S N BOSE NATIONAL CENTRE
FOR BASIC SCIENCES
Block JD, Sector III, Salt Lake, Kolkata 700 106

DEPARTMENTAL SEMINAR
Chemical and Biological Sciences

21st May,2024 **4.00 PM** **ONLINE / FERMION**

SPEAKER

Dr. Debayan Chakraborty
Reader F, The Institute of Mathematical Sciences, Chennai

TITLE OF THE TALK

Understanding amyloid aggregation from the perspective of the monomer conformational ensemble

ABSTRACT

A crucial step in the aggregation of amyloidogenic sequences is the transition from a relatively disordered state to an assembly-competent structure (referred to as the N* state). Using a well-calibrated model for intrinsically disordered proteins (IDPs), we show that these N* states bear considerable resemblance to the fibril polymorphs (U-bend and S-bend) characterized in experiments. The N* states appear as excitations on the monomer free energy landscape and are only sparsely populated.

By relating the populations of the N* states to fibril formation time-scales using an empirical relationship derived from lattice simulations, we can explain nearly quantitatively the relative aggregation propensities of Ab40 and Ab42, the two most common isoforms implicated in Alzheimer's disease. Despite having similar global topographies, the energy landscapes of Ab40 and Ab42 exhibit different extents of local roughness, which we show have profound implications in dictating self-assembly. Using kinetic transition networks, we further show that the N* states are obligatory along the favored assembly routes. The N* theory seems quite general, and also explains the length-dependent polymorphism in the fused in sarcoma (FUS) peptide sequence.

HOST FACULTY

Dr. Suman Chakrabarty
ASSOCIATE PROFESSOR, CHEMICAL and BIOLOGICAL SCIENCES
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