular-dynamics simulations. Our particular interest is in the behaviour of flexibility of protein during the moleculare docking, which is very important in microscopic behaviour of protein.

In the process of drug development molecular dynamics(MD) simulation has become a popular method in the investigation of protein dynamics and has successfully been integrated into virtual screening efforts to optimise lead discovery. In this study we have adopted the flexibility of protein as very important parameter which has key contribution in protein-ligand interaction.In our study , we choose the protein which responsible for Alzheimer deices (pdb code is 1fkn.pdb) [2]. This protein chain contain more then 1000 atoms so for reduces simulation efforts we consider only atoms (hydrophobic active sites) of the protein those are responsible for active molecular docking. Moreover, we can explore and analysis the process during molecular docking in new dimensions those are not possible by laboratory experiments. In the present study, we used NWchem [1] for MD simulation at 128 node based Unix cluster and in 6 hours for completing the single calculation.

[1] M. Valieva et. al. *Computer Physics Communications*, 181:1477-1489, 2010.

[2] Hong, L. et. al. *Science*, 290: 150-153, 2000.