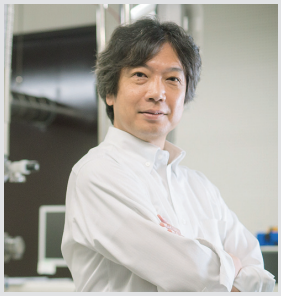
Dynamical Ordering of Biomolecular Systems for Creation of Integrated Functions

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



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Education
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Professional Employment
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2008 Professor, Institute for Molecular Science
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2006 Visiting Professor, Ochanomizu University
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Awards
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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.

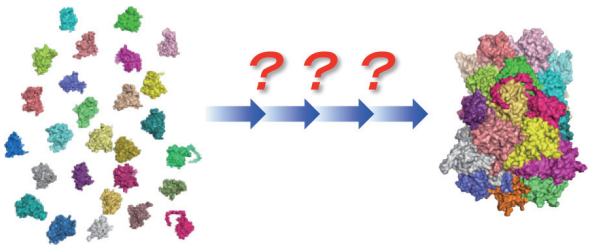

Figure 1. Formation of supramolecular machinery through dynamic assembly and disassembly of biomolecules.

Selected Publications

- H. Yagi, S. Yanaka and K. Kato, "Structural and Functional Roles of the *N*-Glycans in Therapeutic Antibodies," in *Comprehensive Glycoscience, 2nd edition*, J. Barchi, Ed., Elsevier; Oxford, **vol. 5**, pp. 534–542 (2021).
- 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).

1. Methodological Advancements for Analysis of Conformational Dynamics and Interactions of Biomolecules

During the past year, we have made significant progresses in our methods for investigating conformational dynamics and interactions of biomolecules, especially oligosaccharides and glycoproteins. Oligosaccharides play versatile roles in various biological systems but are difficult to characterize from a structural viewpoint due to their remarkable degrees of freedom in internal motion. Therefore, molecular dynamics simulations have been widely used to delineate the dynamic conformations of oligosaccharides. However, hardly any methods have thus far been available for the comprehensive characterization of simulation-derived conformational ensembles of oligosaccharides. We developed a theoretical approach for comprehensive characterization of oligosaccharide conformational ensembles with conformer classification by free-energy landscape via reproductive kernel Hilbert space.[1] This methodology will open opportunities to explore oligosaccharides' conformational spaces, and more generally, molecules with high degrees of motional freedom.

In addition, we sophisticated our experimental methods for stable-isotope-assisted measurements of nuclear magnetic resonance (NMR) and small-angle neutron scattering (SANS) using immunoglobulin G (IgG) as a model glycoprotein. This enabled us to achieve NMR spectral assignments of the N-linked oligosaccharides as well as polypeptide backbones of the Fc portion of IgG.[2,3] Moreover, we combined inverse contrast-matching SANS method with size exclusion chromatography and thereby successfully observed SANS from the non-deuterated IgG glycoprotein in complex with its binding partners with 75% deuteration, which were unobservable in terms of SANS in D_2O.[4] Furthermore, we revealed residual structure of unfolded ubiquitin by employing a dimethylsulfoxide-quenched hydrogen/deuterium-exchange NMR technique with the use of spin desalting columns.[5]

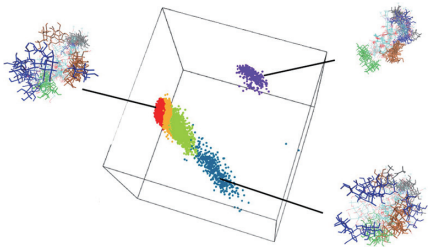

Figure 2. A kernel method for the comprehensive characterization of conformational ensembles of oligosaccharides in association with the conformational free-energy landscape.

2. Integrative Approaches for Characterizing Biomolecular Assembly Systems

We characterized various biomolecular assembling systems using integrative approaches. Cold atmospheric plasma (CAP) has attracted much attention in the fields of biotechnology and medicine owing to its potential utility in clinical applications. Recently accumulating evidence has demonstrated that CAP influences protein structures. However, there remain open questions regarding the molecular mechanisms behind the CAP-induced structural perturbations of biomacromolecules. In view of this situation, we investigated the potential effects of CAP irradiation of amyloid β (Aβ).[6] Based on NMR, mass spectrometry, and kinetics analyses, we demonstrated that the CAP irradiation results in selective oxidation of the methionine residue at position 35 of Aβ, which suppresses amyloid fibril formation. This modification is made by H_2O_2 generated in the plasma-irradiated buffer solution, rather than by the direct action of the plasma.

We also conducted a cryo-electron microscopic study of the proteasome α7 subunit, which self-assembles into a homo-tetradecamer consisting of two layers of α7 heptameric rings.[7] Our observations suggest that the α7 double-ring structure was significantly different from the previously reported crystallographic model and fluctuates considerably in solution.

In addition, we contributed to an IMS Joint Research lead by Dr. Ryo Ohtani (Kyushu University) on two-dimensional coordination polymers as *pseudo-membrane jackets*, which achieve visible phase separation in cell membrane.[8,9] This system opens new avenues for the application of metal complex lipids toward controlling lipid distributions in fluid membranes.

References

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3) S. Yanaka *et al.*, *Biomol. NMR Assignments* **15**, 187–192 (2021).
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5) M. Yagi-Utsumi *et al.*, *Biophys. J.* **119**, 2029–2038 (2020).
6) M. Yagi-Utsumi *et al.*, *Int. J. Mol. Sci.* **22**, 3116 (2021).
7) C. Song *et al.*, *Int. J. Mol. Sci.* **22**, 4519 (2021).
8) R. Ohtani *et al.*, *Angew. Chem., Int. Ed.* **61**, 13603–13608 (2021).
9) R. Ohtani *et al.*, *Angew. Chem., Int. Ed.* **59**, 17931–17937 (2020).

Awards

YAGI-UTSUMI, Maho; 10th Young Researcher Award, National Institutes of Natural Sciences (2021).
YANAKA, Saeko; Award for Young Scientists, the Division of Physical Sciences of the Pharmaceutical Society of Japan (2021).
UMEZAWA, Fumiko; Young Scientist Award, Japanese Biochemical Society Chubu Branch (2021).
SAITO, Taiki; the Young Scientist Award, the 16th Forum of the Glycoscience Base for Chubu (2021).

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