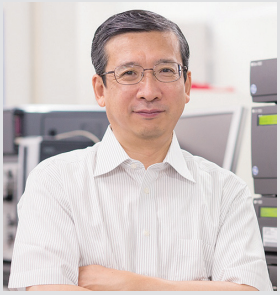
RESEARCH ACTIVITIES
Life and Coordination-Complex Molecular Science

Department of Life and Coordination-Complex Molecular Science is composed of two divisions of biomolecular science, two divisions of coordination-complex molecular science, and one adjunct division. Biomolecular science divisions cover the studies on functions, dynamic structures, and mechanisms for various biomolecules such as sensor proteins, metalloproteins, biological-clock proteins, glycoconjugates, antibodies, and motor proteins. Coordination-complex divisions aim to develop molecular catalysts and functional metal complexes for transformation of organic molecules, and molecular materials with photonic-electronic-magnetic functions and three-dimensional complex structures. Interdisciplinary alliances in this department aim to create new basic concepts for the molecular and energy conversion through the fundamental science conducted at each division.

Bioinorganic Chemistry of Metalloproteins Responsible for Metal Homeostasis and Signal Sensing

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



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Keywords Bioinorganic Chemistry, Metalloproteins, Sensor Protein

Transition metal ions and metalloproteins play crucial roles in meeting the energy demands of the cell by playing roles in intermediary metabolism and in signal transduction processes. Although they are essential for biological function, metal ion bioavailability must be maintained within a certain range in cells due to the inherent toxicity of all metals above a threshold. This threshold varies for individual metal ions. Homeostasis of metal ions requires a balance between the processes of uptake, utilization, storage, and efflux and is achieved by the coordinated activities of a variety of proteins including extracytoplasmic metal carriers, ion channels/pumps/transporters, metal-regulated transcription and translation proteins, and enzymes involved in the biogenesis of metal-containing cofactors/metalloproteins. In order to understand the processes underlying this complex metal homeostasis network, the study of the molecular processes that determine the protein-metal ion recognition, as well as how this event is transduced into a functional output, is required. My research interests are focused on the elucidation of the structure and function relationships of metalloproteins responsible for the regulation of biological homeostasis.

I am also working on gas sensor proteins. Gas molecules such as O_2, NO, CO and ethylene are present in the environment and are endogenously (enzymatically) produced to act as signaling molecules in biological systems. Sensing these gas molecules is the first step in their acting as signaling molecules. Sensor proteins are usually required. Input signals generated by gas sensing have to transduce to output signals that regulate biological functions. This is achieved by biological signal-transduction systems. Recognition of the cognate gas molecules is a general mechanism of functional regulation for gas sensor proteins. This induces conformational changes in proteins that controls their activities for following signal transductions. Interaction between gas molecules and sensor proteins is essential for recognition of gas molecules. Metal-containing prosthetic groups are widely used. In my research group, our research focuses on transition metal-based gas-sensor proteins and the signaling systems working with them.

Selected Publications

- D. Matsui, N. Muraki, K. Chen, T. Mori, A. A. Ingram, K. Oike, H. Gröger, S. Aono and Y. Asano, "Crystal Structural Analysis of Aldoxime Dehydratase from *Bacillus sp.* OxB-1: Importance of Surface Residues in the Optimization for Crystallization," *J. Inorg. Biochem.* **230**, 111770–111779 (2022).
- Y. Ikenoue, Y. Tahara, M. Miyata, T. Nishioka, S. Aono and H. Nakajima, "Use of a Ferritin L134P Mutant for the Facile Conjugation of Prussian Blue in the Apoferritin Cavity," *Inorg. Chem.* **60**, 4693–4704 (2021).
- M. Nishinaga, H. Sugimoto, Y. Nishitani, S. Nagai, S. Nagatoishi, N. Muraki, T. Tosha, K. Tsumoto, S. Aono, Y. Shiro and H. Sawai, "Heme Controls the Structural Rearrangement of Its Sensor Protein Mediating Bacterial Survival," *Commun. Biol.* **4**, 467 (12 pages) (2021).
- N. Muraki, K. Takeda, D. Nam, M. Muraki and S. Aono, "Structural Characterization of Thermoglobin from a Hyperthermophilic Bacterium *Aquifex aeolicus*," *Chem. Lett.* **50**, 603–606 (2021).
- N. Muraki, C. Kitatsuji, Y. Okamoto, T. Uchida, K. Ishimori and S. Aono, "Structural Basis for Heme Transfer Reaction in Heme Uptake Machinery from Corynebacteria," *Chem. Commun.* **55**, 13864–13867 (2019).
- N. Muraki, K. Ishii, S. Uchiyama, S. G. Itoh, H. Okumura and S. Aono, "Structural Characterization of HypX Responsible for CO Biosynthesis in the Maturation of NiFe-Hydrogenase," *Commun. Biol.* **2**, 385 (12 pages) (2019).

1. Structural Characterization of Aldoxime Dehydratase OxdB That Catalyzes Dehydration Reaction of Aldoximes to Form Nitriles

Nitrile compounds are important intermediates in some industrial processes to produce nylon and acrylic fibers, insecticides, and pharmaceuticals. Though one of the most useful methods for nitrile production is dehydration of aldoxime, the chemical dehydration of aldoxime used in the industrial process requires harsh conditions. Therefore, a more environmentally benign process of aldoxime dehydration is expected to be established, for which a biological dehydration of aldoxime is a possible candidate. In nature, some microbes have "aldoxime-nitrile pathway," where aldoximes are metabolized to the corresponding carboxylic acids through nitriles formed by dehydration of aldoximes with aldoxime dehydratase (Oxd; EC4.99.1.-). There are two pathways for the conversion of nitriles to carboxylic acids. One is hydrolysis of nitriles by nitrilase, and the other is the combination of the reactions catalyzed by nitrile hydratase and amidase. Nitriles are the important intermediate not only in some industrial processes but also in this biological system. The detail characterization of such a biological process to produce nitriles will give some useful information to develop an environmentally benign process for the production of nitriles in industrial field.

The crystal structures of OxdRE from *Rhodococcus sp.* N-771 and OxdA from *Pseudomonas chlororaphis* have been reported. Based on the biochemical characteristics of Oxds and the crystal structure of its Michaelis complex, a mechanism for the dehydration of aldoxime to the corresponding nitrile has been proposed. The active site of Oxds includes heme b as a cofactor and a catalytic triad, which consists of, for example, OxdA, arginine, histidine, and serine. The Fe^{2+} ion is additionally coordinated to another histidine. When the substrate enters the active site, it becomes N-coordinated to Fe^{2+}. The hydroxyl moiety of aldoxime also forms hydrogen bonds with serine and histidine. Oxds share a common architecture to achieve this reaction, but show varying substrate selectivities. In particular, OxdB (Oxd from *Bacillus sp.* OxB-1) shows different enantioselectivities from those of OxdRE and OxdA when bulky compounds, such as racemic E/Z-2-methyl-3-(3,4-methylenedioxyphenyl)-propanal oxime, are used as substrates. The structural features of OxdB are considered to be responsible for the difference in substrate selectivity between OxdRE and OxdB. However, the structure of this broadly applicable biocatalyst has not yet been determined due to the challenges associated with its crystallization. Thus, it is difficult to discuss the relationship between protein structure and substrate selectivity.

