

Hybrid approach for structural modeling of biological systems from X-ray free electron laser diffraction patterns

O. Miyashita

RIKEN Advanced Institute for Computational Science, Kobe, Japan

XFEL single particle analysis is an emerging new approach that enables the measurement of individual molecular complexes without necessity of crystallization. Since crystallization is not necessary, it could be applied to a wider variety of systems under various physiological conditions, and exciting new results are being obtained.

However, for biological systems, due to their low diffraction power and complexity of sample delivery, experiments and data analysis are not straightforward. A common approach for XFEL single particle analysis is to obtain 2D real-images from diffraction patterns via phase recovery procedure. Strong diffraction patterns are required for successful and reliable image reconstruction. Reconstruction of 3D structural model is even harder since it requires a large number of diffraction patterns from the samples in the same conformation. It is difficult to obtain enough data to reconstruct a 3D model without additional information.

Therefore, we have been developing hybrid algorithms that combine molecular mechanics and image data processing algorithms. Instead of directly reconstructing the 3D model from diffraction patterns, we first construct hypothetical models using molecular mechanics simulations, computational modeling techniques and/or other experimental data such as X-ray crystallography. Then the models are matched against available XFEL diffraction patterns to identify the model that is most likely to be represented in the experimental data. This approach could be especially useful to study functional dynamics of biological systems. We will present our test calculations for large biological systems, such as ribosomes, and discuss attainable structural accuracy and the required beam intensity for this approach. *Work supported by FOCUS Establishing Supercomputing Center of Excellence.*

Reference:

[1] Tokuhisa, A., Jonic, S., Tama, F. & Miyashita, O. Hybrid approach for structural modeling of biological systems from X-ray free electron laser diffraction patterns. *J Struct Biol* 194, 325-336 (2016)