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Amyloid Structure In Vitro and In Vivo¹

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Solid state nuclear magnetic resonance (NMR) measurements can provide unique information about the structural properties of proteins in noncrystalline states that are of interest from both the biophysical and the biomedical perspectives. I will discuss recent results from my lab's efforts to characterize the molecular structures of amyloid fibrils, especially the A β peptide fibrils that are associated with Alzheimer's disease. From a combination of solid state NMR and electron microscopy measurements, we have developed full structural models for 40-residue wild-type A β fibrils that form in vitro and contain parallel β -sheets with 2-fold and 3-fold overall rotational symmetry. We have recently discovered that the "Iowa mutant" (D23N-A β) peptide can also form metastable fibrils with a surprising antiparallel β -sheet structure. And we are in the process of investigating A β fibril structures that develop in human brain tissue. In addition to recent results, I will briefly describe recent advances in methodology that contribute to this work.

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