

# Adventures in Microcrystallography of Biological Specimens

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With the goal of advancing methods of crystallography for applications to the energy and health sciences, we have been exploring the potential of structure elucidation with specimens that are at least 10,000 times smaller than conventional biological samples. In 2005, we were able to report the atomic structures of two microcrystals containing untwisted amyloid-like fibrils, giving the first glimpse of the atomic arrangement of proteins in the amyloid state. Both structures were short, fibril-forming segments of the yeast prion protein, Sup35, which itself forms amyloid-like fibrils. The microcrystals were of the order of 2  $\mu\text{m}$  in cross section. Diffraction data were collected on ESRF beamline ID13, equipped with a MAR CCD detector. Since then, we have determined structures for some 60 other amyloid-like microcrystals, with X-ray diffraction data collected at ESRF, SLS, and APS.

In recent work, we have found that informative X-ray diffraction patterns can be recorded from even smaller microcrystals and even from subcellular granules containing ordered protein. This work was also carried out at ESRF beamline ID13. The significance of this preliminary work is three fold. First it demonstrates that subcellular organelles can contain protein in highly ordered states. Second, it suggests that in vivo structure determination is feasible. Third, it suggests that X-ray structure determination of nanometer or micrometer-scale biological crystals may become routine, for cases in which only minute amounts of protein are available, or for which only micrometer scale ordered samples can be prepared. This development would accelerate research both in bioenergy sciences and health sciences.

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