Title:	Nanoscale fluorescence imaging of single amyloid fibrils
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Abstract:	Amyloid formation is implicated in a variety of human diseases. It is important to perform high-resolution optical imaging of individual amyloid fibrils to delineate the structural basis of supramolecular protein assembly. However, amyloid fibrils do not lend themselves to the conventional microscopic resolution, which is hindered by the diffraction limit. Here we show super-resolution fluorescence imaging of fluorescently stained amyloid fibrils derived from disease-associated human β 2-microglobulin using near-field scanning fluorescence microscopy. Using this technique, we were able to resolve the fibrils that were spatially separated by ~75 nm. We have also been able to interrogate individual fibrils in a fibril-by-fibril manner by simultaneously monitoring both nanoscale topography and fluorescence brightness along the length of the fibrils. This method holds promise to detect conformational distributions and heterogeneity that are believed to correlate with the supramolecular packing of misfolded proteins within the fibrils in a diverse conformationally enciphered prion strains and amyloid polymorphs.
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