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**Early-Aggregation Studies of Polyglutamine in Solution** AARON FLUITT, JUAN DE PABLO, University of Wisconsin-Madison — Several neurodegenerative diseases, notably Huntington's disease, are associated with certain proteins containing extended polyglutamine tracts. In all polyglutamine diseases, the age of onset is inversely correlated with the length of the polyglutamine domain beyond some pathological threshold. Diseased cells are characterized by intranuclear inclusions rich in aggregated polyglutamine. Experimental evidence suggests that oligomeric aggregate species, not mature amyloid fibrils, are the species most toxic to the cell. Little is known about the structures and aggregation dynamics of polyglutamine oligomers due to their short lifetimes. A better understanding of the pathway through which polyglutamine peptides form oligomeric aggregates will aid the design of therapies to inhibit their toxic activity. In this work, we report structural characterization of polyglutamine monomers and dimers from atomistic molecular dynamics simulations in explicit water. Umbrella sampling simulations reveal that the stability of the dimer species with respect to the disassociated monomers is an increasing function of the chain length.

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