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Structural transitions in the intrinsically disordered Parkinson's protein alpha-synuclein¹

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The protein alpha-synuclein is genetically and histopathologically associated with familial and sporadic Parkinson's disease. Although considered to belong to the category of intrinsically disordered proteins for well over a decade, recent reports have suggested that synuclein may actually exist predominantly in a native, well-structured, tetrameric form. Experiments using in-cell NMR, which bypass potential structural perturbations caused by purification protocols, conclusively demonstrate that recombinant synuclein is in fact highly disordered and monomeric. In the presence of membranes, however, the protein undergoes a coil-to-helix transition to adopt several highly helical conformations, which are proposed to mediate both its normal function and its membrane-induced aggregation into amyloid fibrils.

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