In this work, we have determined the crystal structure of OxdB by adding a site-specific mutation to Glu85 located on the surface of the protein, we succeeded in crystallizing OxdB without reducing the enzyme activity. (Figure 1) The catalytic triad essential for Oxd activity were structurally conserved in

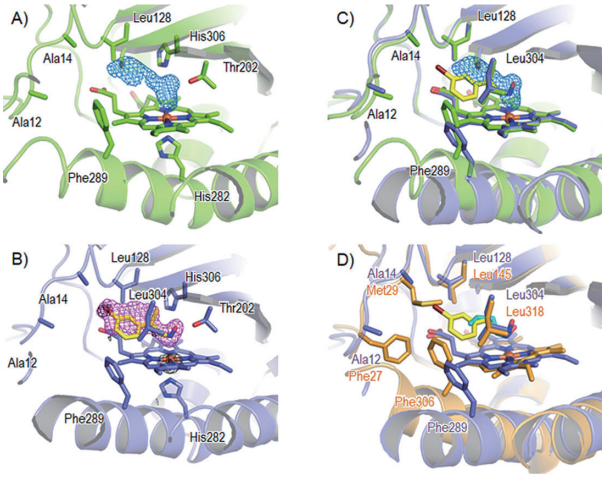

Figure 1. Structure of active site in OxdB-E85A. (A) OxdB-E85A (Substrate-free) is shown in green. *Fo-Fc* map (4σ) in active site is shown in blue mesh. (B) OxdB-E85A and Z-2-(3-bromo-phenyl)-propanal oxime (**1**) complex is shown in slate color. **1** is shown in yellow stick model. Anomalous Fourier map (4σ) in active site is shown in black mesh. Polder map (4σ) of **1** is shown in magenta mesh. (C) Superposition of substrate-free form and substrate-bound form is shown in green and slate color, respectively. *Fo-Fc* map (4σ) of substrate-free form is shown in blue mesh. (D) Superposition of OxdB-E85A and **1** complex, and OxdRE in complex with butyraldoxime. OxdRE is shown in orange. Butyraldoxime is shown in cyan stick model.

OxdB. The catalytic triad were conserved in the structure of OxdB. Based on the crystal structure of OxdB, the molecular mechanism of the aldoxime dehydration in OxdB is as follows. When the substrate is bound to heme in OxdB, Thr202 forms a hydrogen bond with the hydroxyl group of the substrate. Dehydration of the substrate proceeds as a result of the proton supply by His306. His306 receives a proton from Glu126 or Arg159. The imidazole ring of His282 in OxdB was more perpendicular to heme than that of His299 in OxdRE and OxdA. This fact suggests that His282 in OxdB is highly nucleophilic toward heme iron. The experiments with mutagenesis on axial histidine and exogenous imidazole derivatives in OxdB have shown that the enzyme activity increases under conditions of high nucleophilicity by the axial ligand. In this context, the activity of OxdB is expected to be higher than that of OxdRE and OxdA.

In addition, the crystal structure of the Michaelis complex of OxdB and the diastereomerically pure substrate Z-2-(3-bromophenyl)-propanal oxime implied the importance of several hydrophobic residues for substrate selectivity. Mutational analysis implicated Ala12 and Ala14 in the E/Z selectivity of bulky compounds. The N-terminal region of OxdB was shown to be shorter than those of OxdA and OxdRE, and have high flexibility. These structural differences possibly result in distinct preferences for aldoxime substrates based on factors such as substrate size.

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Dynamical Ordering of Biomolecular Systems for Creation of Integrated Functions

Department of Life and Coordination-Complex Molecular Science
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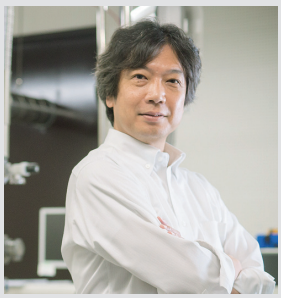

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Keywords Biomolecule Organization, NMR

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.

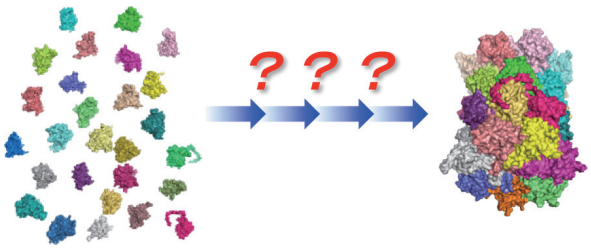

Figure 1. Formation of supramolecular machinery through dynamic assembly and disassembly of biomolecules.

Selected Publications

- M. Yagi-Utsumi and K. Kato, "Conformational Variability of Amyloid-β and the Morphological Diversity of Its Aggregates," *Molecules* **27**, 4787 (2022).
- K. Kato, T. Yamaguchi and M. Yagi-Utsumi, "Experimental and Computational Characterization of Dynamic Biomolecular Interaction Systems Involving Glycolipid Glycans," *Glycoconjugate J.* **39**, 219–228 (2022).
- 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 and T. Satoh, "Structural Insights on the Dynamics of Proteasome Formation," *Biophys. Rev.* **10**, 597–604 (2018).

1. Elucidation of Molecular Mechanisms of Regulation of Protein Glycosylation

Our research on protein glycosylation has made significant progresses over the past year. First, we identified a molecular code embedded in protein for regulating its glycosylation. Many proteins in nature exist as glycoproteins, which are molecules comprised of protein (polypeptide chain) and glycan (sugar chain). While the protein structure is determined on the basis of its genetic blueprint, the information on glycans is not directly encoded by the genome. We recently found a specific 29-amino-acid sequence in the glycoprotein LAMP-1 that promotes a specific glycan structure called Lewis X.[1] This sequence induces Lewis X modification when fused to other proteins such as erythropoietin (Figure 2). These findings on a regulatory code of protein glycosylation are expected to pave the way for controlling glycosylation of biopharmaceuticals, which is critical for their efficacy and safety.

Protein glycosylation also has implications in disease. We previously discovered the presence of a novel post-translational modification, in which glycerol phosphate (GroP) caps the core part of matriglycan, thereby blocking its elongation. We recently found that the GroP modification is mediated by PCYT2, a CDP-Gro synthase in humans, and disrupts glycan-mediated cell adhesion, thereby promoting the migration of cancer cells.[2,3] These findings can contribute to the development of cancer therapies targeting this modification.

Furthermore, we are continuously developing methodologies for structural analyses of glycoproteins, which include updating the web application GALAXY for HPLC/MS-based glycosylation profiling[4] and improving the stable isotope labeling protocol for NMR spectroscopy.[5] These methodological developments have led to the promotion of new collaborative researches as exemplified by identification of distinct N-glycosylation patterns on extracellular vesicles from small-cell and non-small-cell lung cancer cells.[6]

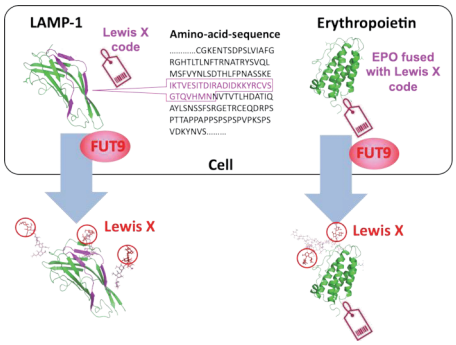

Figure 2. Specific 29-amino-acid sequence from the glycoprotein LAMP-1 serves as a "Lewis X code," which is deciphered by the fucosyltransferase FUT9, and it can be embedded into erythropoietin to evoke Lewis X modification.

2. Characterization of Biomacromolecules that Function in Extreme Environments

Our research also aims to understand the mechanisms of adaptation of life to the environments through analysis of the structure, dynamics, and function of biomacromolecules working in extreme environments. In FY2021, through collaboration with the ExCELLS groups lead by Dr. Uchihashi, Dr. Murata, and Dr. Arakawa, we published several papers on the molecular mechanisms of tardigrade unhydrobiosis. Our integrative spectroscopic and microscopic data demonstrate that CAHS1 (cytosolic-abundant heat-soluble protein 1), an abundant protein in *Ramazzottius varieornatus*, self-assembles into fibrous condensates under desiccation-mimicking conditions in a reversible manner[7] (Figure 3). This dynamic protein organization suggests multistep anhydrobiotic mechanisms, including the reversible formation of protective compartments for desiccation-sensitive biomolecules, water-holding gelation, and maintenance of the integrity of biomolecular complexes under extremely dry conditions. We also characterized structures of g12777 protein, a novel Mn-dependent peroxidase, from *R. varieornatus*,[8] and EtAHS, a novel abundant heat-soluble protein from *Echinisicus testudo*.[9] Our findings illustrate adaptation strategies of organisms to extreme environments without water.

