Tata Institute of Fundamental Research
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Internal Webinar

Exploring Protein Dynamics: Conformational heterogenity and Collective Variables – Introducing NAP

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Proteins are bio-macromolecules, which are basically polymer chains of amino acids, and are one of the most essential nutrients required in the sustenance of a living organism. The various functionalities of proteins can be closely linked with their dynamical properties, which are intrinsically encoded in their amino acids sequence. Thus, decoding various protein functions demands a detailed knowledge about the ensemble of diverse conformational meta-stable states adopted by the protein. As non-static objects, proteins proliferate a huge pool of conformations attained as a consequence of numerous modes of perpetually incessant stochastic fluctuations occurring simultaneously at various locations in the protein 3D structure. Switching between these numerous states calls for transitions occurring over a variety of length scales (ranging from tens of angstrom to nanometers) and time scales (ranging from nanoseconds to seconds) which have been reported to be associated with relevant phenomena such as allosteric signaling and enzymatic catalysis. Tracking systems exhibiting these complex transformations requires development and programming of lower dimensional Collective Variables (CV) which can guide us in capturing and analyzing various crucial bottleneck transition events separating the different metastable states.

In our another work, on apolipoprotein E3, we conform a two-stage reorganisation process of apoE3 tertiary fold in presence of lipids, namely: i) a fast opening of C-terminal domain captured via atomistical simulations, followed by ii) a slow inter-helix separation within N-terminal domain using coarse-grained simulational approaches. Our model confirms that only in the maximal lipidassociated state does apoE3 become adept to act as a ligand for LDL receptor following which the lipid-transport metabolic circuit becomes effective.

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