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Crystallography without Crystals: An Overview[1]

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Protein X-ray crystallography, an "outgrowth of physics," is now the mainstay of biology, biochemistry, and the pharmaceutical industry. However, roughly 40% of biological molecules do not crystallize. And although more than half a million proteins have been sequenced, the structure of less than 40,000 has been determined. By obviating the need for purification and crystallization, the ability to determine the structure of individual biological molecules would constitute a fundamental breakthrough. The confluence of four developments has generated intense interest in achieving this by short-pulse X-ray scattering:

1. The advent of algorithms capable of "solving the phase problem" with practical demonstrations in astronomy, high-energy electron diffraction, and protein crystallography [1,2,3].

2. Development of sophisticated techniques for determining the relative orientation of electron microscope *images* of biological entities such as cells and large macromolecules [4].

3. Development of techniques for producing beams of hydrated proteins [3,5].

4. The promise of ultra-bright, short pulses of X-rays from X-ray Free Electron Lasers (XFELs) under construction in the US, Europe, and Japan.

I will describe how these and other key developments have brought the prospect of single-molecule structure determination "tantalizingly close," perhaps even closer than generally realized in the literature.

[1] J. R. Fienup, Appl. Opt. **21**, 2758 (1982).
[2] J. Miao et al. PNAS **98**, 6641 (2001).
[3] J.C.H. Spence et al. Acta Cryst. **A61**, 237 (2005)
[4] J. Frank, *Three-Dimensional Electron Microscopy of Macromolecular Assemblies* (OUP Press, 2006)
[5] J.B. Fenn, J. Biomolecular Techniques **13**, 101 (2002).

[1]With Dilano Saldin and Valentin Shneerson (see www.uwm.edu/ ourmazd)