Moreover, we applied the integrative biophysical approach to characterize the overall structure of cyanobacterial circadian clock protein complex[10] and single-molecular interactions between the complement component C1 and antibodies.[11]

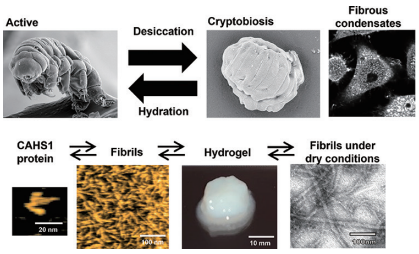

Figure 3. Spontaneous assembling of CAHS1 proteins into fibrous condensates under desiccation-mimicking conditions.

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1) T. Saito *et al.*, *Commun. Biol.* **5**, 676 (2022).
2) F. Umezawa *et al.*, *Int. J. Mol. Sci.* **23**, 6662 (2022).
3) F. Yamasaki *et al.*, *Biochem. Biophys. Res. Commun.* **579**, 8–14 (2021).
4) H. Yagi *et al.*, *Glycobiology* **32**, 646–650 (2022).
5) S. Yanaka *et al.*, *J. Biomol. NMR* **76**, 17–22 (2022).
6) K. Kondo *et al.*, *J. Biol. Chem.* **298**, 101950 (2022).
7) M. Yagi-Utsumi *et al.*, *Sci. Rep.* **11**, 21328 (2021).
8) Y. Yoshida *et al.*, *BMC Genomics* **23**, 405 (2022).
9) Y. Murai *et al.*, *BMC Genomics* **22**, 813 (2021).
10) Y. Yunoki *et al.*, *Commun. Biol.* **5**, 184 (2022).
11) S. Yanaka *et al.*, *Int. J. Mol. Sci.* **23**, 2090 (2022).

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Operation and Design Principles of Biological Molecular Machines

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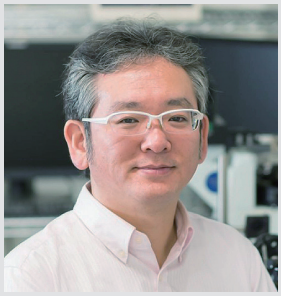
Division of Biomolecular Functions



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Keywords Molecular Motors, Single-Molecule Analysis, Protein Engineering

Activity of life is supported by various molecular machines made of proteins. Protein molecular machines are tiny, but show very high performance, and are superior to man-made machines in many aspects. One of the representatives of protein molecular machines is linear and rotary molecular motors (Figure 1). Molecular motors generate mechanical forces and torques that drive their unidirectional motions from the energy of chemical reaction or the electrochemical potential across the cell membrane. We unveil operation principles of molecular motors with advanced single-molecule functional analysis. With the help of site-saturation mutagenesis and robot-based automation, we also engineer non-natural molecular motors to understand their design principles.

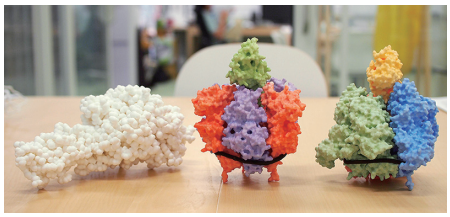

Figure 1. Protein molecular machines. (Left) A linear molecular motor chitinase A. (Center and Right) Rotary molecular motors F_1-ATPase and V_1-ATPase, respectively.

Selected Publications

- A. Nakamura, N. Kobayashi, N. Koga and R. Iino, "Positive Charge Introduction on the Surface of Thermostabilized PET Hydrolase Facilitates PET Binding and Degradation," *ACS Catal.* **11**, 8550–8564 (2021).
- A. Visootsat, A. Nakamura, P. Vignon, H. Watanabe, T. Uchihashi and R. Iino, "Single-Molecule Imaging Analysis Reveals the Mechanism of a High-Catalytic-Activity Mutant of Chitinase A from *Serratia marcescens*," *J. Biol. Chem.* **295**, 1915–1925 (2020).
- J. Ando, T. Shima, R. Kanazawa, R. Shimo-Kon, A. Nakamura, M. Yamamoto, T. Kon and R. Iino, "Small Stepping Motion of Processive Dynein Revealed by Load-Free High-Speed Single-Particle Tracking," *Sci. Rep.* **10**, 1080 (2020).
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- T. Iida, Y. Minagawa, H. Ueno, F. Kawai, T. Murata and R. Iino, "Single-Molecule Analysis Reveals Rotational Substeps and Chemo-Mechanical Coupling Scheme of *Enterococcus hirae* V_1-ATPase," *J. Biol. Chem.* **294**, 17017–17030 (2019).
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- A. Nakamura, T. Tasaki, Y. Okuni, C. Song, K. Murata, T. Kozai, M. Hara, H. Sugimoto, K. Suzuki, T. Watanabe, T. Uchihashi, H. Noji and R. Iino, "Rate Constants, Processivity, and Productive Binding Ratio of Chitinase A Revealed by Single-Molecule Analysis," *Phys. Chem. Chem. Phys.* **20**, 3010–3018 (2018).

1. Direct Observation of Stepping Rotation of V-ATPase Reveals Rigid Component in Coupling between V_o and V_1 Motors[1)]

V-ATPases are rotary motor proteins that convert the chemical energy of ATP into the electrochemical potential of ions across cell membranes (Figure 2). V-ATPases consist of two rotary motors, V_o and V_1, and *Enterococcus hirae* V-ATPase (EhV_oV_1) actively transports Na^+ in V_o (EhV_o) by using torque generated by ATP hydrolysis in V_1 (EhV_1). Here, we observed ATP-driven stepping rotation of detergent-solubilized EhV_oV_1 wild-type, aE634A, and BR350K mutants under various Na^+ and ATP concentrations ([Na^+] and [ATP], respectively) by using a 40-nm gold nanoparticle as a low-load probe. When [Na^+] was low and [ATP] was high, under the condition that only Na^+ binding to EhV_o is rate-limiting, wild-type and aE634A exhibited 10-pausing positions reflecting 10-fold symmetry of the EhV_o rotor and almost no backward steps. Duration time before the forward steps was inversely proportional to [Na^+], confirming that Na^+ binding triggers the steps. When both [ATP] and [Na^+] were low, under the condition that both Na^+ and ATP bindings are rate-limiting, aE634A exhibited 13-pausing positions reflecting 10- and 3-fold symmetries of EhV_o and EhV_1, respectively (Figure 3). The distribution of duration time before the forward step was fitted well by the sum of two exponential decay functions with distinct time constants. Furthermore, occasional backward steps smaller than 36° were observed. Small backward steps were also observed during three long ATP cleavage pauses of BR350K. These results indicate that EhV_o and EhV_1 do not share pausing positions, Na^+ and ATP bindings occur at different angles, and the coupling between EhV_o and EhV_1 has a rigid component (Figure 4).

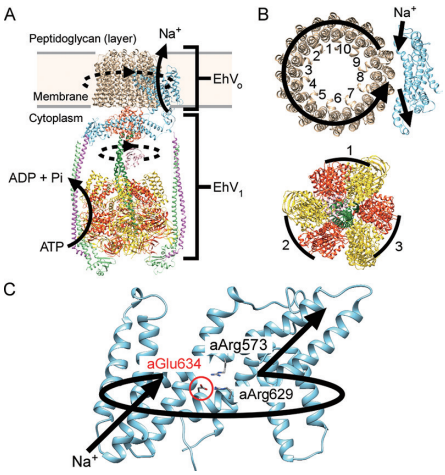

Figure 2. (A) Overall architecture of EhV_oV_1. The dotted circular arcs represent the rotation direction driven by ATP hydrolysis. (B) (top) Top view of a-subunit (cyan) and c_{10}-ring (brown) of EhV_o and (bottom) A- (yellow), B- (orange), D- (green), and F-subunits (pink) of EhV_1. The black arrow at the top indicates the path of Na^+ movement during ATP-driven rotation. The arcs at the bottom represent the catalytic AB pairs. (C) Side view of a-subunit viewed from the c-subunit. The mutated residue, aGlu634, is located on the surface of the entry half-channel of the a-subunit as highlighted in red letters and a circle.

