Femtosecond crystallography of protein nanocrystals.

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We have been developing an injector to fire a single-file beam of hydrated proteins across the femtosecond pulsed X-ray beam of the Linac Coherence Light Source (LCLS), which begins operation at SLAC this year. One diffraction pattern will be read out after each pulse traverses a sub-micron particle and generates a diffraction pattern. The injector has been tested at the Advanced Light Source (LCLS) using Photosystem 1 (PS1) protein, where the "continuous" X-ray beam produced the powder protein patterns which will be shown from a stream of nanocrystals (1). Recent work at Flash, the FEL in Hamburg at DESY, has validated the "diffract-and-destroy" principle for diffractive imaging at low resolution (2). Our aim is to measure resolution limits due to radiation damage in single-shot femtosecond diffraction patterns as a function of pulse duration, in order to understand the damage processes in fast diffraction. For conventional XRD we find that dose is inversely proportional to the fourth power of resolution (3) A sufficiently short pulse is assumed to terminate before significant electron rearangement occurs, yet produce a useful diffraction pattern.

First experiments at LCLS will be based on PS1 nanocrystals consisting of about 20 molecules on a side, which we have learnt to make. This could form the basis of a new form of crystallography for proteins which readily produce a shower of nanocrystals, but fail to produce crystals large enough for conventional crystallography. The analysis of this data (with one nanocrystal per droplet per pattern), which is not angle-integrated, will involve the development of new methods of orientation determination and phasing.

For large molecular complexes and idential virus particles (one in each droplet) , particle orientation determination is needed before data can be merged to fill the three-dimensional reciprocal space for phasing. Four approaches have been described in the literature (4, 5, 6, 7), and we will briefly outline some of these. A method of removing multiple scattering effects from soft X-ray diffraction will also be described (8).

*And others in reference list. Supported by NSF.

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