

MS28-O3 Protein nano-crystallography using optimized quantum area direct electron detectors like the Medipix and Dectris families.

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In recent years new detectors became available for imaging in Electron Microscopy e.g. FEI Falcon and Gatan K2, the DE-series. These detectors gave a huge boost to imaging of tissues, cells and protein complexes. Recently these detectors, together with advances in image processing and computing power, made it possible to break the 2.5 Ångström resolution barrier in imaging of single bio-molecular complexes (Bartesaghi, Nature 2015: the 'resolution revolution' (Kühlbrandt, Nature 2014). These detectors have some drawbacks when it comes to diffraction studies: they are not very radiation hard and have a low dynamic range. These characteristics make it almost impossible to perform a good very low dose diffraction experiment, and one was still dependent on CCD cameras which are characterized by electronic noise, dark currents and noise coming from other sources than electrons (like the huge X-ray background that is present in any EM).

We have recently demonstrated that quantum area electron detectors like the Medipix have a similar impact when switching to diffraction mode [van Genderen, 2016]. We have solved the crystal structures of organic compounds from nano-crystals using electron diffraction with as low a dose as 0.013e-/Å²s. This enabled us to collect sufficient data for structure solution from a single nano-crystal even at room temperature.

I will discuss our recent progress on electron nano-crystallography, how these types of detectors will tear down the boundaries of electron diffraction of organic materials, why we think that diffraction will overcome the resolution problems that single particle faces and what role specialized diffraction cameras play in this process.

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MS28-O4 Serial snapshot crystallography using electron diffraction

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Can electron diffraction be used to perform serial snapshot crystallography? In an attempt to answer this question, we are developing a strategy to collect and process such data on materials that are sensitive to the electron beam, and thus difficult to measure using the conventional methods that rely on long exposure of the same crystal. To avoid beam damage, crystals are measured only once, but by combining snapshots from several sets of randomly oriented crystals, a complete data set can be assembled, and structures of materials that are difficult to analyse otherwise become accessible. This method relies on the ability to reliably retrieve crystal orientations from a snapshot, and this is challenging: (1) accurate orientations have to be retrieved from a single frame, (2) reliable peak positions should be extracted, (3) the unit cells are small, limiting the number of observations per frame, and (4) crystals may overlap, so it should be possible to determine the orientations of multiple crystals from a single frame. We previously developed a strategy to process serial snapshot data based on the broad-bandpass mode that will be offered at the SwissFEL[1] free-electron laser that can overcome several of these problems. The indexing algorithm that we developed can find the orientations of up to 15 crystals at once, and look for several unit cells simultaneously.

To see if such an approach can work with electron diffraction data, we modified our algorithm and applied it to data collected using the rotation method[2] on samples of the mineral garnet, zeolite silicalite-1[3], and isolated crystals of a powder containing 5 different polymorphs of a Ni-Se-O-Cl system[4]. The indexing routine was applied frame by frame, and can find the orientations of these crystals with over 90% success rate. For the multiphasic sample, our algorithm can reliably distinguish between the different polymorphs. This enables automatic screening of beam-sensitive materials for known and unknown phases. The data collection procedure can include precession to increase resolution, improve reflection integration, and reduce dynamical effects. Although our interest is in inorganic materials, the method may also be applied to other beam-sensitive compounds.

[1] Dejoie *et al.* (2015) *IUCrJ*, **2**, 361; [2] Wan *et al.* (2013) *J. Appl. Cryst.* **46**, 1863; [3] Su *et al.* (2014) *Micropor. Mesopor. Mat.* **189**, 115; [4] Yun *et al.* (2014) *J. Appl. Cryst.* **47**, 2048

Keywords: serial snapshot crystallography, electron diffraction, beam-sensitive materials