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

Internal Webinar

Conformational characterisation of a-synuclein and its modulation by small-molecule using atomistic simulations

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140-residue intrinsically disordered protein, a-synuclein (aS) is known to be susceptible to environmental cues/crowders and adopts conformations that are vastly variable in the extent of secondary structure and tertiary interactions. The nature of these interactions determines if a particular conformation is susceptible to self-assemble into amyloids or resists aggregation. Computer simulations have tremendous potential in exploring the dynamics and broad conformational landscapes of IDPs.

In the first part of the talk, I will present the insights we gained from fully atomistic simulations of a-synuclein monomer in conjunction with Markov state models to characterise the key metastable states and kinetics of their interconversion. We further incorporate crowded conditions and elucidate the impact of crowding on monomeric conformations. In the second part of the talk, I will describe how small molecule (fasudil) interaction modulates the structural ensemble of a-synuclein monomer. We further test the observation on the initial dimerisation of a-synuclein in aqueous conditions and in the presence of fasudil.

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11:30AM