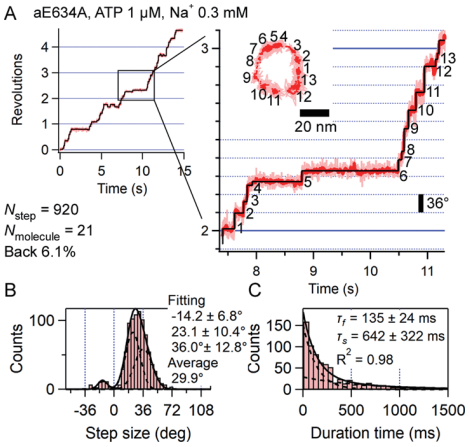

Figure 3. (A) Typical trajectory of rotation at 1 μM ATP and 0.3 mM Na^+ recorded at 1,000 fps. Enlarged view of one revolution (360°) is shown on the right. Pink, red, and black traces represent raw, median-filtered (current ± 7 frames), and fitted trajectories, respectively. The inset shows the corresponding *x*-*y* trajectory. Pink lines and red dots represent the raw and median-filtered (current ± 7 frames) coordinates, respectively. (B) Distribution of the step size fitted with the sum of three Gaussians: One peak in backward (minus) direction and two peaks in forward (plus) direction, one of which was fixed at 36°, assuming that it was the step of EhV_o. (C) Distribution of the duration time before the forward step fitted with the sum of two exponential decay functions.

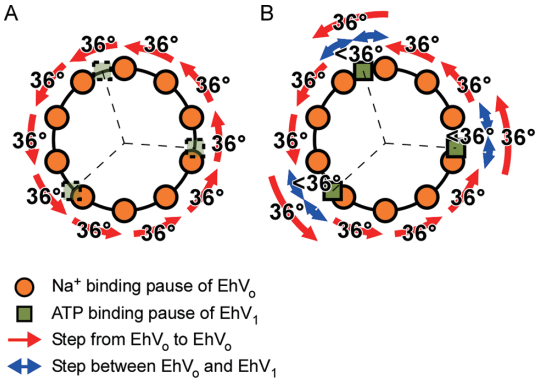

Figure 4. Schematic models of the stepping rotation and rigid coupling of EhV_oV_1. The orange circles and dark green squares indicate the pausing positions waiting for Na^+ binding to EhV_o and ATP binding to EhV_1, respectively. The red arrows indicate the 36° steps between adjacent pausing positions for the EhV_o. The blue arrows indicate the backward and forward steps smaller than 36° between adjacent pausing positions for EhV_o and EhV_1. (A) Condition in which only Na^+ binding to EhV_o is rate-limiting. In this condition, the pauses waiting for ATP binding to EhV_1 are too short to be detected, and EhV_oV_1 rotates unidirectionally without backward steps. (B) Condition in which both Na^+ and ATP bindings are rate-limiting. The pausing positions waiting for ATP binding are visualized, and then 13-pausing positions are detected per single turn. Because no torque is generated during the pauses waiting for ATP binding to EhV_1, EhV_oV_1 rotates to the backward and forward pausing positions of EhV_o driven by Brownian motion.

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Development of Novel Catalytic Organic Transformations

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2003 Research Project Leader, JST CREST Project (–2008)
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2011 Deputy Research Project Leader, JST CREST (–2016)
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Awards
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Keywords Transition Metal Catalysis, Green Chemistry, Photocatalysis

Our research interests lie in the development of catalytic reaction systems toward ideal (highly efficient, selective, green, safe, simple, etc.) organic transformations. In particular, development of a wide variety of the heterogeneous aqua-catalytic systems, continuous flow catalytic systems, and super active catalysts working at ppm-ppb loading levels, have been achieved. Furthermore, we have recently been developing a novel photocatalysis where, for example, the electrophilic substitution of carbonyl groups took place under visible-light irradiation (Figure 1).

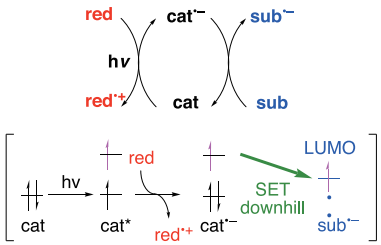

Figure 1. The outlined concept of photocatalytic reductive activation of substrate (*e.g.* carbonyls).

Selected Publications

- G. Hamasaka, D. Roy, A. Tazawa and Y. Uozumi, "Arylation of Terminal Alkynes by Aryl Iodides Catalyzed by a Parts-per-Million Loading of Palladium Acetate," *ACS Catal.* **9**, 11640–11646 (2019).
- R. David and Y. Uozumi, "Recent Advances in Palladium-Catalyzed Cross-Coupling Reactions at ppm-ppb Molecular Catalyst Loadings (review)," *Adv. Synth. Catal.* **360**, 602–625 (2018).
- T. Osako, K. Torii, S. Hirata and Y. Uozumi, "Chemoselective Continuous-Flow Hydrogenation of Aldehydes Catalyzed by Platinum Nanoparticles Dispersed in an Amphiphilic Resin," *ACS Catal.* **7**, 7371–7377 (2017).
- Y. M. A. Yamada, S. M. Sarkar and Y. Uozumi, "Self-Assembled Poly(imidazole-palladium): Highly Active, Reusable Catalyst at Parts per Million to Parts per Billion Levels," *J. Am. Chem. Soc.* **134**, 3190–3198 (2012).
- G. Hamasaka, T. Muto and Y. Uozumi, "Molecular-Architecture-Based Administration of Catalysis in Water: Self-Assembly of an Amphiphilic Palladium Pincer Complex," *Angew. Chem., Int. Ed.* **50**, 4876–4878 (2011).
- Y. Uozumi, Y. Matsuura, T. Arakawa and Y. M. A. Yamada, "Asymmetric Suzuki-Miyaura Coupling in Water with a Chiral Pallasium Catalyst Supported on Amphiphilic Resin," *Angew. Chem., Int. Ed.* **48**, 2708–2710 (2009).
- Y. M. A. Yamada, T. Arakawa, H. Hocke and Y. Uozumi, "A Nanoplatinum Catalyst for Aerobic Oxidation of Alcohols in Water," *Angew. Chem., Int. Ed.* **46**, 704–706 (2007).

1. Photocatalytic Carbinol Cation/Anion Umpolung: Direct Addition of Aromatic Aldehydes and Ketones to Carbon Dioxide[1)]

We have developed a new photocatalytic umpolung reaction of carbonyl compounds to generate anionic carbinol synthons. Aromatic aldehydes or ketones reacted with carbon dioxide in the presence of an iridium photocatalyst and 1,3-dimethyl-2-phenyl-2,3-dihydro-1*H*-benzimidazole (DMBI) as a reductant under visible-light irradiation to furnish the corresponding α-hydroxycarboxylic acids through nucleophilic addition of the resulting carbinol anions to electrophilic carbon dioxide.

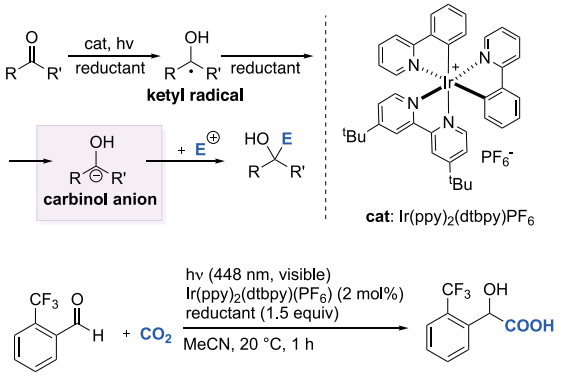

Figure 2. Photocatalytic Eelectrophilic Substitution of Carbonyls with Carbon Dioxide via Carbinol Anion Species.

2. Palladium-Catalyzed Aminocarbonylation of Aryl Halides with *N,N*-Dialkylformamide Acetals[2)]

We developed a protocol for the palladium-catalyzed aminocarbonylation of aryl halides using less-toxic formamide acetals as bench-stable aminocarbonyl sources under neutral conditions. Various aryl (including heteroaryl) halides reacted with *N,N*-dialkylformamide acetals in the presence of a catalytic amount of $Pd_2(dba)_3$ and xantphos to give the corresponding aromatic carboxamides at 90–140 °C without any activating agents or bases in up to quantitative chemical yield. This protocol was applied to aryl bromides, aryl iodides, and trifluoromethanesulfonic acid, as well as to relatively less-reactive aryl chlorides. A wide range of functionalities on the aromatic ring of the substrates were tolerated under the aminocarbonylation conditions. The catalytic aminocarbonylation was used to prepare the insect repellent *N,N*-diethyl-3-methylbenzamide as well as a synthetic intermediate of the dihydrofolate reductase inhibitor triazinate.

