B 研究室

計算生物物理研究室

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Overview of Computational Biophysics Lab

Biophysics is a field of study that aims to understand biological phenomena using the principles and tools of physics. Every living organisms must be following the laws of physics, however, due to their complexity, our understanding on biological systems is still limited.

B laboratory focuses on the studies of biological molecules such as proteins and nucleotides. Biological complexes, structured ensembles of proteins and nucleic acids, perform many vital cellular functions and dysfunctions of those result in severe diseases. In order to understand diseases and develop treatments, the functional mechanisms of these biological complexes need to be elucidated. A crucial step in this process is the characterization of the structures and dynamics of these complexes. We use computational techniques, often in collaboration with experimental groups, to study important biological systems.

Current research focuses are described in the following.

Hybrid Approaches - Computational Modeling and Experimental Data

One of our goals is to develop computational algorithms to obtain atomic level structural models of biological complexes by utilizing multiple experimental data. Currently, atomic level structures of biological molecules are mostly determined by X-ray crystallography. However, some important biological systems are difficult to study by crystallography. Other techniques such as cryo-Electron Microscopy (cryo-EM), Small Angle X-ray Scattering (SAXS) and X-ray Free Electron Lasers (XFEL) could be useful to provide additional information, however these provide only low-resolution structural information, such as overall shapes of the complexes.

We use computational modeling techniques, which utilize simple concepts of mechanics in physics, to simulate the dynamics of biological molecules and combine various experimental data into the modeling process (hybrid approach). Multi-scale modeling, which describes the system at different level of details, from atomic description to continuum representation, needs to be used to study a variety of biological systems. Accurate description of molecular mechanics and computational algorithms for efficient sampling are the key components of these researches. We develop these tools to study important biological molecules in collaboration with experimental groups. Previously we studied important macromolecular machines, such as ribosomes and myosin, and revealed the mechanisms of their conformational transitions.

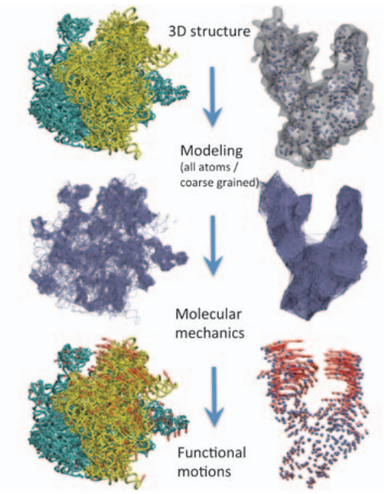

Fig 1：Dynamics of biological molecules: molecular mechanics using full atom description or coarse-grained representation

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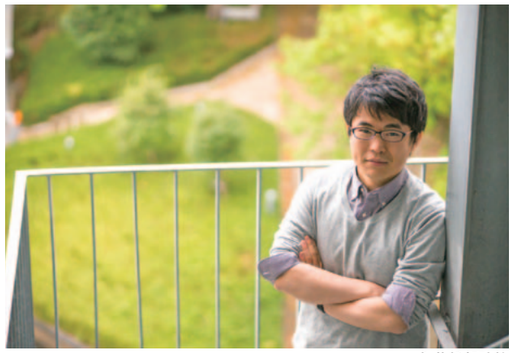

永井哲郎助教

Molecular Dynamics Simulation to study Biological Functions

Dynamics of biological molecules are essential for their functions. Biological molecules interact with other molecules (small chemical or biological molecules) and undergo conformational transitions through out their functional processes. Thus characterization of these motions are important to understand the mechanisms, however biological molecules are small in scale and direct observation of their motions is still difficult in the current experimental techniques.

Molecular dynamics simulation is a powerful technique to obtain additional insights by providing atomistic level details of molecular motions. Molecular dynamics simulation is a computational technique to simulate the dynamics of biological molecules. In this approach, the potential energy functions that represent physicochemical properties of proteins and nucleotides are defined and equation of motion is numerically solved using high performance computers. Being computer simulations, the whole descriptions of atomic motions can be examined.

We perform molecular dynamics simulations of biological molecules to examine a variety of functions. We can study their interactions with other molecules, for example, other proteins or drug molecules. We also study conformational transitions following such interactions. Observations from simulations are examined carefully to discover new insights that have not been accessible from experimental studies. Recent studies include small heat shock proteins and organic cation transporter proteins.

Life in the lab

The research in the lab is interdisciplinary. We use physics, chemistry, and computational science to study biological systems. In addition, we work on hybrid approaches, where computational modeling techniques are combined with experimental data.

Therefore a variety of students with different scientific interests could join our research lab. For example, students interested in physics and chemistry should enjoy the computational modeling and molecular mechanics simulations. Students interested in programming and mathematics can contribute in the development of algorithms for computational modeling. Students more interested in biochemistry can study specific biological systems using established program packages. All students will initially explore, briefly, all of these aspects, and afterward select a thesis theme based on his/her interest and skills through discussion with advisors. Students can continue onto graduate courses, potentially followed by post-doc and academic positions, or industry, such as pharmaceutical or computational company.

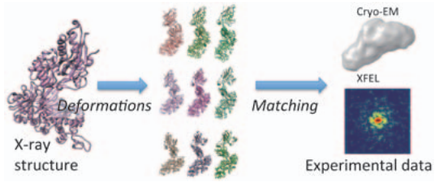

Fig 2：Hybrid approaches: combining computational modeling and experimental data

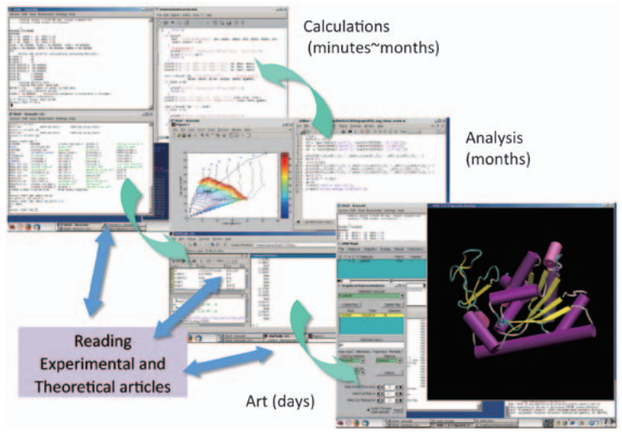

Fig 3：Work in the lab