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

# Biological cluster: dynamic assembly and functional properties of supramolecular complexes in cells（Cluster Cell Biology）


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| Project Information | Project Number : 24A302　Project Period (FY) : 2024-2028<br>Keywords : Supramolecular complex, High-precision imaging, Cellular functions, Soft matter physics, Mathematical simulation |


## Purpose and Background of the Research

### ●Outline of the Research

In cells, molecular complexes formed by proteins are further assembled into higher-order "supramolecular complexes" that create various structures and functions. In recent years, many studies have been conducted to elucidate the structure of molecular complexes reconstituted in vitro, but such studies alone often fail to understand how the complexes function in cells. This is because in vitro complexes do not capture the whole picture of supramolecular complexes functioning in cells, stable complexes in vitro do not reproduce the dynamic structure in cells, and disordered aggregates that form in vitro do not reproduce the organized supramolecular complexes. In this research project, we define ”Biological Clusters" as functional "supramolecular complexes", and aim to understand how they generate cellular functions and to clarify their formation mechanisms and functional properties. We will promote research on the targeted supramolecular complexes by analyzing their ultra-structures and molecular dynamics, and by linking physical quantity measurement, theory, and computational simulation. By clarifying how various Biological Clusters are formed, what properties they possess, and the relationship between these properties and cellular functions, we aim to establish a new view of cells as Biological Clusters.

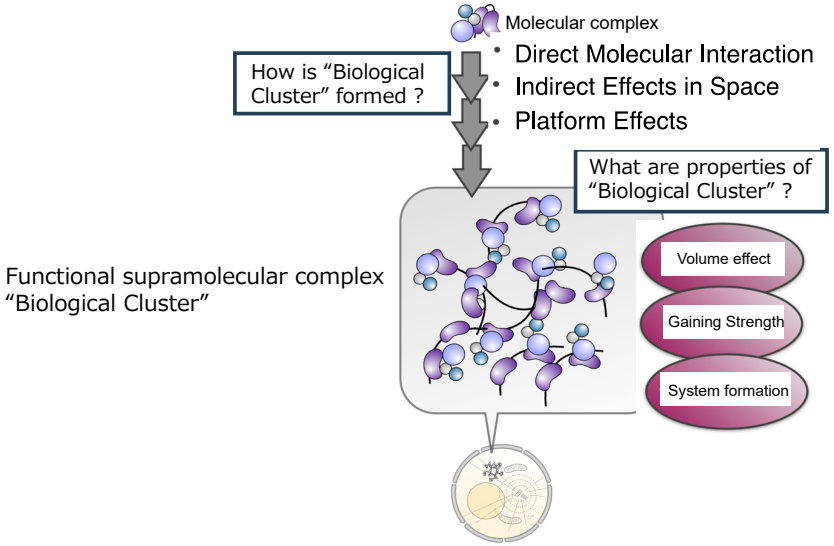


Figure 1. Goal of this project: To clarify what properties supramolecular complexes have, how they are formed, and how they relate to cellular functions.

### ●Research Strategy

To understand Biological Clusters, both capturing their substance in the cells and using reconstituted systems seem to be effective. In addition, orthogonal to this, it is necessary to elucidate both the structure of the cluster and to understand its dynamics. In this project, the research groups are arranged to cover all four quadrants. From the understanding of the four quadrants listed on the right, through the collaboration of Group A01, Group A02, and Group A03, we would like to elucidate the properties of Biological Clusters, their mechanisms of formation, and their relationship to cellular functions, and to submit a new view of the cells.

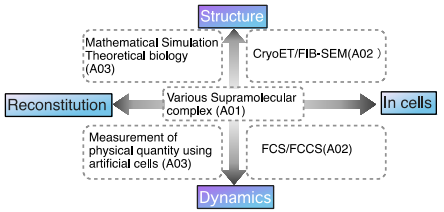


Figure 2. Groups within this research project

## Expected Research Achievements

The purpose of this research project is to elucidate how supramolecular complexes are formed and acquire functional properties as ”Biological Clusters" through the analysis of their intracellular structure and dynamics. To achieve this purpose, the following basic approaches will be taken in all research subjects.

1) To analyze the three factors involved in the formation of supramolecular complexes (direct molecular interactions, indirect effects in space of cells, and platform effects) (see Figure 3) and to clarify the mechanism of their ordered formation.
2) To analyze the properties acquired by the formation of supramolecular complexes (volume effect, gaining strength, system formation) and to clarify how these properties relate to cellular functions.

Within the project, the following three research groups have been established to unite the different specialties.

### ●Group A01 Elucidation of the molecular basis of Biological Clusters and their relationship to cellular functions

Comprehensive elucidation of the target supramolecular complexes, from the molecular basis of the basic units to regulation of supramolecular complex formation and acquisition properties.

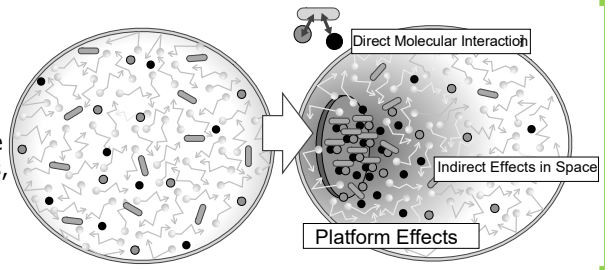


Figure 3. Elements promoting a formation of Biological Cluster in cells

### ●Group A02 Visualization of Biological Clusters and elucidation of its regulation of its molecular dynamics

Capture supramolecular complexes in cells by advanced high-precision imaging analysis to characterize and regulate their molecular dynamics

### ● Group A03 Formation and characterization of Biological Clusters through physical and theoretical analysis

The physical quantities related to supramolecular complexes will be measured, and in parallel with mathematical and theoretical analysis, the functional properties of the clusters and the factors involved in their formation will be elucidated.

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| Homepage Address, etc. | https://www.cluster-biology.f.u-tokyo.ac.jp/ |