【Grant-in-Aid for Scientific Research on Innovative Areas (Research in a proposed research area)】

Interdisciplinary Area

Title of Project：Non-equilibrium-state molecular movies and their applications

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Research Project Number：19H05776　Researcher Number：60452330

【Purpose of the Research Project】

In order to understand the functions of biological macromolecules essential for life, it is most effective to capture their chemical reactions and structural changes in real time. X-ray free electron laser (XFEL) is a unique tool to observe these reactions and changes with outstanding time and spatial resolutions. Promote and develop this method as a versatile technology applicable to a wide range of biological macromolecules, we will integrate various methodologies including organic chemistry, computational science and biophysics to understand basic questions such as switching and signalling mechanisms of proteins and reaction mechanisms of enzymes. Based on these results, we will also develop controlling methods of biological macromolecules using light and other stimulations.

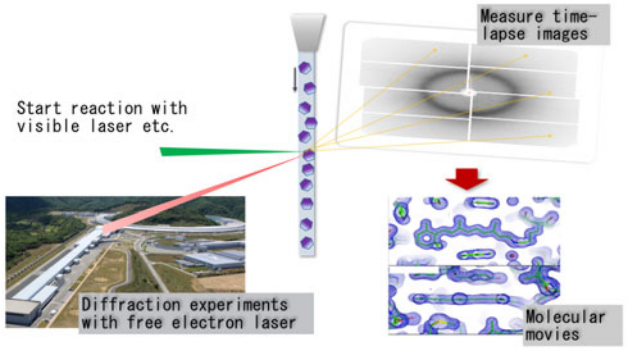

Figure 1. Making molecular movies

【Content of the Research Project】

We use XFEL's femtosecond pulses like strobes for making molecular movies to study macromolecular dynamics with a wide range of time resolution from femtoseconds to seconds. This research field is new and includes a wide range of disciplines such as physics, engineering, chemistry and biology. The group to study the chemical reactions and structural changes (A01, in the figure) in a wide variety of macromolecules, which forms the core part of this project, will closely collaborate with the group responsible for technical development of molecular movies (B01) and the group of computational science and physical chemistry (C01). In the group A01, we will study a variety of interesting biological and chemical systems to understand these molecular mechanisms. For this purpose, we will introduce and develop a wide range of new technologies. In addition, by using computational science, we aim to understand these systems theoretically and quantitatively to design proteins and compounds with new functions.

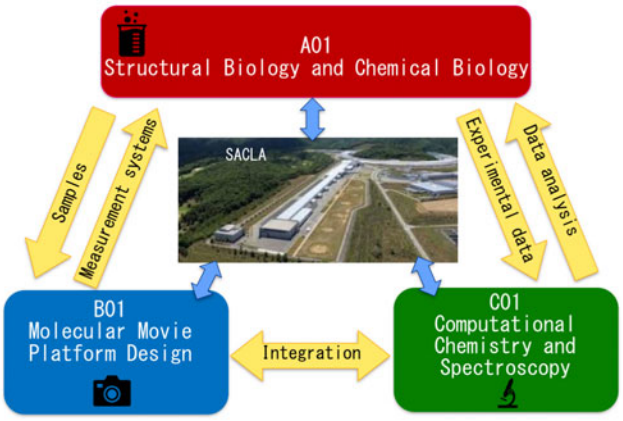

Figure 2. Project design

【Expected Research Achievements and Scientific Significance】

Outstanding time and spatial resolutions of the method will be used to study structural changes and chemical reactions in biological macromolecules to understand their functions at molecular level. Based on the results, rational molecular design will be carried out to produce proteins controlled by various stimulations and compounds switched *in vivo* controlling protein functions. Integrated research in a wide range of fields such as structural biology, protein engineering, chemical biology, and computational science is also expected to accelerate the further development of each field.

【Key Words】

X-ray free electron laser (XFEL): An X-ray laser characterized by ultrahigh brightness, ultrashort pulse duration and high spatial coherence. Using the source, one X-ray diffraction image can be collected within 10 femtosecond.

Molecular movies: Using XFEL, it is possible to capture extremely fast motions of molecules such as chemical reactions, at the time resolution of femtoseconds and spatial resolution of Angstroms and to visualize them as "molecular movies".

【Term of Project】

FY2019-2023

【Budget Allocation】

1,064,000 Thousand Yen

【Homepage Address and Other Contact Information】

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