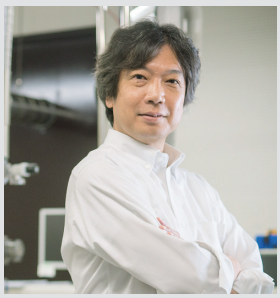
Dynamical Ordering of Biomolecular Systems for Creation of Integrated Functions

Department of Life and Coordination-Complex Molecular Science
Division of Biomolecular Functions



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Education
1986 B.S. The University of Tokyo
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Professional Employment
1991 Assistant Professor, The University of Tokyo
1997 Lecturer, The University of Tokyo
2000 Professor, Nagoya City University
2008 Professor, Institute for Molecular Science
Professor, Okazaki Institute for Integrative Bioscience (–2018)
Professor, The Graduate University for Advanced Studies
2006 Visiting Professor, Ochanomizu University
2013 Project Leader, JSPS Grant in Aid for Scientific Research on Innovative Areas "Dynamical Ordering of Biomolecular Systems for Creation of Integrated Functions"
2018 Professor, Exploratory Research Center on Life and Living Systems (ExCELLS)

Awards
2000 The Pharmaceutical Society of Japan Award for Young Scientists
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Living systems are characterized as dynamic processes of assembly and disassembly of various biomolecules that are self-organized, interacting with the external environment. The omics-based approaches developed in recent decades have provided comprehensive information regarding biomolecules as parts of living organisms. However, fundamental questions still remain unsolved as to how these biomolecules are ordered autonomously to form flexible and robust systems (Figure 1). Biomolecules with complicated, flexible structures are self-organized through weak interactions giving rise to supramolecular complexes that adopt their own dynamic, asymmetric architectures. These processes are coupled with expression of integrated functions in the biomolecular systems.

Toward an integrative understanding of the principles behind the biomolecular ordering processes, we conduct multidisciplinary approaches based on detailed analyses of dynamic structures and interactions of biomolecules at atomic level, in conjunction with the methodologies of molecular and cellular biology along with synthetic and computational technique.

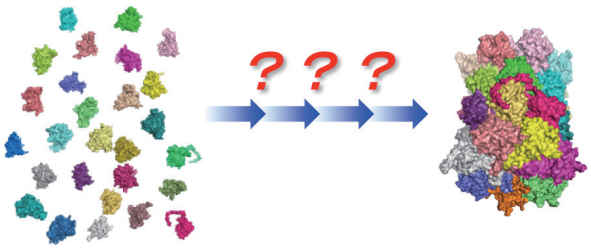

Figure 1. Formation of supramolecular machinery through dynamic assembly and disassembly of biomolecules.

Selected Publications

- S. Yanaka, R. Yogo and K. Kato, "Biophysical Characterization of Dynamic Structures of Immunoglobulin G," *Biophys. Rev.* **12**, 637–645 (2020).
- T. Satoh and K. Kato, "Structural Aspects of ER Glycoprotein Quality-Control System Mediated by Glucose Tagging," in *Glycobiophysics*, Y. Yamaguchi and K. Kato, Eds., Springer Nature; Singapore, pp. 149–169 (2018).
- K. Kato, H. Yagi and T. Yamaguchi, "NMR Characterization of the Dynamic Conformations of Oligosaccharides," in *Modern Magnetic Resonance, 2nd Edition*, G. A. Webb, Ed., Springer International Publishing, pp. 737–754 (2018).
- T. Yamaguchi and K. Kato, "Molecular Dynamics of Gangliosides," in *Gangliosides*, S. Sonnino and A. Prinetti, Eds., Methods in Molecular Biology, Humana Press; New York, **vol. 1804**, pp. 411–417 (2018).
- K. Kato and T. Satoh, "Structural Insights on the Dynamics of Proteasome Formation," *Biophys. Rev.* **10**, 597–604 (2018).
- K. Kato, S. Yanaka and H. Yagi, "Technical Basis for Nuclear Magnetic Resonance Approach for Glycoproteins," in *Experimental Approaches of NMR Spectroscopy*, The Nuclear Magnetic Resonance Society of Japan, Ed., Springer Nature; Singapore, pp. 415–438 (2018).

1. Conformational Dynamics of Post-Translational Protein Modifiers

A majority of proteins encoded in genomes of limited size are post-translationally diversified by covalent modifications such as glycosylation and ubiquitination. The modifiers, *i.e.*, glycans and ubiquitin (Ub) chains, carry distinct biological information in forms of "glycocode" and "Ub code," respectively, which are read out by specific interacting proteins. Because these modifiers possess considerable degrees of motional freedom, we develop methodologies for characterizing their conformational dynamics in solution by NMR spectroscopy.

