SUPPLEMENTARY INFORMATION

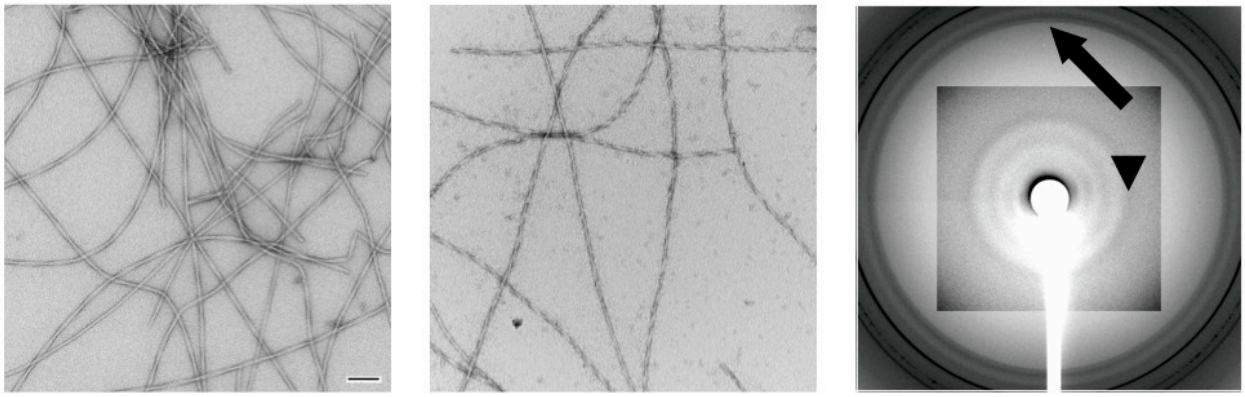

Fig. S1 Electron micrographs and diffraction from Aβ samples prepared by different protocols. (a) Fibrils made at pH 7.4. Electron microscopy procedures for this image were described by Paravastu *et al*.[1] Scale bar: 100 nm; also applies to (b). (b) Fibrils made without buffer at pH ~2. Electron microscopy procedures are described in Materials and Methods. (c) Diffraction pattern from the fibrils shown in (a). Different color tables are used for the inner and outer parts of the pattern, in order to show the diffraction in regions of very different backgrounds and intensities. As in Figs. 1a and 1b, the arrow indicates meridional intensity at 4.7 Å and the arrowhead equatorial intensity at ~10 Å.

The pH 2 fibrils in (b) are fibrils from the specific preparation whose diffraction pattern is shown in Fig. 1b. Electron micrographs were not available for the fibrils whose diffraction pattern is shown in Fig. 1a, but the pH 7.4 fibrils shown here in (a) were made following exactly the same protocol in the same laboratory as the fibrils whose diffraction pattern is shown in Fig. 1a, using fibrils from ssNMR measurements as seeds. As further confirmation that the fibrils shown in (a) are comparable to those whose diffraction pattern is shown in Fig. 1a, a diffraction pattern from the fibrils in (a) is shown in (c). This diffraction pattern is not as good as the one in Fig. 1a;

because of difficulties obtaining well-oriented fibers and obtaining time at beamlines set up for low-angle, low-background data collection, it was not possible to obtain a diffraction pattern from the sample shown in (a) at a beamline optimized for fiber diffraction. However, the pattern in (c), obtained at the BioCARS beamline, shows clearly that the diffracted intensity at 22 Å, 15 Å, and 10 Å is very similar to the intensity in Figs. 1a and 1b. The intensity at ~50 Å in Figs. 1a and 1b is not seen in (c) because the BioCARS beamline did not allow low-angle diffraction data collection, but fibers made from other samples using the same protocols consistently produced the strong 50 Å diffraction seen in Figs. 1a and 1b.

Although there are superficial differences in the appearances of the fibrils in (a) and (b), including a difference in the apparent twist of the fibrils, these are differences that can easily be caused by variations in negative stain electron microscopy technique. Most importantly, the diameters of the fibrils are very similar (80 to 100 Å), and the uniformity of diameter along the fibrils is similar. Two-subfilament fibrils would be expected to show significantly more variation in diameter than fibrils made from three or more subfilaments.

