Towards automated serial electron diffraction for macromolecular crystallography

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Introduction

We are developing software and methodology to automate the collection of electron diffraction (ED) data for macromolecular crystallography

Structure determination of (sub)micron-sized crystals

- With electron diffraction, high-resolution data can be collected on crystals orders of magnitude smaller than those needed for X-ray diffraction experiments

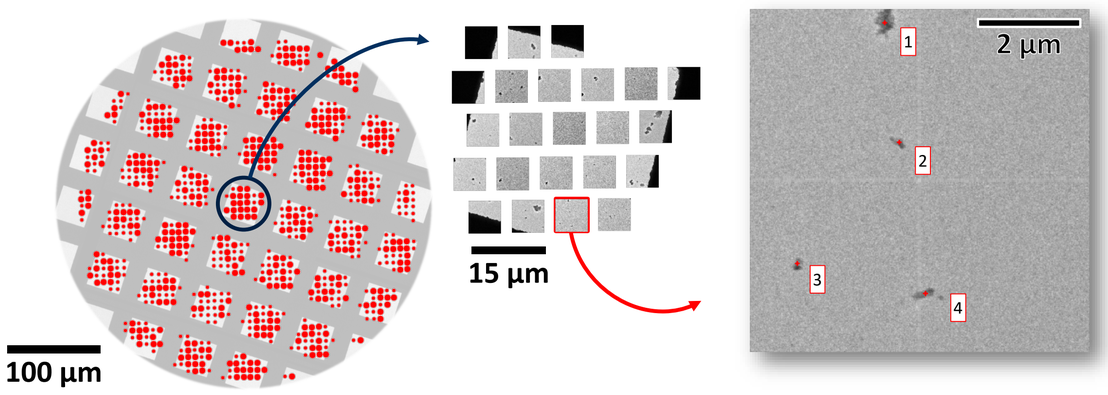
High-throughput serial electron diffraction

- We are developing serial electron diffraction to collect snapshot (~1000 crystals/hour) and rotation (~50 crystals/hour) data automatically

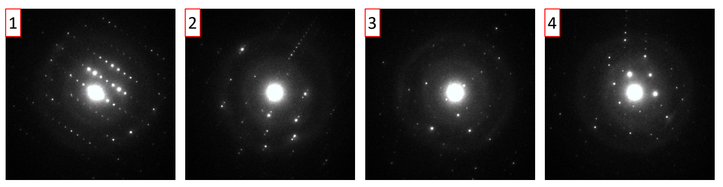
Low-dose data collection and crystal tracking

- Minimize radiation damage through automated experiments and using a trajectory prediction algorithm to correct for crystal drift

Serial snapshot electron diffraction



Stage map: 400 x 400 µm
836 images



Collect data on 1019 crystals in 80 minutes

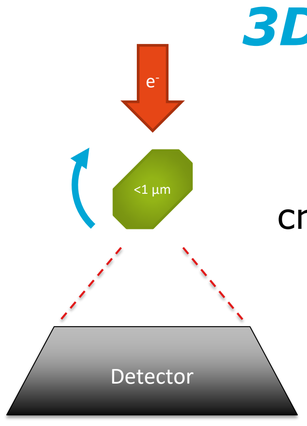
Applications

Screening
Identify crystals suitable for 3D ED data collection

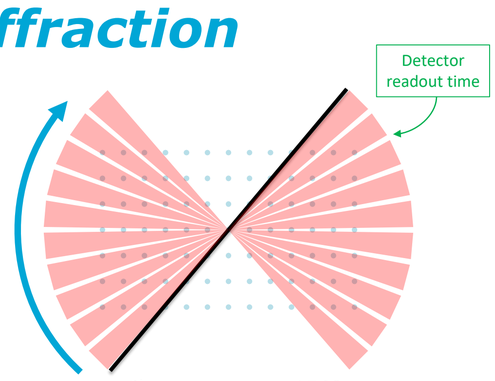
Crystal identification
Identify individual crystalline phases in a multiphasic materials

Structure analysis
Combine ~200 diffraction patterns for structure determination

3D electron diffraction

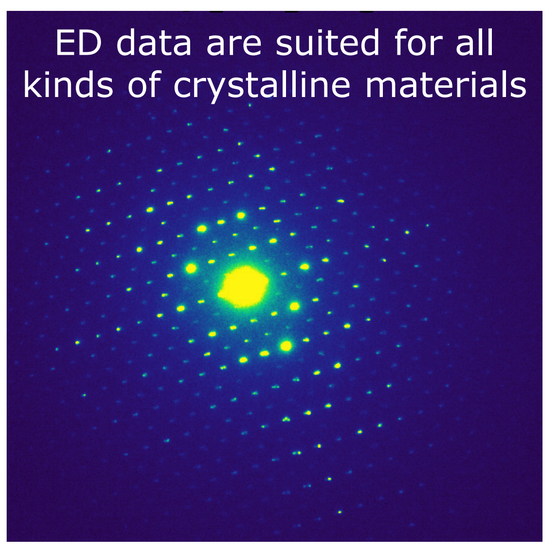


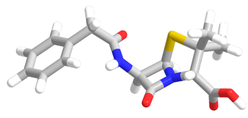
Continuously tilt crystal while reading out camera