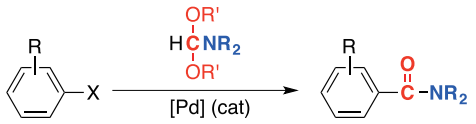

Figure 3. Palladium-Catalyzed Aminocarbonylation with *N,N*-Dialkylformamide Diacetals.

3. Cyanide-Free Cyanation of Aryl Iodides with Nitromethane by Using an Amphiphilic Polymer-Supported Palladium Catalyst[3)]

A cyanide-free aromatic cyanation was developed using nitromethane as a cyanide source in water with an amphiphilic polystyrene–poly(ethylene glycol) (PS–PEG) resin-supported palladium catalyst and an alkyl halide (*i.e.*, 1-iodobutane). The cyanation proceeded through the palladium-catalyzed cross-coupling of aryl halides and nitromethane, followed by transformation of the resultant nitromethylarene intermediates into nitriles by 1-iodobutane.

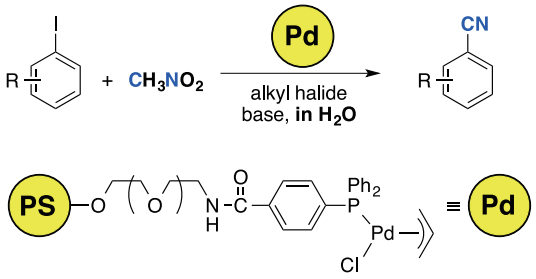

Figure 4. Cyanation of Aryl Iodides with Nitromethane by Using an Amphiphilic PS-PEG resin-Supported Palladium Catalyst in Water.

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2) S. Hirata, T. Osako and Y. Uozumi, *Helv. Chim. Acta* **104**, e2100162 (2021). DOI: 10.1002/hlca.202100162

3) T. Suzuka, R. Niimi and Y. Uozumi, *Synlett* **33**, 40–44 (2022). DOI: 10.1055/a-1675-0018

Award

OKUMURA, Shintaro; The Society of Synthetic Organic Chemistry, Fujifilm Research Proposal Award (2021).

Design and Synthesis of Chiral Organic Molecules for Asymmetric Synthesis

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Keywords Synthetic Chemistry, Molecular Catalyst, Non-Covalent Interaction

The field of molecular catalysis has been an attractive area of research to realize efficient and new transformations in the synthesis of functional molecules. The design of ligands and chiral molecular catalysts has been recognized as one of the most valuable strategies; therefore, a great deal of effort has been dedicated to the developments. In general, "metal" has been frequently used as the activation center, and conformationally rigid catalyst framework has been preferably components for the catalyst design. To develop new type of molecular catalysis, we have focused on the use of hydrogen and halogen atom as activation unit, and have utilized non-covalent interactions as organizing forces of catalyst framework in the molecular design of catalyst, which had not received much attention until recently. We hope that our approach will open the new frontier in chiral organic molecules from chiral molecular chemistry to chiral molecular science.

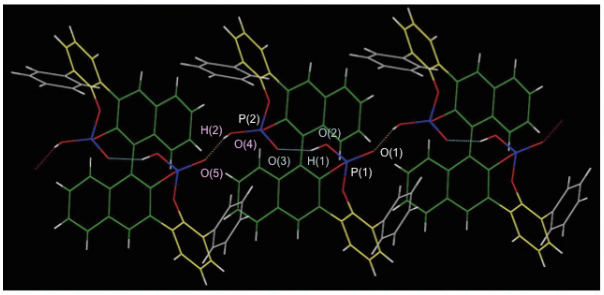

Figure 1. Hydrogen bonding network in chiral bis-phosphoric acid catalyst derived from (*R*)-3,3'-di(2-hydroxy-3 -arylphenyl)binaphthol. Hydrogen bond acts as activation unit for the substrate in asymmetric reaction space and controls atropisomeric behavior in naphthyl–phenyl axis.

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- T. P. Yoon and E. N. Jacobsen, *Science* **299**, 1691–1693 (2003).
- N. Momiyama and H. Yamamoto, "Brønsted Acid Catalysis of Achiral Enamine for Regio- and Enantioselective Nitroso Aldol Synthesis," *J. Am. Chem. Soc.* **127**, 1080–1081 (2005).
- N. Momiyama, H. Tabuse and M. Terada, "Chiral Phosphoric Acid-Governed Anti-Diastereoselective and Enantioselective Hetero-Diels–Alder Reaction of Glyoxylate," *J. Am. Chem. Soc.* **131**, 12882–12883 (2009).
- N. Momiyama, T. Konno, Y. Furiya, T. Iwamoto and M. Terada, "Design of Chiral Bis-Phosphoric Acid Catalyst Derived from (*R*)-3,3'-Di(2-hydroxy-3-arylphenyl)binaphthol: Catalytic Enantioselective Diels–Alder Reaction of α,β-Unsaturated Aldehydes with Amidodienes," *J. Am. Chem. Soc.* **133**, 19294–19297 (2011).
- N. Momiyama, H. Tabuse, H. Noda, M. Yamanaka, T. Fujinami, K. Yamanishi, A. Izumiseki, K. Funayama, F. Egawa, S. Okada, H. Adachi and M. Terada, "Molecular Design of a Chiral Brønsted Acid with Two Different Acidic Sites: Regio-, Diastereo-, and Enantioselective Hetero-Diels–Alder Reaction of Azopyridinecarboxylate with Amidodienes Catalyzed by Chiral Carboxylic Acid–Monophosphoric Acid," *J. Am. Chem. Soc.* **138**, 11353–11359 (2016).

1. Design of Hydrogen Bond-Based Molecular Catalysts

Allylation of imines with allylic metal reagents has been one of the most valuable tools to synthesize enantioenriched homoallylic amines. Due to the inherent nature of allylic metal reagent, however, regioselectivity has been a long-standing subject in this area. To develop the synthetic reaction for enantioenriched linear homoallylic amines, we discovered chirality transferred formal 1,3-rearrangement of ene-aldimines in the presence of Brønsted acid, and developed it as synthetic method for variety of enantioenriched linear homoallylic amines.[1] Furthermore, we studied details of reaction mechanism and succeeded catalytic asymmetric version of this rearrangement.[2] On the basis of our discovery, catalytic asymmetric version of this reaction was developed.[3] To the best our knowledge, our discovery is the first example of catalytic asymmetric methylene migration.

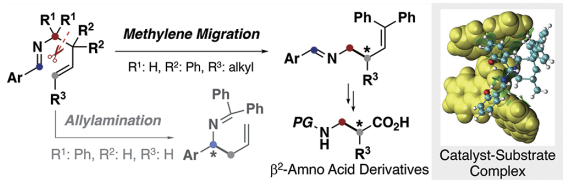

Figure 2. Asymmetric counteranion-directed catalysis *via* OH···O, CH···O, CH···π, π···π interactions.

