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

EPIC Assembly: Emergence of Novel Functional Assembly by Evo-Physico Information Coupling

Principal Investigator	The University of Tokyo, Institute of Industrial Science, Professor KOBAYASHI J. Tetsuya	Researcher Number : 90513359
Project Information	Project Number : 25A401	Project Period (FY) : 2025-2029
	Keywords : Molecular machines, Reaction networks, multicellular systems, Nonequilibrium phenomena, Evolution, Complex Systems	

Purpose and Background of the Research

● **Outline of the Research.** Biological systems exhibit a wide range of highly functional features. This research area aims to elucidate the principles underlying the emergence and development of such biological functions through evolution. To address the increase in complexity and diversity of the functions, we focus on the concept of "assemblies" as a unifying framework that spans molecular to multicellular levels. Assemblies refer to systems composed of heterotypic interacting elements. Assemblies can become combinatorially complex as the number and diversity of constituent elements increase, offering a structural basis for the evolutionary exploration of novel functions.

However, this combinatorial potential also poses a fundamental challenge: as the number of elements increases, the number of possible assemblies grows exponentially. How biological systems navigate this immense space to arrive at functional configurations remains an open question. We hypothesize that functional assemblies emerge and evolve through non-equilibrium dynamics, and that such dynamics are coordinated with evolutionary processes. Our goal is to understand the conjugate actions of non-equilibrium and evolutionary dynamics that drive the emergence, development, and increasing complexity of novel functions.

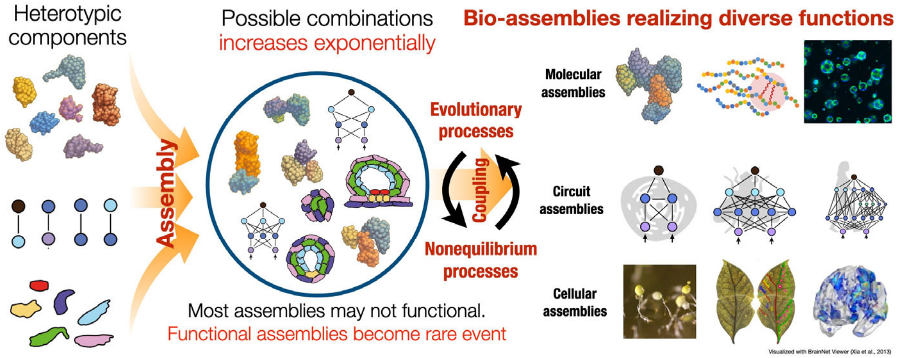

Figure 1. Outline of the idea of assemblies

● **Research Strategy.** To address this challenge, we integrate state-of-the-art imaging technologies and evolutionary analysis. Recent advances have enabled high-resolution measurement of dynamics across scales. In addition, next-generation sequencing and novel phylogenetic techniques allow the reconstruction of ancestral assemblies, whose functions will be verified by their experimental reconstitution.

We also construct mathematical frameworks to capture both the non-equilibrium and evolutionary dynamics of diverse assemblies, integrate these models with the experimental data, and identify the general principles by which non-equilibrium and evolution contribute to the emergence of novel functions in biology.

● **Team organization**

To achieve this strategy, we organize five main projects and teams:

[Project A01] Focusing on proteins and their intrinsically disordered regions (IDRs), team A01 investigates the non-equilibrium processes underlying the emergence of novel molecular behaviors. They also examine the evolutionary paths of protein assemblies by analyzing the evolutionary biases encoded in IDR sequences.

[Project A02] Focusing on GPCR signaling pathways, team A02 analyzes how heterogeneous receptor assemblies contribute to information transmission. By examining the evolutionary diversification of taste receptor gene assemblies, they also uncover the evolutionary dynamics of the functionalities of circuit assemblies.

[Project A03] Targeting multicellular assemblies and tissue formation, team A03 analyzes the physical principles governing non-equilibrium cellular assembly dynamics and spatial organization. They also examine the evolutionary conservation and divergence of cell surface molecules and their impact on forming cellular assemblies.

[Project B01] Team B01 develops theoretical and computational tools to capture the non-equilibrium dynamics of molecular and cellular assemblies. They also extend statistical inference techniques for extracting interaction rules from experimental data.

[Project B02] Team B02 extends mathematical theories of non-equilibrium dynamics of biochemical reaction networks and develops phylogenetic methods for various assemblies. They also construct variational approaches to capture the interplay among non-equilibrium dynamics, evolution, and information.

The theories developed by team B01-B02 will be verified with the experiments of team A01–A03. We also employ the theories and technologies to be developed for designing functional and intelligent biological and artificial systems.

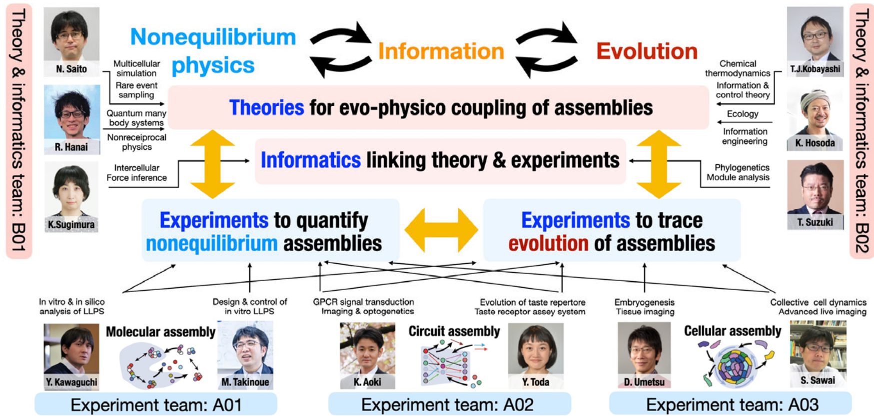

Figure 2. Team organization and research topics

Expected Research Achievements

The experimental, computational, and theoretical methodologies developed in this area are expected to contribute to the design of various biological systems, such as synthetic smart droplets, information-processing biochemical circuits, and functional organoids. Furthermore, the theoretical insights into the interface of information, evolution, and non-equilibrium dynamics may open up novel theoretical paradigms for intelligent systems in information sciences.

Homepage Address, etc.	Homepage : https://epic-assembly.crmind.net/ X account : https://x.com/EpicAssemblyJp Bluesky account : https://bsky.app/profile/epicassemblyjp.bsky.social