TATA INSTITUTE OF FUNDAMENTAL RESEARCH

DEPARTMENT OF CHEMICAL SCIENCES

DCS SEMINAR

Speaker	Dr. Sanjoy Paul Department of Chemistry, Boston University, USA
Day, Date	Tuesday, April 11, 2023
Time	2.30 P.M.
Venue	AG-80
Title	Atomistic insights into the Sar1 mediated membrane remodeling activity

Abstract:

The Coat Protein Complex II (COPII) is an essential molecular machinery that delivers protein payloads from Endoplasmic Reticulum (ER) to Golgi Bodies in the protein secretory pathway of a cell. After being activated by GDP/GTP exchange, Sar1, a COPII component protein, starts the protein transport mechanism by budding vesicles on the ER subdomains. We employ atomistic MD simulation to compare Sar1's ability to insert into the membrane and create curvature in the GDP and GTP bound states. To yield efficient membrane insertion we consider the Highly Mobile Membrane Mimetic (HMMM) model which was converted into fully atomistic models later. We evaluate Sar1's ability to bend membranes in both nucleotide states and the GTP-bound dimeric state using simulations of large membrane ribbons and membrane bicelles. Our results(1) suggest a molecular mechanism for how Sar1 interacts with membranes in which GTP binding triggers stable Sar1 penetration into the membrane through its N-terminal anchor, significantly improving membrane bending ability. While the precise amino acid sequence and insertion depth of the amphipathic helix are relevant, the generated membrane curvature is most correlated with the volume of protein insertion into the membrane.

References:

1. Paul, Sanjoy, Anjon Audhya, and Qiang Cui. "Molecular mechanism of GTP binding-and dimerization-induced enhancement of Sar1-mediated membrane remodeling." Proceedings of the National Academy of Sciences 120.8 (2023): e2212513120.

S.K. Kadam