Title:	Studying backbone torsional dynamics of intrinsically disordered proteins using fluorescence depolarization kinetics
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Abstract:	Intrinsically disordered proteins (IDPs) do not autonomously adopt a stable unique 3D structure and exist as an ensemble of rapidly interconverting structures. They are characterized by significant conformational plasticity and are associated with several biological functions and dysfunctions. The rapid conformational fluctuation is governed by the backbone segmental dynamics arising due to the dihedral angle fluctuation on the Ramachandran ϕ–ψ conformational space. We discovered that the intrinsic backbone torsional mobility can be monitored by a sensitive fluorescence readout, namely fluorescence depolarization kinetics, of tryptophan in an archetypal IDP such as α-synuclein. This methodology allows us to map the site-specific torsional mobility in the dihedral space within picosecond-nanosecond time range at a low protein concentration under the native condition. The characteristic timescale of ~ 1.4 ns, independent of residue position, represents collective torsional dynamics of dihedral angles (ϕ and ψ) of several residues from tryptophan and is independent of overall global tumbling of the protein. We believe that fluorescence depolarization kinetics methodology will find broad application to study both short-range and long-range correlated motions, internal friction, binding-induced folding, disorder-to-order transition, misfolding and aggregation of IDPs.
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