【Grant-in-Aid for Transformative Research Areas（B）】

Section III

Title of Project： Autonomous biological systems of megadalton complexity

Tomoya Tsukazaki
(Nara Institute of Science and Technology, Graduate School of Science and Technology, Professor)

Number of Research Area：21B308 Researcher Number：80436716

【Purpose of the Research Project】

Understanding how living organisms, including us, are created from non-living molecules is the answer to the most fundamental question of life science, which can provide an essential clue to solving the mystery of how life appeared on Earth. Structural life science is a field of study that describes, at the atomic level, the mechanism of life functions arising from molecules and has made significant contributions to life science in recent years. However, there is a considerable gap between understanding molecular structures and understanding life as a macroscopic system. Meanwhile, synthetic biology is developing as a new academic field that views life phenomena as a system. The aims are to manipulate and produce life phenomena artificially, utilizing the vast amount of genetic and biochemical knowledge obtained so far. Strangely enough, the fusion of these two research fields, which will drive the life sciences of the future, has never been done before, nor has the possibility of doing so ever been discussed. The fusion of structural life science, which seeks to understand cells at the molecular level, and synthetic biology, which aims to understand cells as systems, will undoubtedly accelerate the two fields in complementary ways. By combining structural life science, synthetic biology, and a field of artificial cell research, among others, we will understand constitutive biological systems at multiple scales based on structural information and also develop next-generation structural modeling methods based on the high-purity data produced from the fusion of the two fields. We aim to generate transformative research of life science by breaking away from existing concepts. This will open the way to the future of "structural life system science," in which we can understand biological phenomena as a system with atomic-level resolution and intuitively understand complex biological systems composed of multiple elements through sophisticated molecular dynamics simulations.

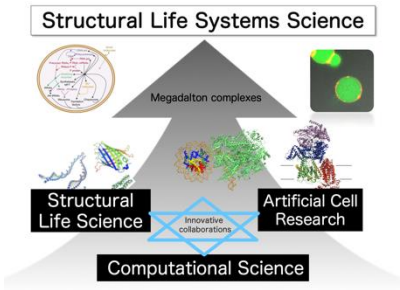

Figure 1. Innovative collaborations

【Content of the Research Project】

This transformative Research Area consists of Group A, which is based on structural life science; Group B, which is based on artificial cell research; and Group C, which is based on computational science. Group A01 (Kayo Nozawa group) and Group A02 (Tomoya Tsukazaki group) will research dynamics of biomolecules in the megadalton class based on structural life science, titled "Structural analysis of megadalton complexes in the dynamic genome" and "4D dynamics and assembly of protein translocation machinery," respectively. In addition, they will collaborate with Group B01 (Yutetsu Kuruma group) and Group C01 (Takaharu Mori group) to conduct new analyses and computer simulations. Group B01's research title is "The construction of cell functions in multi-component artificial cells." In particular, they are trying to synthesize lipids, which are the components of membranes, inside membrane vesicles and in vitro reproduce growth and division like living cells. In parallel, this artificial cell research procedure will be used as a new platform for structural life science in collaboration with Groups A01 and A02. Furthermore, group C01 has developed an experimental data-driven simulation method that incorporates Bayesian statistics-based estimation in the research project "Next-generation biomolecular structure modeling based on the Bayesian statistics." and visualizes the life phenomena handled by Groups A and B as movies.

【Expected Research Achievements and Scientific Significance】

The advanced interdisciplinary research in this area is expected to have a significant ripple effect in the field of life sciences by providing a research platform that will serve as a model for future structural life science research, as well as a ripple effect that will demonstrate the wide range of academic applications of artificial cell research and molecular dynamics calculations. In this area, we will pioneer a new field, "structural life system science," that will become the standard for the future by leading an advanced approach that integrates protein structure/function analysis and artificial cells.

【Key Words】

Megadalton: Dalton (Da) is a unit of mass used to represent molecules and atoms. The mass of ^{12}C is 12 Da. We used megadalton in the area's title because we are studying mega (10^6) Dalton-class complexes in living organisms in this area.

【Term of Project】FY2021-2023

【Budget Allocation】104,500 Thousand Yen

【Homepage Address and Other Contact Information】

http://megashinka.org