MAR13-2012-020112

Abstract for an Invited Paper
for the MAR13 Meeting of
the American Physical Society

Yeast prion architecture explains how proteins can be genes

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Prions (infectious proteins) transmit information without an accompanying DNA or RNA. Most yeast prions are self-propagating amyloids that inactivate a normally functional protein. A single protein can become any of several prion variants, with different manifestations due to different amyloid structures. We showed that the yeast prion amyloids of Ure2p, Sup35p and Rnq1p are folded in-register parallel beta sheets using solid state NMR dipolar recoupling experiments, mass-per-filament-length measurements, and filament diameter measurements. The extent of beta sheet structure, measured by chemical shifts in solid-state NMR and acquired protease-resistance on amyloid formation, combined with the measured filament diameters, imply that the beta sheets must be folded along the long axis of the filament. We speculate that prion variants of a single protein sequence differ in the location of these folds. Favorable interactions between identical side chains must hold these structures in-register. The same interactions must guide an unstructured monomer joining the end of a filament to assume the same conformation as molecules already in the filament, with the turns at the same locations. In this way, a protein can template its own conformation, in analogy to the ability of a DNA molecule to template its sequence by specific base-pairing.

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