Tata Institute of Fundamental Research
Survey No. 36/P, Gopanpally Village, Serilingampally, Ranga Reddy Dist., Hyderabad – 500 046

Internal Seminar

Characterisation of the structural plasticity and small-molecule mediated modulation of an intrinsically disordered protein

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α-synuclein (αS) is an intrinsically disordered protein (IDP) that has a vastly heterogeneous conformational ensemble and is known to be susceptible to environmental cues/crowders. The inherent structural plasticity renders αS highly prone to aggregate, a process that eventually leads to disease. Therefore, it is imperative to understand the nature of interactions that determines if a monomeric protein is susceptible to self-assemble into amyloids or resists aggregation. Furthermore, the lack of a defined binding pocket presents challenges in efforts of targeting IDPs like αS with small-molecules for clinical purposes.

In the first part of the talk, I will present the insights we gained from fully atomistic simulations of α-synuclein monomer in conjunction with Markov State Models to characterize the key metastable states from the fuzzy αS ensemble. We further study the impact of a crowded environment on the overall structural features of these metastable states. In the second part of the talk, I will describe our efforts to characterize the process of small molecule (fasudil) interacting with αS in terms of modulation of its structural ensemble.

Thursday, May 11th 2023

10:00 AM

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