

TIFR Centre for Interdisciplinary Sciences

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Students' Annual Seminar

Towards understanding the disaggregation of amyloid fibrils

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Dissolution of the amyloid plaques has been the primary focus of the therapeutic approaches to Alzheimer's disease. However, molecular mechanisms of disaggregation of the amyloids are poorly understood. Here we use amyloid aggregates of tetramethylrhodamine labelled Aβ (TMR-Aβ) to examine the kinetic and thermodynamic properties of disaggregation of the AB amyloids. We use fluorescence recovery of TMR to monitor fibril disaggregation. Dilution of TMR-Aβ fibrils in urea and GdnCl led to disaggregation of the fibrils. Both kinetics and the extent of disaggregation are strongly dependent shown be on denaturant concentration. However, the fraction of disaggregated state was found to be independent of the total fibrils concentration contrary to what is expected in equilibrium systems. Furthermore, disaggregation behaviour of the aggregates is also found to be dependent on growth conditions such as pH, temperature and ageing. Taken together our results suggest that amyloid aggregates consist of a heterogeneous assembly of metastable states.

Thursday, May 25th 2017 4:30 PM (Tea/Coffee at 3:45 PM) Seminar Hall, TCIS