

MS25 3D electron diffraction for structure solution of organics and proteins

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Serial Electron Diffraction: Strategies for Data Collection and Analysis

R. Bücker¹, **P. Hogan-Lamarre**², **P. Mehrabi**³, **E.C. Schulz**³, **G.H. Kassier**⁴, **R.J.D. Miller**²

¹Centre for Structural Systems Biology - Hamburg (Germany), ²University of Toronto - Toronto (Canada),

³University of Hamburg - Hamburg (Germany), ⁴DESY - Hamburg (Germany)

Abstract

Serial electron diffraction (SerialED) [1] is an emerging three-dimensional electron diffraction (3D ED/MicroED) [2] method performed in a scanning transmission electron microscope (STEM), where, in analogy to fixed-target serial X-ray crystallography at XFELs or synchrotrons, data from a large ensemble of nano-crystals is merged into a high-resolution structure solution. The characteristics of electron diffraction, such as high interaction cross sections at relatively low inelastic energy deposition, and high sensitivity to hydrogens and charge states, are combined with the ability of serial data collection to provide virtually damage-free structures, pushing the boundaries of 3D ED to the smallest and most sensitive of crystals, and opening up new avenues towards time-resolved measurements.

Like its X-ray counterpart, SerialED is typically performed in the limit of rapidly acquired single or dose-fractionated diffraction snapshots, minimizing deleterious effects of radiation damage. However, the flexibility of a STEM enables a much broader range of data collection strategies, blurring the lines between serial crystallography (SX), momentum-resolved STEM (4D-STEM), and massively automated rotation electron diffraction [3].

I will present results from a range of highly radiation-sensitive biological and organic small-molecule samples, discuss approaches for collection, data processing [4] and sample preparation, and give an outlook on ongoing projects towards time-resolved SerialED and new sample classes.

References

[1] R. Bücker, et al., Serial Protein Crystallography in an Electron Microscope, *Nature Communications* 11, 996 (2020). S. Smeets, et al., Serial electron crystallography for structure determination and phase analysis of nanocrystalline materials, *Journal of Applied Crystallography* 51, 1 (2018).

[2] M. Gemmi, et al., 3D Electron Diffraction: The Nanocrystallography Revolution, *ACS Central Science* 5, 1315 (2019).

[3] B. Wang, X. Zou, and S. Smeets, Automated Serial Rotation Electron Diffraction Combined with Cluster Analysis: An Efficient Multi-Crystal Workflow for Structure Determination, *IUCrJ* 6, 854 (2019).

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SerialED: (a) grid mapping; (b) data collection

