iNEXT workshop on Integrated methodologies and approaches for structural biology

Name of Speaker: **Tim Gruene**
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Title of Lecture: **Structure Determination with Electron Crystallography**

Abstract:

The use of electrons for crystallography was discovered only a few decades after the work of von Laue and the Braggs. Unlike X-ray crystallography, inorganic, organic, and biological electron crystallography were developed rather independently. Until about 2000, electron crystallography in all three sections was essentially two-dimensional: mostly thin layers were investigated. This changed with the work of the groups of Ute Kolb and of Xiaodong Zou/Sven Hovmoeller, who introduced the rotation method to electron crystallography. This and similar developments have their origin in the material sciences, blended with elements from the classical rotation method.

Single Crystal 3D Electron crystallography of organic and macromolecular compounds benefits greatly from the developments in X-ray crystallography of many, many decades. E.g. profile fitting and data scaling are concepts that are unusual in the crystallography of material science. For electron diffraction, these concepts reduce the impact of dynamic scattering. My work has focused on the methods development of electron crystallography with the perspective from macromolecular crystallography and structural chemistry. Modern X-ray integration software like XDS, SAINT, and DIALS bring new aspects into the field of electron crystallography. These program produce reliable structures from crystals that are minute compared to samples used in X-ray crystallography.
This talk will present the results of the nanoArgovia project "A3EDPI". We mounted a DECTRIS EIGER detector onto a transmission electron microscope and ensured fast and reliable determination of those parameters required for data processing with XDS. With this setup, we created a prototype electron diffractometer. We determined the new structure of a methylene blue derivative, and extracted the structure of paracetamol out of the powder of Grippostad, taken to the TEM directly from the pharmacy. I will extrapolate the experience from our experiment to provide my perspective of electron diffraction for macromolecular crystallography.

Research Profile:

T. Gruene studied physics at TH Karlsruhe and learned his basics of crystallography at Imperial College. During his PhD in molecular biology, he approached crystallography from a user's side and became a method developer with focus the needs of those using crystallography as a tool. He has

recently been fascinated by 3D electron crystallography, where structures are determined from submicron crystals, too small for the strongest X-ray sources. His publication in Angewandte Chemie [1], shortly followed by a similar work by several groups from the US (Jones *et al., ACS Central Science(2018*), created great attention and was selected as one of nine *Runners-up* of the year 2018 by *Science* (http://science.sciencemag.org/content/362/6421/1346).

Three selected publications:

1. T. Gruene *et al., "Rapid Structure Determination of Microcrystalline Molecular Compounds Using Electron Diffractio", Angw. Chemie Int. Ed. (2018), 57, 16313-16317*
2. T. Gruene *et al., "Characterization at the level of individual crystals: single crystal MFI type zeolite grains",* Chem. Eur. J. (2018), 27, 2384-2388
3. J. Heidler, R. Pantelic, J. T. C. Wennmacher, C. Zaubitzer, A. Fecteau-Lefebvre, K. N. Goldie, E. Müller, J. J. Holstein, E. van Genderen, S. De Carlo and T. Gruene, *"Design guidelines for an electron diffractometer for structural chemistry and structural biology"*, Acta Cryst D75 (2019)