Perfluorinated aryls have emerged as an exquisite class of motifs in the design of molecular catalysts, and their electronic and steric alterations lead to notable changes in the chemical yields and the stereoselectivities. We developed the perfluoaryls-incorporated chiral mono-phosphoric acids as chiral Brønsted acid catalysts that can deliver high yields and stereoselectivities in the reactions of imines with unactivated alkenes. We have described the first example of a diastereo- and enantioselective [4+2] cycloaddition reaction of *N*-benzoyl imines, as well as the enantioselective three-component imino–ene reaction using aldehydes and $FmocNH_2$.[4]

We have developed (*R*)-3,3'-di(2-hydroxy- 3-arylphenyl) binaphthol derived chiral bis-phosphoric acid which efficiently catalyzed enantioselective Diels–Alder reaction of acroleins with amidodienes.[5,6] We demonstrated that two phosphoric acid groups with individually different acidities can play distinct roles in catalyst behavior through hydrogen bonding interactions. Therefore, we developed a Brønsted acid with two different acidic sites, aryl phosphinic acid-phosphoric acid.[7] Furthermore, molecular design of a chiral Brønsted acid with two different acidic sites, chiral carboxylic acid–cyclic mono-phosphoric acid, was identified as a new and effective concept in asymmetric hetero-Diels–Alder reaction of 2-azopyridinoester with amidodienes.[8]

2. Design of Halogen Bond-Based Molecular Catalysts

Halogen bonds are attractive non-covalent interactions between terminal halogen atoms in compounds of the type R—X (X = Cl, Br, I) and Lewis bases LBs. It has been known that strong halogen bonds are realized when "R" is highly electronegative substituents such as perfluorinated alkyl or aryl substituents. On the basis of electrophilic feature for halogen atom, we have examined it to develop catalysis with halogen bond for carbon–carbon bond forming reactions.[9,10]

We found that perfluorinated iodoaryls are able to catalyze the allylation reaction to *N*-activated heteroaromatics. On the basis of this discovery, a quantitative approach was studied using 4-substituted perfluorinated iodobenzene.[11] Examination of the electrostatic potential surfaces showed that substituent R groups significantly affected the charge density of iodine, fluorine, and carbon on the benzene ring. ^{19}F NMR titrations were used to determine the binding constants *K* for chloride, and their catalytic activities were evaluated in the allylation reaction. We revealed that the log *K* and product yields were linearly correlated, and that they were dependent on the Hammett substituent parameter, σ_{meta}. This linear correlation provided a quantitative predictive model for both the binding constant and the reaction yield. Concomitantly, this efficiently permitted the development of a highly active anion-binding catalyst, namely 4-CNC_6F_4I. The catalytic activity of 4-CNC_6F_4I was established in the allylation and crotylation of silatrane reagents to *N*-activated isoquinolines.

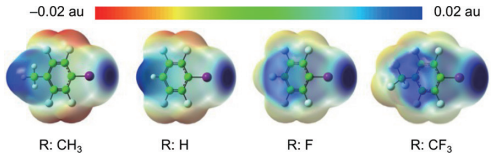

Figure 3. Molecular electrostatic potential surfaces of 4-RC_6F_4I (R: CH_3, H, F, and CF_3) at the M06-2X-D3/6-311+G(d,p)-SDD level of theory.

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2) N. Momiyama, Y. Honda, T. Suzuki and C. Jongwohan, *Asian J. Org. Chem.* **10**, 2205–2212 (2021). [Invitation only, special collection on the Topic of Organocatalysis]
3) N. Momiyama, A. C. Jongwohan, N. Ohtsuka, P. Chaibuth, T. Fujinami, K. Adachi and T. Suzuki, *J. Org. Chem.* **87**, 9399–9407 (2022).
4) N. Momiyama, H. Okamoto, J. Kikuchi, T. Korenaga and M. Terada, *ACS Catal.* **6**, 1198–1204 (2016).
5) N. Momiyama, T. Konno, Y. Furiya, T. Iwamoto and M. Terada, *J. Am. Chem. Soc.* **133**, 19294–19297 (2011).
6) N. Momiyama, K. Funayama, H. Noda, M. Yamanaka, N. Akasaka, S. Ishida, T. Iwamoto and M. Terada, *ACS Catal.* **6**, 949–956 (2016).
7) N. Momiyama, T. Narumi and M. Terada, *Chem. Commun.* **51**, 16976–16979 (2015).
8) N. Momiyama, H. Tabuse, H. Noda, M. Yamanaka, T. Fujinami, K. Yamanishi, A. Izumiseki, K. Funayama, F. Egawa, S. Okada, H. Adachi and M. Terada, *J. Am. Chem. Soc.* **138**, 11353–11359 (2016).
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Creation of Novel Photonic-Electronic-Magnetic Functions Based on Molecules with Open-Shell Electronic Structures

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Keywords Radical, Open-Shell Electronic States, Photonic-Electronic-Magnetic Properties

The molecules with open-shell electronic states can exhibit unique properties, which are difficult to achieve for conventional closed-shell molecules. Our group develops new open-shell organic molecules (= radicals) and metal complexes to create novel photonic-electronic-magnetic functions.

While conventional closed-shell luminescent molecules have been extensively studied as promising components for organic light-emitting devices, the luminescent properties of radicals have been much less studied because of their rarity and low chemical (photo-)stability. We have developed highly photostable luminescent organic radicals, PyBTM and its analogues, and investigated photofunctions attributed to their open-shell electronic states. We have discovered that (i) PyBTM-doped molecular crystals exhibit photoluminescence at RT with φ_{em} = 89%, which is exceptionally high in radicals, (ii) radical-doped crystals and radical-based coordination polymers exhibit drastic changes in the emission spectra by applying a magnetic field. These are the first demonstrations of magnetoluminescence in radicals, and are attributed to interplay between the spin and the luminescence. Our studies provide novel and unique concepts in molecular photonics, electronics, and spintronics, and also bring innovative ideas in the development of light-emitting devices.

Our group focuses on strongly-interacted spins in molecular crystals. The anisotropic assembly of open-shell molecules in crystalline states enables unique molecular materials with exotic electrical and magnetic properties, such as superconductors, ferromagnets, and quantum spin liquids.

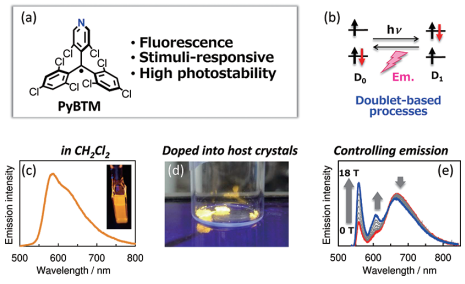

Figure 1. (a) Molecular structure of PyBTM and its characteristics. (b) Schematic photoexcitation-emission processes. (c) Emission in CH_2Cl_2. (d) Emission of PyBTM-doped molecular crystals. (e) Controlling emission by magnetic field.

Selected Publications

- S. Kimura, M. Uejima, W. Ota, T. Sato, S. Kusaka, R. Matsuda, H. Nishihara and T. Kusamoto, "An Open-Shell, Luminescent, Two-Dimensional Coordination Polymer with a Honeycomb Lattice and Triangular Organic Radical," *J. Am. Chem. Soc.* **143**, 4329–4338 (2021).
- S. Kimura, T. Kusamoto, S. Kimura, K. Kato, Y. Teki and H. Nishihara, "Magnetoluminescence in a Photostable, Brightly Luminescent Organic Radical in a Rigid Environment," *Angew. Chem., Int. Ed.* **57**, 12711–12715 (2018).
- Y. Hattori, T. Kusamoto and H. Nishihara, "Enhanced Luminescent Properties of an Open-Shell (3,5-Dichloro-4-pyridyl)bis(2,4,6-trichlorophenyl)methyl Radical by Coordination to Gold," *Angew. Chem., Int. Ed.* **54**, 3731–3734 (2015).
- Y. Hattori, T. Kusamoto and H. Nishihara, "Luminescence, Stability, and Proton Response of an Open-Shell (3,5-Dichloro-4-pyridyl)bis(2,4,6-trichlorophenyl)methyl Radical," *Angew. Chem., Int. Ed.* **53**, 11845–11848 (2014).

