

MAR09-2008-000224

Abstract for an Invited Paper
for the MAR09 Meeting of
the American Physical Society

Structures of Amyloid Fibrils and Protein Folding Intermediates: New Insights from Solid State NMR
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I will present recent results from two projects: (1) We are using a combination of solid state NMR techniques and electron microscopy techniques to develop full molecular models for amyloid fibrils formed by the beta-amyloid peptide of Alzheimer's disease and by other peptides and proteins. Amyloid fibrils are often polymorphic, so that the detailed molecular structure depends on growth conditions or other factors. I will describe two structural models for beta-amyloid fibrils with two distinct morphologies. I will also describe efforts to determine which fibril structure develops in the brains of Alzheimer's disease patients, and solid state NMR methods that contribute to our amyloid studies; (2) Structural properties of unfolded or partially folded states of proteins are not well understood. In principle, solid state NMR measurements on freeze-trapped samples can reveal site-specific, quantitative aspects of protein structures in unfolded states. I will describe experiments on thermodynamically unfolded states (i.e., denatured states) and on transient states that are trapped by freezing on the microsecond time scale. Both types of experiments reveal structural properties that are unanticipated and could not be detected by more conventional protein folding measurements.