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

Seminar

Beyond the structural picture: key role of conformational changes for biological function and activity

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The ability to determine three-dimensional molecular structures of biomolecules was one of the major revolutions in biology during the second half of the twentieth century, providing atomistic insights into biomolecular function. Structural determination by X-ray crystallography, and later by NMR and cryo-EM, has therefore had profound scientific impact. More recently, artificial-intelligence–based approaches such as AlphaFold, trained on extensive structural databases, have provided an additional transformative advance by predicting native protein structures with remarkable accuracy.

Atomistic simulations make it possible to probe the dynamical evolution of these structures and their conformational fluctuations. However, despite substantial efforts to refine molecular interactions in these models, the exploration of conformational space often remains incomplete. Numerous cases exist in which experimentally determined static structures (or AlphaFold models), even when complemented with molecular dynamics simulations, fail to explain other experimental observations related to biomolecular activity or function.

In this presentation, I will discuss selected recent work from our group demonstrating that a detailed characterisation of biomolecular conformations, often hidden from experimentally resolved structures, is essential. Using a variety of enhanced-sampling techniques, recently augmented with deep-learning approaches, we uncover conformational states that allow us to explain the temperature dependence of enzymatic activity, the catch-bond behaviour of complex biomolecular interactions, and the function of a small ribozyme that serves as a model for the emergence of early auto-catalytic “living” systems.

Tuesday, Dec 16th 2025

16:00 Hrs (Tea / Coffee 15:45 Hrs)

Auditorium, TIFRH