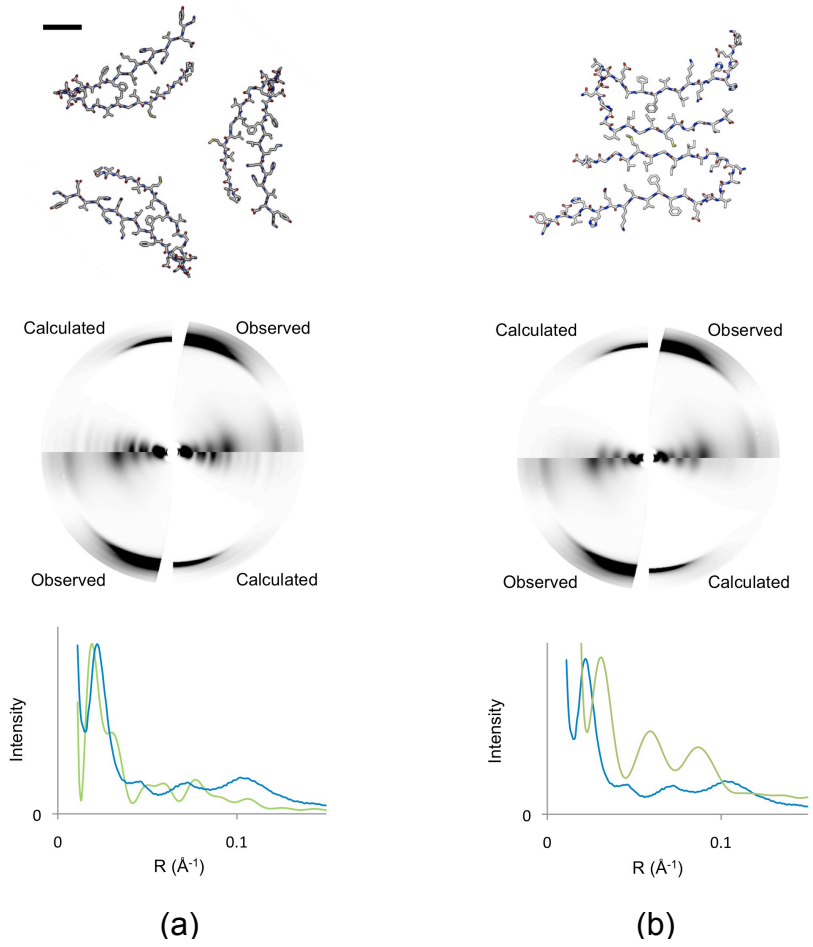

Fig. S2 Comparison of diffraction predicted from additional Aβ models with observed data. (a) ssNMR model[1] with cross-β units moved to higher radius, approximating a hollow cylinder. (b) Model based on the two-fold symmetric ssNMR model of Petkova *et al*.,[2] derived from fibrils formed under agitating conditions. Coordinates were from subunit 4 of chains D and J in PDB ID: **2LMO**. Within each part, the top image is the cross-section of the Aβ model (bar = 10 Å), the middle image compares predicted with observed fiber diffraction data, and the bottom image represents intensity on a line through the equator of the corresponding diffraction pattern. Observed (blue) and calculated (green) intensities are scaled to match the peak intensities at R = ~0.02 Å^{-1}.

Supplemental References

1. Paravastu, A. K., Leapman, R. D., Yau, W. M. & Tycko, R. (2008). Molecular structural basis for polymorphism in Alzheimer's β-amyloid fibrils. *Proc. Natl. Acad. Sci. U.S.A.* **105**, 18349-18354.

2. Petkova, A. T., Yau, W. M. & Tycko, R. (2006). Experimental constraints on quaternary structure in Alzheimer's β-amyloid fibrils. *Biochemistry* **45**, 498-512.