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A route to synchrotron nanocrystallography via fluctuation scattering analysis

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Serial crystallography has opened up possibilities for the study of micron-sized macromolecular crystals at synchrotrons, but there are several instances where even smaller crystal sizes – genuine nanocrystals – are unavoidable[1]. Protein nanocrystals occur in the natural world (e.g. insecticides). They are advantageous for enabling fast timing in diffusion-limited time-resolved experiments. They also arise in studies of the crystallization process itself. Many of these experiments can only be considered at an X-ray free-electron laser. This is because protein nanocrystals can be too small for synchrotron-based crystallography and their unit cells can be too large for powder diffraction, due to peak overlap. There is scope to fill this gap with new analysis techniques that exploit the large datasets of serial crystallography and innovative new approaches to extracting 3D structural information.

Fluctuation x-ray scattering (FXS) [2,3,4] aims to measure the local angular structure in materials using a small x-ray beam to enhance angular scattering fluctuations. Large serial diffraction datasets are analysed statistically via correlation functions. We have developed a method of inverting FXS correlation functions to recover the structure of crystals. This approach is applicable to nanocrystals because it uses dose fractionation, like powder diffraction, while providing 3D structure factors like conventional crystallography. It is also works with multiple crystals in the beam. Hence, it has the potential to give the "best of both worlds" between crystallography and powder diffraction.

We also know how to map FXS correlations into a three- and four-atom distribution call the Pair-Angle Distribution Function (PADF) [5,6,7]. It is a natural generalisation of the widely used 1D PDF to higher dimensions. The PADF contains, for example, a bond angle distribution and greatly increases the amount of structural information beyond that of the PDF. It suitable for both ordered and disordered samples. We will give examples of PADF studies of liquid crystals and proteins.

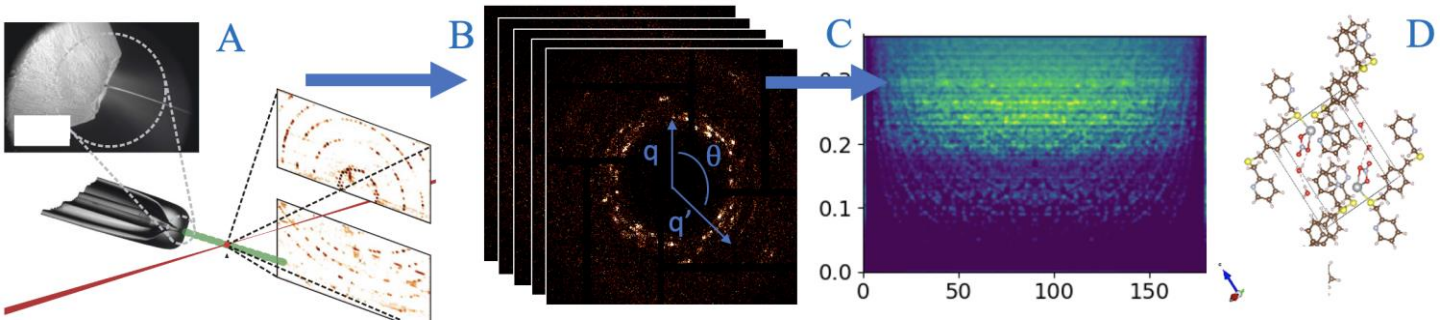

Figure 1. A) Serial crystallography experiment with a liquid injector. Detector pixels are correlated and binned using polar coordinates (B) and then averaged over a large dataset to produce the correlation function shown in (C). The intensity correlations can be used to extract structure factors and solve the structure (D) or converted in to the PADF (not shown).

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