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

Seminar

Protein dynamics and kinetics with applications to neurodegeneration studied by NMR spectroscopy

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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 emphasized.

In the 2nd 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 1 and the fibrillar endpoint. Intermediate 1 has the functional characteristics of a toxic oligomer and the structure of the tetramer will be presented. In addition, we determined the structure of anle138b, a clinical drug candidate, bound to lipidic fibrils. The small molecule binds in a cavity of the lipidic fibril. The same is found for the PET candidate MODAG-005 when bound to the lipidic fibrils. Comparison with binding of this molecule to lipidic Aβ fibrils will be discussed searching for commonalities. Toxicity mechanisms by the comparison of the aSyn tetramer in the presence and absence of anle138b will be discussed that provide first insight into detoxification of oligomers.

Wednesday, Mar 5th 2025

11:30 Hrs (Tea / Coffee 11:15 Hrs)

Auditorium, TIFRH