

MAR10-2009-000657

Abstract for an Invited Paper
for the MAR10 Meeting of
the American Physical Society

Mid-infrared pulse shaping permits the pathway of amyloid aggregation to be determined with rapid-scan 2D IR spectroscopy

MARTIN ZANNI, University of Wisconsin-Madison

We have developed a means for rapidly acquiring 2D IR spectra in a continuous fashion to monitoring protein kinetics. Our method relies on a mid-IR pulse shaper that generates precise pulse trains for collecting 2D IR spectra. The phase, amplitude and now the polarization of the pulse trains can be automatically generated without optical alignment, which produces higher accuracy spectra in a much easier fashion than with standard 4-wave mixing. Using this new technology as well as site-specific isotope labeling, we have measured the development of secondary structures for six residues during the aggregation process of the 37-residue polypeptide associated with type 2 diabetes, the human islet amyloid polypeptide (hIAPP), also called amylin. By monitoring the kinetics at six different labeled sites, we find that the peptides initially develop well ordered structures near the ordered loop of the fibrils, followed by formation of the two parallel β -sheets with the N-terminal β -sheet likely forming before the C-terminal sheet. This experimental approach provides residue-by-residue details on the aggregation pathway of hIAPP fibril formation as well as a general methodology for studying other amyloid forming proteins without the use of structure perturbing labels. Moreover, this approach is also applicable to membrane catalyzed amyloid formation, and experiments along these lines will be presented as well.