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

Seminar

Fast Protein Dynamics and Small Molecules Triggering Transmembrane Signalling and Interfering with Aggregation Important in Neurodegeneration

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NMR spectroscopy is a powerful tool to study dynamics and kinetics of conformational ensembles. While pico-second to one digit Nano-seconds are well covered by relaxation measurements and several 10 micro-seconds to millisecond by relaxation dispersion, relying on the variation of isotropic chemical shifts, the region between one digit Nano-seconds and several 10 micro-seconds is difficult to access. High power relaxation dispersion can assess the amount and kinetics of motion in this region. This will be discussed in the context of protein motion and protein/protein recognition with approaches to get information about the region between ns and µs. The importance of optimal control pulses for high field NMR of proteins will be emphasised. The second topic will be on the signal transduction of two-component systems. They are the GPCRs of bacteria. The sensory part is a dimer which receives the signal on the periplasmic side, transmits it through the membrane to the cytosolic side which induces cross phosphorylation of histidine kinases which form one subunit of the sensory protein. The cross-phosphorylation happens only in the activated state. In the case of citrate sensor, two conformational states can be identified, with and without citrate. Transmembrane signalling due to citrate binding will be discussed and includes an amplification of an Angstrom scale to a nanometre scale. In the third project, we have studied the process of aggregation of α-synuclein on membranes in vitro and identified key time points in the aggregation process, that enable targeted isolation of a so called intermediate I and the fibrillar endpoint. Intermediate I has the functional characteristics of a toxic oligomer. In addition, we determined the structure of anle138b, a clinical drug candidate, bound to lipidic fibrils that are doped with anle138b. Comparison with binding of this molecule to lipidic Aβ fibrils will be discussed searching for commonalities.

Wednesday, Jul 24th 2024

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

Seminar Hall, TIFR-H