**PHYSICS UPDATE**

# Atomic and hierarchical structure of an amyloid fibril

## A suite of techniques has laid bare the mysterious and physiologically debilitating structures.

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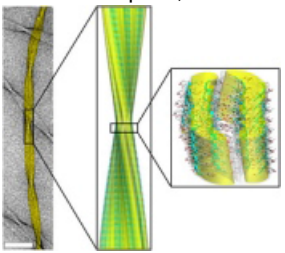

When proteins and peptides go awry, bad things can happen. For example, sometimes various of those biomolecules not only fail to fold correctly but also then self-assemble into amyloid fibrils—structurally robust micron-long threads just a few nanometers in diameter that are implicated in many human disorders, notably Alzheimer's and Parkinson's diseases. The misfolded proteins are known to gather into so-called $\beta$-strands, but the detailed hierarchical assembly of the strands into amyloid fibrils is elusive. So an international team led by Christopher Dobson of the University of Cambridge in the UK systematically approached the problem with a multitude of techniques, including solid-state nuclear magnetic resonance; scanning electron transmission, atomic force, and cryoelectron microscopies; and x-ray fiber diffraction. Collectively, the measurements produced structural information spanning five orders of magnitude in length scales that revealed crucial elements in the overall self-assembly. Different variants of a fibril were studied: The left panel—with a scale bar of 50 nm—shows a transmission electron micrograph of one variant. In the center is a cryo-EM reconstruction of electron density, and at right is the detailed atomic-resolution structure obtained from the various biophysical techniques. The structure shows how the proteins' individual amino acids are assembled into $\beta$-strands (green), which stack into $\beta$-sheets that run the length of the entire structure. Those $\beta$-sheets then group with increasing rigidity into protofilaments, filaments, and finally mature and tough fibrils. Besides the intricate structure, the team could also detail many of the packing interactions that drive the amyloid self-assembly process. (A. W. P. Fitzpatrick et al., *Proc. Natl. Acad. Sci. USA* **110**, 5468, 2013.)—Stephen G. Benka