Tata Institute of Fundamental Research
Survey No. 36/P, Gopanpally Village, Serilingampally, Ranga Reddy Dist., Hyderabad - 500107

Seminar

Modulating Protein Self-Assembly with External Influence: Molecular Insights from Computer Simulations

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Self-assembled amyloid conformations are more resistant to 'denaturation' that the folded states of globular proteins. This corresponds, in large part, to the nature of their conformational energy landscape. Folding is typically associated with a rough, yet 'funnel-shaped' energy landscape corresponding to an identifiable conformational minimum ('folded' state). In contrast, the landscape corresponding to amyloid formation is thought to feature several equivalent minima separated from a highly stable 'amyloid' conformation by large kinetic barriers. A recurring challenge in protein biophysics has been to identify perturbative ways to disrupt stable amyloids; consequences range from proteopathic amelioration to preservation of bio-specimens. Such goals, however, necessitate molecular-level details of the response of the amyloidogenic assemblies to perturbative conditions. I will begin first by highlighting some of our earlier efforts using non-biological surfaces for disrupting the early oligomerization of Amyloid beta (Aβ), followed by the effects of using a glucose as a co-solvent on the self-assembly. I will then discuss our recent efforts towards leveraging thermodynamic dynamic conditions to affect the stability of the self-assembled amyloid-like assembly of a segment of αB-Crystallin. Cold thermal conditions affect the hydrophobic core of this assembly in a way expected in a typical globular protein, but is not adequate for 'denaturing' the amyloid state. Our analyses indicate key roles of solvent water molecules in the thermodynamic and dynamical response of the amyloid to thermal perturbation.

Monday, Nov 25th 2019

4:00 PM (Tea/Coffee at 3:30 PM)

Auditorium, TIFR-H