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

DEPARTMENTAL SEMINAR
Chemical and Biological Sciences

20th June, 2023 **4.00 PM** **ONLINE / FERMION**

SPEAKER

Dr. Prabir Khatua
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TITLE OF THE TALK

Exploring Nucleosome Dynamics and Protein Folding/Aggregation Mechanism through Molecular Simulations

ABSTRACT

The basic packaging unit of eukaryotic chromatin is the nucleosome that contains 145-147 base pair duplex DNA wrapped around an octameric histone protein. While DNA sequence plays a crucial role in controlling the positioning of the nucleosome, the molecular details of the interplay between DNA sequence and nucleosome dynamics remains poorly explored. During the first part of my talk, I will present the findings of 12-microsecond long atomistic simulations, which revealed occurrence of partial unwrapping of nucleosome, leading to the formation of loop and breathing motion. I will further discuss about base-pair level analysis of the nucleosome, enabling us to predict novel shift-roll deformation mechanism that offers insights into the sequence dependent nucleosome dynamics.

Proteins play many critical roles in the molecular machinery of cells. The classical model of protein folding states that a protein has a unique three-dimensional structure in its native state, which defines the function. Despite success of this model in describing structure-function relationship of many proteins, this mechanism fails in explaining folding of intrinsically disordered proteins (IDPs) or metamorphic proteins, where the amino acid sequence of a protein encodes not only a single native state but also an ensemble of structures, allowing a single protein to simultaneously perform multiple functions. The absence of specific native structure in IDPs can sometimes contribute to protein aggregation, potentially leading to the development of amyloidosis diseases.

However, neither folding of metamorphic protein nor the molecular mechanisms for the aggregation of IDPs are clearly understood. In the second part of my talk, I will present how an advanced simulation technique called Replica-Exchange-with-Tunneling (RET) allowed us to study folding switch of a metamorphic protein called Lymphotactin within reasonable computer time. This special simulation method enabled us to predict a unique role of bifurcated hydrogen bonds for the fold switching process. I will further discuss about our investigation into the molecular mechanism of protein aggregation, which contributes to amyloidosis diseases like Alzheimer's disease and secondary amyloidosis, using atomistic molecular dynamics simulations.

HOST FACULTY

Prof. Rajib K Mitra
PROFESSOR, CHEMICAL and BIOLOGICAL SCIENCES

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