Title:	Nanoscopic Amyloid Pores Formed via Stepwise Protein Assembly
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Abstract:	Protein aggregation leading to various nanoscale assemblies is under scrutiny due to its implications in a broad range of human diseases. In the present study, we have used ovalbumin, a model non-inhibitory serpin, to elucidate the molecular events involved in amyloid assembly using a diverse array of spectroscopic and imaging tools such as fluorescence, laser Raman, circular dichroism spectroscopy, and atomic force microscopy (AFM). The AFM images revealed a progressive morphological transition from spherical oligomers to nanoscopic annular pores that further served as templates for higher-order supramolecular assembly into larger amyloid pores. Raman spectroscopic investigations illuminated in-depth molecular details into the secondary structural changes of the protein during amyloid assembly and pore formation. Additionally, Raman measurements indicated the presence of antiparallel β-sheets in the amyloid core. Overall, our studies revealed that the protein conformational switch in the context of the oligomers triggers the hierarchical assembly into nanoscopic amyloid pores. Our results will have broad implications in the structural characterization of amyloid pores derived from a variety of disease-related proteins.
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