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

Seminar

Novel and established approaches for structural characterisation of crystalline proteins and amyloid polymorphs using solid-state NMR

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Solid-state nuclear magnetic resonance NMR (ssNMR) can be employed to characterise crystalline proteins, membrane proteins, filamentous proteins and fibrils. Amyloid polymorphism is considered important in neurodegenerative diseases arising from different aggregates of the same protein. Polymorphs show different morphology, different biochemical and biophysical properties and different abilities to induce toxicity and propagate in the brain. We demonstrate that an *in-vitro* heterogenous population of α-synuclein intermediates forms different polymorphs under identical conditions with substantially different properties. Atomic-level differences between these polymorphs of α-synuclein were characterised using ssNMR. p53 is a tumour suppressor gene whose inactivation converts normal cells into cancerous. Aggregates of p53 have been reported from the patient's tissues. *In-vitro* preparation of p53 fibril is challenging, preventing its characterisation. I will discuss some approaches employed by us to obtain *in-vitro* homogeneous population of p53 DBD fibrils and initial NMR observation. The second part of the talk will discuss approaches for the structural characterisation of proteins at fast MAS. The NMR structural characterisation of aromatic residues has routinely been achieved through specific isotope labelling and mutagenesis. We propose novel NMR methods to structurally characterise aromatic side-chain atoms in proteins using one uniformly labelled sample. We also propose different approaches to generate a higher density of distance restraints that are central for protein structure determination by NMR.

Friday, Jul 7th 2023

4:00 PM (Tea / Coffee 3.45 PM)

Auditorium, TIFR-H