1. A Novel Organic Quantum Spin Liquid Material with a Triangular Lattice

Quantum spin liquid (QSL) is a novel quantum state of matter, in which charges are localized while spins are highly fluctuating. In general, interacting spins with antiferromagnetic (AFM) exchange couplings result in long-range ordered magnetic ground state at low temperatures, with vanishing the spin entropy. On the other hand, spins in QSL that are entangled strongly remain highly fluctuating with high entropy even at very low temperatures. In QSL materials, geometrical frustrations, in addition to quantum fluctuations, are suggested to play a critical role. Among them, organic crystalline solids with triangular lattices have attracted much attention because of their intriguing properties at low temperatures. So far, organic QSL materials are rarely reported, which limits in-depth investigation for elucidating the fundamental characteristics of the QSL. In this study, we prepared a novel triangular-lattice organic QSL material (Et-4IT)[Ni(mnt)$_2$]$_2$, and the structure and physical properties were investigated (Figure 2a).[1] The Ni(mnt)$_2$ anions constructed *k*-type molecular arrangement in the crystal. The two crystallographically independent anion layers both realized Mott insulating states, showing that (Et-4IT)[Ni(mnt)$_2$]$_2$ is a novel bilayer Mott system. The magnetic susceptibility and magnetic torque measurements and low-temperature heat capacity measurements confirmed the absence of the long-range magnetic ordering down to 25 mK with an appreciably significant γ value of 94 ± 7 mJ K^{-2} mol^{-1}. The AFM interaction ($J/k_B \sim -24$ K) detected between the spins was much smaller than that in the other organic QSLs, while χ_0 and γ values were larger. We found significant relationships, χ_0, $\gamma \propto 1/J$, for all the organic QSLs (Figure 2b). These results suggest the presence of the spinon Fermi surface in the QSLs.

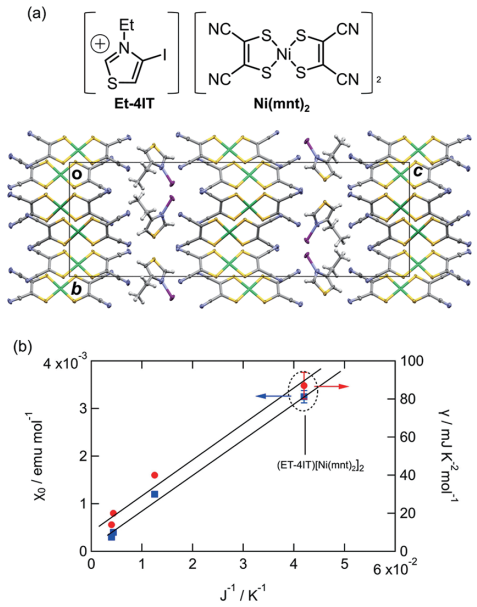

Figure 2. (a) Chemical and crystal structures of (Et-4IT)[Ni(mnt)$_2$]$_2$. (b) γ-J^{-1} and χ_0-J^{-1} plots for organic QSLs.

2. Development of Two-Dimensional Kagome-Honeycomb Lattice Coordination Polymer Based on Triangular Radical

Two-dimensional (2D) open-shell coordination polymers (CPs) with honeycomb, Kagome, and Kagome-honeycomb hybrid lattices have attracted growing interest because of the exotic electronic structures and physical properties attributed to the structural topology. Employing organic radicals as building blocks is a promising approach to producing open-shell CPs, where structural topology and efficient electronic and magnetic interaction between the radical ligands and the metal ions enable peculiar electrical, magnetic, and photonic properties. Recently, we have prepared a highly-crystalline 2D honeycomb lattice CP, trisZn, via coordination of a triangular-shaped organic radical tris(3,5-dichloro-4-pyridyl)methyl radical (trisPyM) to Zn ions.[2] The coordination structure of trisZn was stable under evacuation at 60 °C. trisZn exhibited photoluminescence below 79 K at λ_{em} = 695 nm. Importantly, trisZn demonstrated magnetoluminescence below 20 K.[3] This is the first example showing magnetoluminescence of pure (*i.e.*, non-doped) radical compounds. trisPyM can be a promising building block in constructing a new class of 2D CPs with spin-correlated novel photofunctions. In this study, we aimed to create a Kagome-honeycomb hybrid lattice CP with magnetic functions by employing a magnetic ion Cu^{II} instead of the nonmagnetic Zn^{II}. The synthesized 2D CP, trisCu, was isostructural to trisZn, where the Cu^{II} ions constructed a Kagome lattice while trisPyMs formed a honeycomb lattice. In this situation, efficient magnetic couplings between the Cu^{II} ions and the radicals extended onto two dimensions were expected to induce strong magnetic anisotropy.

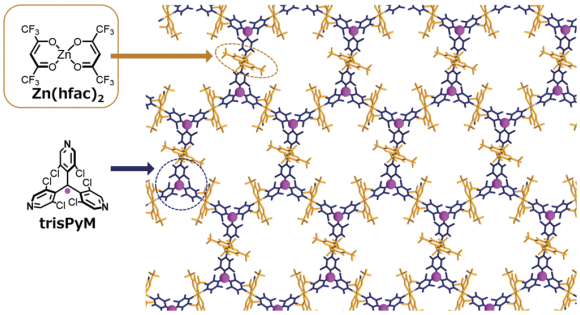

Figure 3. Crystal structure of trisZn and the chemical structure of the components.

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Design and Synthesis of Three-Dimensional Organic Structures

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2017 Chemical Society of Japan Award for Young Chemists
2018 The Commendation for Science and Technology by the Minister of Education, Culture, Sports, Science and Technology
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Keywords π-Conjugated Molecules, Molecular Topology, 3D Network Polymer

Aromatic compounds are potentially useful as functional electronic materials. However, the controlled synthesis and assembly of three-dimensional complex molecules are still very difficult, especially for the crystal engineering of organic molecules. This group aims to create novel topological and reticular organic structures by using synthetic organic chemistry and geometric insights.

To achieve our purpose, this group will start electron-diffraction crystallography (MicroED) for the rapid structure determination of organic compounds. While X-ray crystallography is a general and reliable method for structure determination, it requires ~0.1 mm single crystals and making such crystal sometimes needs tremendous times and efforts. Since electron beam have much higher diffraction intensity than X-ray, structural analysis can be performed even with ultra-small crystals (1 μm or less). There are many fields such as covalent organic crystals with a three-dimensional structure and molecules with complex molecular topologies, where structural analysis has not been sufficiently developed.

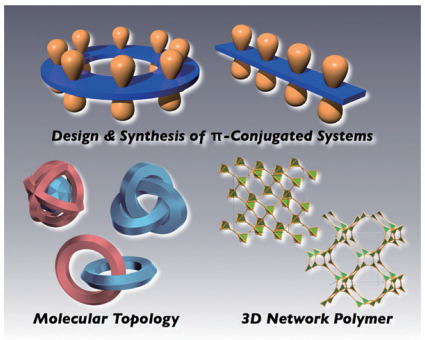

Figure 1. Design and synthesis of π-conjugated organic molecules (top); Development of novel molecular topology (bottom left); Construction of three-dimensional network polymers (bottom right).

Selected Publications

- Y. Segawa, T. Watanabe, K. Yamanoue, M. Kuwayama, K. Watanabe, J. Pirillo, Y. Hijikata and K. Itami, "Synthesis of a Möbius Carbon Nanobelt," *Nat. Synth.* **1**, 535–541 (2022).DOI: 10.1038/s44160-022-00075-8
- K. Kato, K. Takaba, S. Maki-Yonekura, N. Mitoma, Y. Nakanishi, T. Nishihara, T. Hatakeyama, T. Kawada, Y. Hijikata, J. Pirillo, L. T. Scott, K. Yonekura, Y. Segawa and K. Itami, "Double-Helix Supramolecular Nanofibers Assembled from Negatively Curved Nanographenes," *J. Am. Chem. Soc.* **143**, 5465–5469 (2021).
- K. Y. Cheung, K. Watanabe, Y. Segawa and K. Itami, "Synthesis of a Zigzag Carbon Nanobelt," *Nat. Chem.* **13**, 255–259 (2021).
- Y. Segawa, D. R. Levine and K. Itami, "Topologically Unique Molecular Nanocarbons," *Acc. Chem. Res.* **52**, 2760–2767 (2019).
- Y. Segawa, M. Kuwayama, Y. Hijikata, M. Fushimi, T. Nishihara, J. Pirillo, J. Shirasaki, N. Kubota and K. Itami, "Topological Molecular Nanocarbons: All-Benzene Catenane and Trefoil Knot," *Science* **365**, 272–276 (2019).
- G. Povie, Y. Segawa, T. Nishihara, Y. Miyauchi and K. Itami, "Synthesis of a Carbon Nanobelt," *Science* **356**, 172–175 (2017).
- Y. Segawa and D. W. Stephan, "Metal-Free Hydrogenation Catalysis of Polycyclic Aromatic Hydrocarbons," *Chem. Commun.* **48**, 11963–11965 (2012).

