Title:	Studying Conformational Dynamics of Amyloidogenic Proteins using Fluorescence Spectroscopy
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Keywords:	Chemistry Spectroscopy Fluorescence Spectroscopy Proteins Protein Misfolding
Issue Date:	29-Jul-2015
Publisher:	IISER M
Abstract:	Protein misfolding leading to amyloid aggregation has attracted considerable interest due to its connection to a range of neurological disorders. It is important to characterize the conformational behaviour of the early oligomeric state of amyloidogenic proteins that serve as precursor to toxic amyloid in order to understand the molecular mechanism of amyloidogenesis. Fluorescence Spectroscopy has been an invaluable tool for the study of biomolecular systems. It is one of the most powerful methods to study protein folding, dynamics, assembly and interactions. In the structural and dynamical studies of proteins, fluorescence spectroscopy is well suited because of its high experimental sensitivity and selectivity to a protein's environment. The present work comprises the study of two amyloidogenic proteins, namely a-synuclein and B2-microglobulin (B2m), aggregation of which are involved in Parkinson's disease and dialysis-related amyloidosis, respectively. a–synuclein is an intrinsically disordered protein that is preferentially expressed in presynaptic nerve terminals. It undergoes a large-scale conformational rearrangement upon binding to synaptic vesicle membranes. In order to obtain the structural insights into the membrane-bound a-synuclein in the residue specific manner, we incorporated single cysteine (Cys) at various positions along the sequence. These Cys mutants were labelled with an extrinsic fluorophore, IAEDANS and were used as site-specific fluorescence marker to characterize the dynamical aspects of B2-synuclein. On the other hand, B2m has a classical B-sandwich fold comprising seven antiparallel B-strands and is a component of the major histocompatibility complex class I. Here we have focused on conformational states of B2m that would be involved in unfolding process as an intermediate state using a host of fluorescence spectroscopic tools. These tools allowed us to monitor the conformational changes of B2m during its unfolding process.

URI:	http://hdl.handle.net/123456789/523 (http://hdl.handle.net/123456789/523)
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