Probing the structure and dynamics of unfolded and intrinsically disordered proteins with single-molecule spectroscopy

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Single-molecule spectroscopy provides new opportunities for investigating the structure and dynamics of intrinsically disordered proteins. The combination of single-molecule Förster resonance energy transfer (FRET) with nanosecond correlation spectroscopy, microfluidic mixing, and related methods can be used to probe intramolecular distance distributions and reconfiguration dynamics on a wide range of timescales, and even in heterogeneous environments, including live cells. In view of the large structural heterogeneity of disordered proteins, a description in terms of polymer physical principles is often a powerful way of conceptualizing their behavior.