Tilt range: up to 150°
Oscillation angle: 0.1-0.5°
Rotation speed: 0.5-3.0°/s
<5 minutes

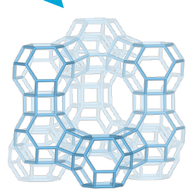
ED data are suited for all kinds of crystalline materials





Pharmaceuticals

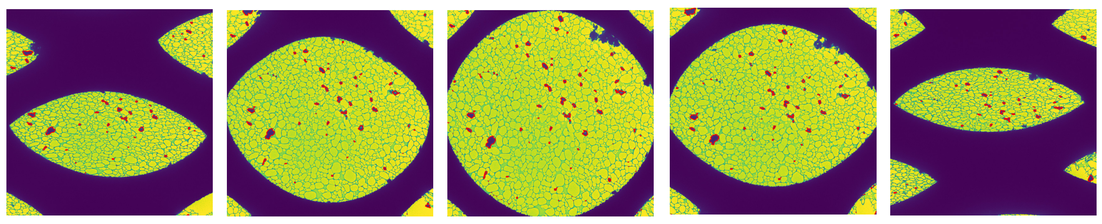
Proteins



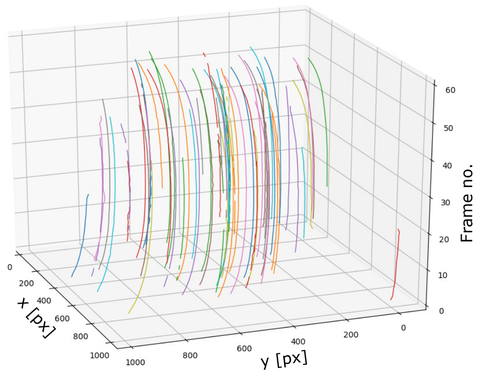
Inorganic materials

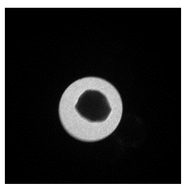
Low-dose crystal tracking

Trace crystal position at low magnification

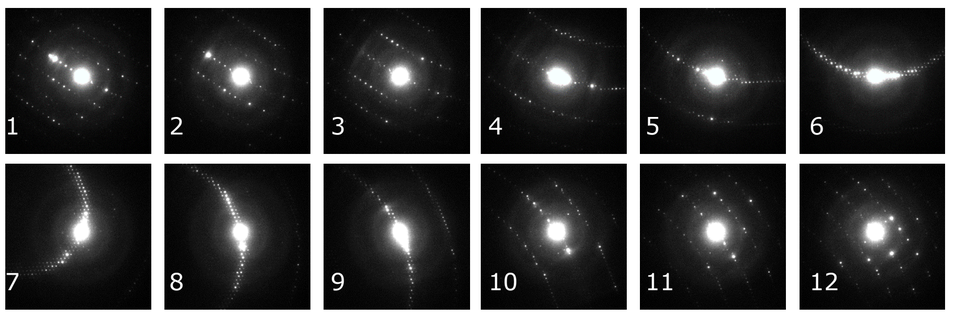


-60° -30° 0° 30° 60°





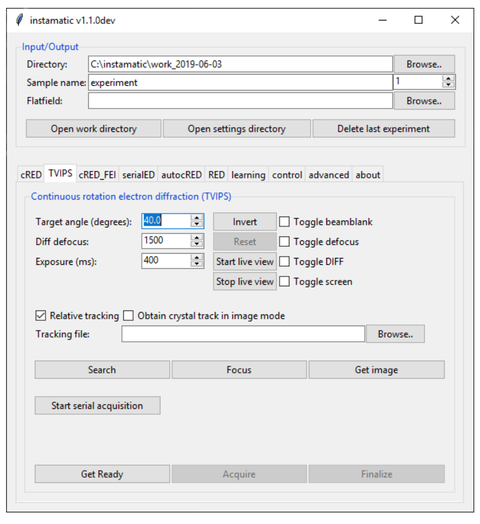
Obtain crystal trajectories to keep crystal in the beam or aperture during rotation



Serial rotation electron diffraction

- Select crystals to measure from map
- Collect ED data while continuously rotating the crystal in the electron beam (-70° to +70°)
- Adjust goniometer (x, y) during rotation

Software development



Software *Instamatic* for orchestrating electron diffraction data collection

Camera communication

TVIPS (X)F416

ASI Cheetah

Microscope control

JEOL 1400/2100/3200
Goniometer
Beam blank
Beam optics
Diff. mode
Lens settings
Beam position

Source code (Python 3.6+)
https://github.com/stefsmeets/instamatic

References

- S. Smeets, B. Wang, M.O. Cichocka, J. Ångström & W. Wan, Instamatic 1.0. Zenodo (2018), doi: 10.5281/zenodo.1090388
- S. Smeets, X. Zou & W. Wan. *J. Appl. Crystallogr*. 51 (2018), 1262–73
- B. Wang, X. Zou & S. Smeets, *IUCrJ* (2019), *In Press.*