Contribution ID: **255** Type: **Oral**

Structure ensemble determination from ultrashort pulse single molecule X-ray scattering: a Bayesian approach

Tuesday, 16 May 2023 10:45 (30 minutes)

Single molecule scattering experiments with femtosecond high-intensity free-electron laser (XFEL) pulses provide a new route to macromolecular structure determination. In these serial crystallography experiments, and despite the ultra-high brilliance of XFEL lasers, the signal to noise is expected to be in the extreme Poisson regime with only 10-100 recorded diffracting photons per image. Further, in each single scattering event, the orientation of the specimen molecule is random and unknown. As a further layer of complexity, many biomolecules show structural heterogeneity and conformational motions between different distinct structures; these structural dynamics are averaged out by existing refinement methods. To overcome these limitations, here we developed and tested a rigorous Bayesian approach and demonstrate that it should be possible to determine not only a single structure, but an entire structural ensemble to near-atomistic resolution from these experiments. We further show that as few as three photon per scattering image suffice for this purpose. Unexpectedly, much fewer images are required to determine an ensemble of n structures of m atoms each than a single structure of n × m atoms, i.e., of the same total number of degrees of freedom. These findings shows that X-ray scattering experiments using state-of-the-art free electron lasers should allow one to determine not only biomolecular structures, but whole structure ensembles and, ultimately, 'molecular movies'.

Select Topic 1

Modern Methods in Structural Biology and Dynamics

Select Topic 2

Primary author: GRUBMÜLLER, Helmut (Max Planck Institute for Multidisciplinary Sciences)

Co-authors: VON ARDENNE, Benjamin (Max Planck Institute for Biophysical Chemistry); SCHULTZE, Steffen (Max Planck Institute for Multidisciplinary Sciences)

Presenter: GRUBMÜLLER, Helmut (Max Planck Institute for Multidisciplinary Sciences)

Session Classification: Modern Methods