1. Möbius Carbon Nanobelt

Technologies for the creation of topological carbon nanostructures have greatly advanced synthetic organic chemistry and materials science. Although simple molecular nanocarbons with a belt topology have been constructed, analogous carbon nanobelts with a twist—more specifically, Möbius carbon nanobelts (MCNBs), have not yet been synthesized owing to their high intrinsic strain. Herein, we report the synthesis, isolation and characterization of a MCNB. Calculations of strain energies suggest that large MCNBs are synthetically accessible. Designing a macrocyclic precursor with an odd number of repeat units led to a successful synthetic route via *Z*-selective Wittig reactions and nickel-mediated intramolecular homocoupling reactions, which yielded (25,25) MCNB over 14 steps (Figure 2a). NMR spectroscopy and theoretical calculations reveal that the twist moiety of the Möbius band moves quickly around the MCNB molecule in solution (Figure 2b,c). The topological chirality originating from the Möbius structure was confirmed experimentally using chiral HPLC separation and CD spectroscopy.

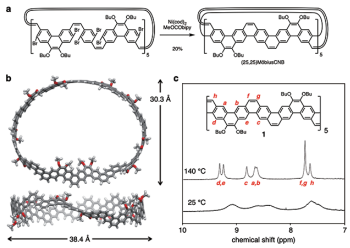

Figure 2. (a) Synthesis of (25,25)MCNB. (b) Structure of (25,25) MCNB. (c) ^{1}H NMR spectra of (25,25)MCNB.

2. Perfluorocycloparaphenylene

Perfluorinated aromatic compounds, the so-called *perfluoroarenes*, are widely used in materials science owing to their high electron affinity and characteristic intermolecular interactions. However, methods to synthesize highly strained perfluoroarenes are limited, which greatly limits their structural diversity. Herein, we report the synthesis and isolation of perfluorocycloparaphenylenes (PFCPPs) as a class of ring-shaped perfluoroarenes. Using macrocyclic nickel complexes, we succeeded in synthesizing PF[*n*]CPPs (*n* = 10, 12, 14, 16) in one-pot without noble metals (Figure 3a). The molecular structures of PF[*n*]CPPs (*n* = 10, 12, 14) were determined by X-ray crystallography to confirm their tubular alignment (Figure 3b,c). Photophysical and electrochemical measurements revealed that PF[*n*]CPPs (*n* = 10, 12, 14) exhibit wide HOMO–LUMO gaps, high reduction potentials, and strong phosphorescence at low temperature. PFCPPs are not only useful as electron-accepting organic materials but can also be used for accelerating the creation of topologically unique molecular nanocarbon materials.

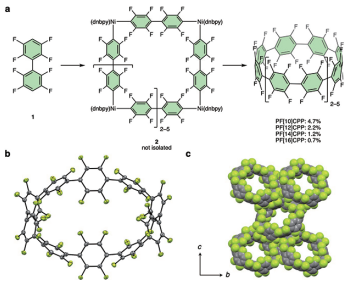

Figure 3. (a) Synthesis of PFCPPs. (b) ORTEP of PF[10]CPP. (c) Packing structure of PF[10]CPP.

3. A Photochromic Carbazolyl-Imidazolyl Radical Complex

Optical phenomena which occur on a timescale of microseconds to milliseconds are instantaneous or invisible for human visions, whereas they can be easily detected by conventional photodetectors. Therefore, fast photoswitching materials that work in these time ranges have received considerable attention for the applications to bioimaging, anti-counterfeiting, and dynamic holographic materials. Here we report the synthesis of carbazole-incorporated photochromic radical complex.[3] The molecular structure of **CIC-tBuPh** was determined by X-ray crystallography (Figure 4a). The long-wavelength photosensitivity of the photochromic reaction of the molecule is enhanced up to ~580 nm by substituting a triphenyl amine group to the 3-position of the carbazole moiety. These photochromic reactions are investigated by subpicosecond-to-microsecond transient absorption measurements (Figure 4b).

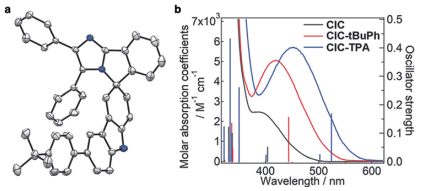

Figure 4. (a) ORTEP representation of **CIC-tBuPh** with thermal ellipsoids (50% probability), where the nitrogen atom is highlighted in blue. Hydrogen atoms and solvent molecules are omitted for clarity. (b) Steady-state absorption spectra of **CIC**, **CIC-tBuPh** and **CIC-TPA** in benzene at room temperature. Vertical lines indicate the theoretical spectra of each molecule.

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3) Y. Kawanishi, Y. Segawa, K. Mutoh, J. Abe and Y. Kobayashi, *Chem. Commun.* **58**, 4997–5000 (2022).

Awards

SEGAWA, Yasutomo; Chemist Award BCA 2021 (2021).
SEGAWA, Yasutomo; Thieme Chemistry Journals Award 2022 (2022).
SEGAWA, Yasutomo; 62nd Academic Encouragement Award from the Ube Industries Foundation (2022).

Visiting Professors

Visiting Professor
FUKAZAWA, Aiko *(from Kyoto University)*

Renaissance of Nonbenzenoid π-Conjugated Systems toward Functional Materials

The work of our group has focused on exploring functional organic compounds with unusual superb optical and/or electronic properties, based on the molecular designs of novel π-conjugated scaffolds as well as unusual functional groups. In particular, we have recently proposed a rational design of stable yet unusual π-conjugated systems based on the characteristics of nonbenzenoid hydrocarbons such as dehydroannulenes and non-alternant hydrocarbons by annulation of weakly aromatic (hetero)arenes. This year, we have succeeded in synthesizing several thiophene-fused antiaromatic π-systems that exhibit high thermal stability even without bearing bulky substituents while retaining pronounced antiaromatic character. Moreover, we have recently succeeded in synthesizing the fulvalene-based π-conjugated oligomers that exhibit exceptional electron-accepting character as well as robustness toward multi-electron reduction.

Visiting Associate Professor
UEDA, Akira *(from Kumamoto University)*

Development of Neutral Radical Molecular Conductors with Intramolecular Charge Degrees of Freedom

Design and synthesis of novel molecular materials have been a central issue for the development of molecular science. In this work, we have successfully developed a new type of neutral radical molecular conductor crystals with intramolecular charge degrees of freedom. Measurements of X-ray diffraction, electrical resistivity, and magnetic susceptibility have revealed that this new type of charge degrees of freedom is coupled to the intermolecular charge degrees of freedom, leading to unique strongly correlated electron phenomena and properties in molecular materials. In particular, we emphasize that the successful formation of a 3/4-filled electron band in this system is an unprecedented event in neutral molecular solids, which allows not only the realization of an ambient-pressure metallic state but also the emergence of exotic Mott insulating states relevant to the charge degrees of freedom. These results offer new possibilities of neutral radical solids as a molecular strongly correlated electron system.

Visiting Associate Professor
KAMIYA, Yukiko *(from Nagoya University)*

Expand the Artificial Nucleic Acid World Based on the Studies of Molecular Science

Nucleic acids (DNA and RNA) are essential biopolymers that carry genetic information in all living organisms. On the other hand, various artificial nucleic acids (XNAs) having ribose-modified or non-ribose type backbone and nucleic acid recognition ability have been developed. One of the motivation of XNA study is development of nucleic acid drugs. Another big motivation is addressing the fundamental question why nature selected ribose as backbone of genetic materials. Our group has focused on amino acid-type artificial nucleic acids and we are studying on characterization of their molecular recognition properties, design of unique structures, and development of molecular tools and drugs that target RNA as applications. The unique feature of the XNAs is that they form highly stable homo-duplex than XNA/RNA hetero duplex. In the recent study we have developed the methodology that can control the hybridization of XNA/XNA and XNA/RNA by designing the nucleobase structures.