Title:	The dynamic personality of α- synuclein: Intrinsic disorder, conformational dynamics, internal friction , and amyloid formation
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Abstract:	Proteins perform a myriad of biological functions, and their functional attributes are governed by their both structural and dynamic properties. Apart from the well-structured folded proteins, there is an emerging class of proteins known as intrinsically disordered proteins (IDPs) that do not autonomously fold to a unique 3D structure and can be best described by a heterogeneous ensemble of rapidly interconverting conformers. IDPs are characterized by significant conformational plasticity whose misfolding and aggregation is implicated in several neurodegenerative diseases such as Alzheimer's, Parkinson's, Huntington's, and so forth. The conformational ensemble of IDPs uniquely populates the Ramachandran dihedral space resulting in a heterogeneous dynamic ensemble of conformers. Therefore, the intrinsic backbone segmental dynamics of IDPs arises due to the fundamental dihedral rotations in the Ramachandran Φ-Ψ conformational space that governs the course of their binding-induced folding, misfolding, aggregation, assembly, and so forth. In this work, the efforts were directed towards understanding the conformational dynamics of an IDP in its native monomeric and amyloid states by using an array of molecular biological, biophysical, and spectroscopic tools. We used α-synuclein (α-syn) as a model extended IDP, misfolding and aggregation of which is implicated in Parkinson's disease. In my talk, I will discuss the diverse application of ultrasensitive picosecond time-resolved fluorescence anisotropy measurements to capture the short-range backbone dihedral rotations and long-range correlated dynamics of α-syn under physiological conditions. Next, I will discuss the molecular underpinning of internal friction in IDPs by characterizing the backbone dihedral relaxation of the polypeptide chain by measuring fluorescence depolarization kinetics. Additionally, I will talk about the utility of excitation energy migration via homo-FRET to elucidate the unique structural attributes of the supramolecular assembly of amyloid fibrils of α-syn. Together, my thesis work sheds light on the intriguing dynamical personalities of IDPs involved in a mosaic of fundamental biophysical phenomena.
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