

Internal Seminar

Understanding the molecular mechanism of allostery in proteins and conformational plasticity of natively disordered human CD4 peptide using molecular dynamics simulations and network models

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The talk consists of two parts. The first part would deal with the computational study of allosteric regulation in proteins. Allostery is a form of signaling in which perturbation by an effector to a site in protein affects the function or activity of a distant site. I will discuss three different studies carried out during my graduate research: nucleotide dependent allosteric regulation of AMP-activated protein kinase (AMPK), activation mechanism of corticotropin-releasing factor 1 (CRF1) G-protein coupled receptor, and understanding the extraordinary ligand-binding ability of human serum albumin (HSA). We have used a number of theoretical approaches to address these problems, including advanced molecular dynamics (MD) simulations, elastic network model (ENM), principal component analysis (PCA), and graph theory. Our results are in good agreement with experiments and provide detail explanation of allosteric communications in the studied systems.

The second part will focus on the structural characterization of natively disordered human CD4-peptide. Experimental characterization of IDPs is challenging due to their structural heterogeneity. MD simulation is a powerful tool in providing information on both structure and dynamics at atomic-resolution and becoming popular to study IDPs. The cytoplasmic tail of CD4 (residues 402-419) is known to be involved in direct interaction with the HIV-1 proteins Vpu and Nef. We carried out extensive replica exchange MD simulations in explicit water to characterize the equilibrium conformational ensemble of CD4-tail. Markov state model (MSM) and clustering analysis show that this peptide adapts multiple, rapidly interconverting distinct conformations with varying degree of residual secondary structures. Our results could help to understand the key molecular mechanisms of T-cell activation and HIV-mediated receptor interference.

Wednesday, Aug 31st 2016

2:00 PM (Tea/Coffee at 1:45 PM)

Seminar Hall, TCIS