学位申請論文公開講演会

日時：2023 年 01 月 27 日(金)　10:30~

申請者：ASI HAN（B 研）

場所：物理会議室（C207）

題目：Development and integration of computational tools to decipher the structure & dynamics of biomolecules from low-resolution experimental data

（低解像度の実験データから生体分子の構造とダイナミクスを明らかにする計算手法の開発と統合）

主論文の要旨

Biomolecules, such as nucleic acids and proteins, are essential in all life processes as they perform many vital cellular functions. The structural and dynamic characterization of biomolecules is crucial in the endeavor to understand their functional mechanisms. Computational structural biology has advanced our understanding of the structure and dynamics of biomolecules by leveraging data from many low-resolution experimental methods. In this thesis, we explored a novel hybrid method and integrated multiple computational tools to decipher the structure and dynamics of biomolecules from low-resolution experimental data.

X-ray Free Electron Laser (XFEL) is the latest generation of X-ray source which could enable the observation of single molecules free of radiation damage. We proposed an algorithm for characterizing biomolecular conformational transitions by using a single 2D low-resolution XFEL diffraction pattern with another known conformation. We explored the strategy to obtain plausible 3D structural models by optimizing an initial structural model to maximize the similarity between the target XFEL diffraction pattern and simulated diffraction pattern from candidate models using Monte-Carlo sampling. We tested the proposed algorithm on two biomolecules represented by a set of Gaussian kernels using synthetic XFEL data. The results show that, with the proposed algorithm, conformational transitions could be described from 2D XFEL data. In addition, we showed that the incident beam orientation has some effect on the accuracy of the 3D structure modeling and discussed the reasons for the inaccuracies for certain orientations.

Structural information on the green alga *Chlamydomonas reinhardtii* (CraCRY) protein is key to elucidate its functional mechanism. However, the C-terminal extension of CraCRY remains unknown and is difficult to study due to its intrinsic disorder. Currently, the experimental data available on full-length CraCRY is from Small Angle X-ray Scattering (SAXS) experiments, which provide low-resolution information under near-native conditions in solution. We combined protein structure prediction via AlphaFold2 and MD simulations to propose a complete 3D model of CraCRY in agreement with experimental SAXS data.

Through the development of a novel hybrid method and the integration of multiple computational tools, we have demonstrated that structural and dynamic information on biomolecules can be obtained from low-resolution experimental data. Such integration of computational methods with experimental information is expected to play an increasingly crucial role in structural biology.