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

Construction of membrane-structure theory: Regulation of biological function via functional membrane-structure unit.

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Project Information	Project Number : 26B302　Project Period (FY) : 2026-2028 Keywords : membrane protein complexes, single-molecule biology, physiology, reconstitution systems, computational science

Purpose and Background of the Research

●Outline of the Research

We define large membrane–protein complexes, which cells have evolutionarily refined to perform specialized functions, as “functional membrane-structure units.” By integrating experimental, computational, and reconstitution approaches, we aim to construct an innovative “membrane-structure theory” that can predict the architectures of large complexes. This will provide a fundamental understanding of a wide range of membrane–protein complexes and offer a new approach to biological phenomena beyond conventional frameworks.

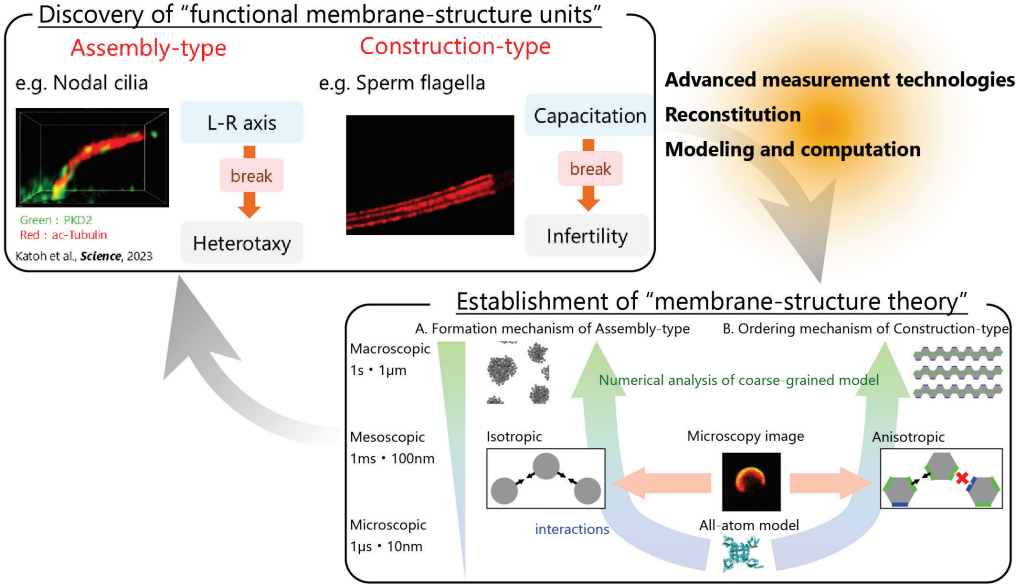

Figure 1. Based on the discovery of the “functional membrane-structure unit,” we will establish a “membrane-structure theory” by combining advanced measurement technologies, reconstitution systems, and computational science.

●Discovery of “functional membrane-structure units”

Super-resolution analyses of membrane-molecule distribution, including the asymmetric localization of mechanosensitive molecules in nodal cilia (organelles that function as cellular antennas and govern left–right body patterning; Katoh *et al.*, *Science*, 2023), have revealed that cells possess functional membrane-structure units that have evolved to perform specialized physiological functions. However, such units have been identified in only a limited number of cell types, and in many cases, even their mechanisms of formation cannot be explained within existing frameworks.

Expected Research Achievements

●Establishment of the concept of “functional membrane-structure units”

We aim to move beyond conventional methodologies that focus on individual molecules and instead establish a new theoretical framework for describing membrane-molecule collectives.

1. Classification and conceptualization of these units, and systematization of their physiological roles
2. Elucidation of the mechanisms underlying their formation and dynamics
3. Construction of a membrane-structure theory

A01 Katoh & Kambara: Assembly-type units; Advanced microscopy

Among functional membrane-structure units, we classify disordered assemblies as assembly-type units. By focusing primarily on nodal cilia, where such assemblies have already been identified, we will use advanced microscopy to investigate their formation mechanisms and conservation, thereby establishing the concept of assembly-type units.

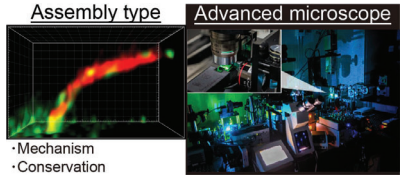

Figure 2. membrane assemblies

A02 Kawai: Construction-type units; Electrophysiology

Among functional membrane-structure units, we define ordered membrane–protein structures as “Constructions”. Focusing on neuronal axons and sperm flagella, in which the existence of such structures has been suggested, we will use advanced electrophysiological approaches to elucidate their dynamics and physiological functions at the single-molecule level.

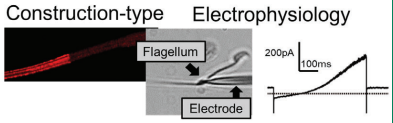

Figure 3. construction-type units

B01 Nishimura: Artificial reconstitution; Reconstitution technique

By using protein reconstitution technologies and interaction assays on giant unilamellar vesicles, we will artificially reconstitute functional membrane-structure units to analyze their functions and, in collaboration with C01, promote the establishment of membrane-structure theory.

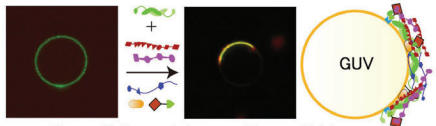

Figure 4. Reconstitution of the “functional membrane structure units”

C01 Adachi & Yamamoto: Construction of membrane-structure theory; Modeling

By integrating all-atom simulation data with experimental data generated in A01–B01, we will establish a new framework, “membrane-structure theory,” for predicting macroscopic phase behavior from microscopic chemical structures.

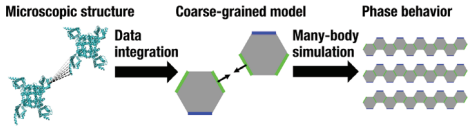

Figure 5. membrane-structure theory

Website(s)	Website: https://membrane-unit.notion.site/unit-35dae2f8376680cdb5e1d69e9f6cc05c Website of PI: https://sites.google.com/view/katoh