

Internal Webinar

Characterization of monomeric alpha synuclein in soluble and crowded conditions using computer simulations

Sneha Menon

TIFR, Hyderabad

Intrinsically disordered proteins (IDPs) can adopt a broad ensemble of conformations and aggregate to form amyloid fibrils with functional or pathological consequences. α -synuclein is one such IDP whose aggregation is implicated in Parkinson's disease. It is therefore critical to identify the key disorder-to-order transitions of monomeric α -synuclein that can initiate the formation of amyloids. Computer simulations have tremendous potential in exploring the dynamics and conformational landscapes of IDPs.

In this talk, I will mainly describe the insights we gained from fully atomistic simulations of α -synuclein monomer in conjunction with Markov state models to characterise the key conformational species and kinetics of their inter-conversion. We further used these meta-stable conformations in simulations emulating crowded conditions used in experiments. In these ensembles, we identify various fibril-like and non-fibrillar interactions that may be potential on- and off-pathway intermediates in the aggregation process.

Wednesday, June 23rd 2021

2:30 PM