TIFR Centre for Interdisciplinary Sciences
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Seminar

Nanoscale Biophysics of Protein Amyloids

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Amyloids are ordered protein aggregates that are implicated in a variety of debilitating human disorders such as Alzheimer's, Parkinson's and prion diseases. The transition from a normal functional protein to an altered (misfolded) form involves a profound conformational change that triggers the aberrant protein assembly resulting in a wide variety of nanostructures including amyloid oligomers, pores and fibrils. My laboratory utilizes a diverse array of methodologies to unravel the key molecular events that are crucial in amyloid formation from a number of proteins. We are particularly interested in combining scanning probe microscopy and optical imaging in order to simultaneously monitor nanoscale topography and supramolecular packing of proteins within the amyloid architecture. Using Raman spectroscopy in combination with atomic force microscopy, we have been able to delineate the key structural transitions during amyloid formation. Additionally, we have adapted a super-resolution nanophotonic technology that allows us to optically image individual amyloids at the nanoscopic spatial resolution. Due to the optical diffraction-limit, conventional optical microscopy does not allow us to monitor the nanoscale organization at a high spatial resolution. Therefore, we have utilized near-field scanning fluorescence microscopy to optically map the amyloid fibrils far beyond the diffraction-limit. Interrogation of individual fibrils by simultaneously monitoring both nanoscale topography and fluorescence brightness revealed heterogeneous packing of the cross-β spine within amyloids. Our results provide structural underpinnings of diverse amyloid polymorphs that underlie the strain phenomenon in prion and amyloid biology. I will also discuss our recent results on the generation of a range of amyloid nanostructures from human prion protein that exhibits cytotoxicity in human cell lines.

Thursday, Oct 16th 2014

11:30 AM (Tea/Coffee at 11:15 AM)

Seminar Hall, TCIS