

Understanding the structure of polyglutamine (polyQ) amyloid-like fibril aggregates is crucial to gaining insights into the etiology of at least ten neurodegenerative disorders, including Huntington's disease. Here, we determine the structure of D2Q10K2 (Q10) fibrils using ultraviolet resonance Raman (UVRR) spectroscopy and molecular dynamics (MD). Using UVRR, we determine the fibril peptide backbone Ψ and glutamine (Gln) side chain χ_3 dihedral angles. We find that most of the fibril peptide bonds adopt antiparallel β -sheet conformations; however, a small population of peptide bonds exist in parallel β -sheet structures. Using MD, we simulate three different potential fibril structural models that consist of either β -strands or β -hairpins. Comparing the experimentally measured Ψ and χ_3 angle distributions to those obtained from the MD simulated models, we conclude that the basic structural motif of Q10 fibrils is an extended β -strand structure. Importantly, we determine from our MD simulations that Q10 fibril antiparallel β -sheets are thermodynamically more stable than parallel β -sheets. This accounts for why polyQ fibrils preferentially adopt antiparallel β -sheet conformations instead of in-register parallel β -sheets like most amyloidogenic peptides. In addition, we directly determine, for the first time, the structures of Gln side chains. Our structural data give new insights into the role that the Gln side chains play in the stabilization of polyQ fibrils. Finally, our work demonstrates the synergistic power and utility of combining UVRR measurements and MD modeling to determine the structure of amyloid-like fibrils.