Tata Institute of Fundamental Research
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Internal Webinar

Segmental labelling of α-Synuclein: Purification and Characterization

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The aggregation of proteins into amyloid fibrils is implicated in several neurodegenerative diseases. Synucleinopathies is a group of neurodegenerative diseases originating from misfolding and aggregation of the α-Synuclein protein in the cytoplasm of neurons. The different diseases of Synucleinopathies show deposition of α-Synuclein but have different symptoms and pathology and accumulations in different parts of the brain. Alpha-Synuclein is a 140 residue intrinsically disordered protein, abundant in brain. The oligomers play a crucial role in defining the polymorphism associated with α-Synuclein aggregation. We are interested in structural characterization of different oligomers using solid-state NMR spectroscopy. However, oligomers are structurally heterogeneous due to their transient nature, thereby compromising the resolution in the spectra. In order to overcome the problem of resolution associated with studying oligomers, we adopted the approach of segmental isotopic labelling for this project.

For the segmental isotopic labelling, we have employed a hybrid synthesis approach, combining both recombinant protein production and chemical synthesis. Various C-terminal and N-terminal fragments of α-Synuclein were combinatorially labelled and ligated in vitro to create the full length protein. Thus, differentially labelled α-Synuclein will be used to prepare transient oligomers and will be subsequently studied by various biophysical techniques and NMR spectroscopy.

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11:30 AM