TIFR Centre for Interdisciplinary Sciences
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Internal Seminar

Deciphering structures of multi-domain protein using computer simulation

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This presentation will cover my recent work which is based on understanding biophysically and biochemically the relevant multi-domain protein systems using all-atom Molecular Dynamics (MD) simulations.

Firstly, I will discuss about the structural differences between ApoE3 and ApoE4 that we could predict from MD simulation studies. The ApoE4 variant of Apolipoprotein E is known to be the strongest causative factor for late-onset Alzheimer's Disease (AD) whereas; the other variants ApoE2 and ApoE3 have been found to be respectively protective and neutral in terms of propensity to develop the disease. The relationship between the structure of these three ApoE isoforms and their contribution to the cause of AD is still not known completely. We have tried to explore structural differences between the two isoforms ApoE3 and ApoE4 by using all-atom MD simulations, Umbrella Sampling and Markov State Modeling techniques. We have also observed some strong structural differences between the two isoforms on the basis of their secondary structures, contact-map, salt-bridges involved and domain-domain interactions. We could also propose a probable mechanism for propagation of fluctuation/instability caused due to C112R mutation in ApoE4.

Secondly, I will be discussing the preliminary work related to silk protein that I have already started and will pursue during the next year. In silk labs around the world, concentrated aqueous LiBr solution is used to dissolve silk fibroin for further processing and we expect to gain a fundamental understanding of this process by which LiBr helps dissolution of silk fibroin. We have performed MD simulations with the reported N-terminal domain crystal structure in different concentration of LiBr solution. Since, the central part of the sequence has no reported crystal structure, we used modern structure prediction methodology to predict the secondary structure of these repetitive domains and then used these de novo predicted structures to computationally study the effect of small molecules and salts on their structures.

Wednesday, Feb 22nd 2017

4:00 PM (Tea/Coffee at 3:45 PM)

Seminar Hall, TCIS