Our NMR analyses enabled the quantification of populations of individual conformers of Lys48-linked Ub chains, which serve as tags for proteasomal degradation. The data indicate that the most distal Ub unit in the Ub chains is the most apt to expose its interaction surface with the Ub-recognizing proteins. We also demonstrate that a mutational modification of the distal end of the Ub chain can remotely affect the solvent exposure of the interaction surfaces of the other Ub units, suggesting that Ub chains could be unique design frameworks for the creation of allosterically controllable multidomain proteins.[1)]

We also developed an approach to improve the protein-binding affinity of an oligosaccharide by remodeling its conformational space in the precomplexed state. In this approach, based on NMR-validated molecular dynamics simulations, we created an oligosaccharide analogue with an increased population of on-pathway metastable conformers that were originally very minor but exclusively accessible to the target protein without steric hindrance (Figure 2).[2)]

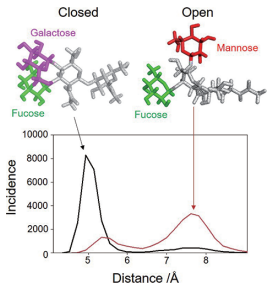

Figure 2. Remodeling of the oligosaccharide conformational space in the prebound state to improve lectin-binding affinity.

2. Integrative Biophysical Approaches to Exploring Protein Assembly Dynamics

The integrative biophysical approaches we have been developing in collaboration with several research groups in ExCELLS and our external research network could be successfully applied to a variety of biomolecular assembling systems, yielding fruitful results in the past year, as summarized below (Figure 3).

We revealed that the two functionally unannotated archaeal proteins, PbaA and PF0014, are co-assembled into a unique ancient Greek tholos-like architecture, offering a novel framework for designing functional protein cages.[3)] We successfully visualized the dynamic process by which the antibodies bound to antigens in membranes spontaneously assemble to form a hexameric ring structure, thereby recruiting complement component C1q on the membrane, which is the initial step of complement-mediated cell lysis.[4)] Assembly of amyloid β (Aβ) under microgravity conditions were explored using the International Space Station, showing that the Aβ fibrillization process significantly slowed down in the microgravity environment, giving rise to distinct morphologies of Aβ.[5)]

Furthermore, we demonstrated that the cargo receptor complex responsible for the intracellular transportation of blood coagulation factors V and VIII recognizes 10-amino acid sequence built into these glycoproteins as a "passport" in the secretory pathway.[6)] The secretion levels of recombinant glycoproteins were significantly increased simply by tagging it with the passport sequence. Our findings offer a potentially useful tool for improving the production yields of recombinant glycoproteins of biopharmaceutical interest.

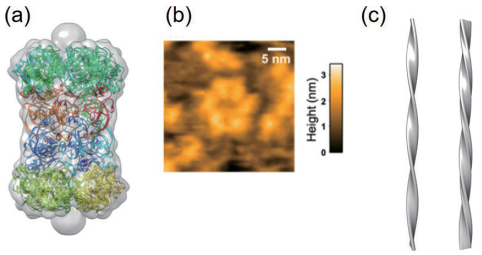

Figure 3. Integrative biophysical approaches to exploring protein assembly dynamics. The simulated model structure of the PbaA/PF0014 complex superimposed onto the cryo-EM map (a), high-speed AFM image of IgG hexamers formed on membrane (b), distinct morphologies of Aβ fibrils formed under microgravity conditions (c).

References

1) M. Hiranyakorn *et al. Int. J. Mol. Sci.* **21**, 5351 (2020).
2) T. Suzuki *et al. Biochemistry* **59**, 3180–3185 (2020).
3) M. Yagi-Utsumi *et al. Sci. Rep.* **10**, 1540 (2020).
4) S. Yanaka *et al. Int. J. Mol. Sci.* **21**, 147 (2020).
5) M. Yagi-Utsumi *et al. NPJ Micorgravity* **6**, 17 (2020).
6) H. Yagi *et al. Nat. Commun.* **11**, 1368 (2020).

Awards

SAITO, Taiki; Young Scientist Award, The Japanese Biochemical Society Chubu Branch (2019).
UMEZAWA, Fumiko; Young Scientist Award, the 3rd Glycolleague (2019).
YUNOKI, Yasuhiro; poster prize, the 26th Annual Meeting of the Japanese Society for Chronobiology (2019).

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