Prions: how a pathogen can propagate without a nucleic acid

PrPSc prions are the infectious agents behind fatal neurodegenerative diseases such as Creutzfeldt-Jakob and "mad cow" diseases. Prions can propagate yet they lack any nucleic acids. How can they do it? PrPSc is an alternatively folded variant of a normal brain protein, PrPC. While the structure of PrPC is well studied, the structure of PrPSc resisted high-resolution determination due to its general insolubility. Cryo-electron microscopy, X-ray fiber diffraction, and other approaches have finally defined the architecture of PrPSc as a four-rung β-solenoid, which provides a molecular framework for the propagation mechanism. The surprising conclusion is that the same forces operating during nucleic acid propagation are at play, and opens the way for rational approaches to anti-prion drug discovery.