Serial Electron Diffraction for Proteins and Small Molecules

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Serial crystallography, where diffraction snapshots of a large ensemble of randomly oriented crystals are taken, evades the cumulative damage inherent to rotation diffraction techniques. This approach has facilitated the use of sub-micron crystals in latest-generation X-ray sources, making large classes of small, radiation-sensitive systems such as recalcitrant protein nano-crystals or nano-porous materials amenable to crystallographic structure solution. We recently demonstrated a new scheme for dose-fractionated serial electron nano-crystallography in a scanning TEM, which combines the benefits of serial crystallography with the favorable scattering properties of electrons. It can be conducted in standard microscopes in a highly automated manner and without requiring specific sample delivery devices [1]. I will present our data collection and processing pipeline, show results from protein and small-molecule crystals, and discuss specific advantages and challenges of a serial crystallography approach as compared to conventional rotation techniques for different types of samples. [1] R. Bücker, P. Hogan-Lamarre, P. Mehrabi, E. C. Schulz, L. A. Bultema, Y. Gevorkov, W. Brehm, O. Yefanov, D. Oberthür, G. H. Kassier, and R. J. D. Miller, Nat. Commun. 11, 996 (2020).