RESEARCH ACTIVITIES
Theoretical and Computational Molecular Science

The Department aims to advance the understanding and prediction of static and dynamic properties, reactions, and functions in condensed-phase systems, such as biomolecular and heterogeneous catalytic systems, through the development of novel theories and computational methodologies grounded in quantum mechanics, statistical mechanics, and solid-state physics. The Department collaborates with the Research Center for Computational Science on research.

Theoretical Studies on Reactions, Functions, and Fluctuations in Condensed-Phase Systems

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Division of Theoretical Molecular Science I

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Professional Employment
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Keywords Reactions, Functions, Fluctuations

Our research centers on complex fluctuations in condensed systems, including supercooled liquids and biomolecules. These fluctuations significantly influence various properties, functions, and reactions. By investigating the dynamics and fluctuations in these molecular systems, we aim to uncover the molecular origins of these properties, functions, and reactions.

We have pioneered advanced computational methods for multi-dimensional nonlinear spectroscopy, enabling us to elucidate the molecular basis of ultrafast energy relaxation and the temporal evolution of nonuniform fluctuations in liquid water that conventional linear spectroscopy has not revealed. Additionally, we have delved into the dynamical heterogeneity of supercooled liquids, characterized by slow, inhomogeneous structural changes driven by fluctuations. Using a three-time correlation function, we unveiled the dynamic coupling of structural fluctuations across different time scales in proteins.

Our research has also focused on the anomalous properties of water, establishing a link between these anomalies and previously hidden structural and dynamical characteristics. Recently, we developed a novel analytical method for studying dynamical disorder based on stochastic process theory, elucidating the mechanisms behind slowing structural changes as systems approach the glass transition.

In the realm of biomolecular systems, structural fluctuations and conformational changes are crucial for functional expression. Our studies on enzymatic reactions underscore the importance of specific prepared conformational states that facilitate these reactions. Furthermore, we have probed the molecular origins of dynamic disorder within protein conformational dynamics, revealing the complexity of these processes. Our investigations also extend to the molecular mechanisms underlying efficient excitation energy transfer in photosynthetic systems.

Through these efforts, we are engaged in a broad spectrum of theoretical and computational studies to unravel the dynamical phenomena that govern condensed-phase systems.

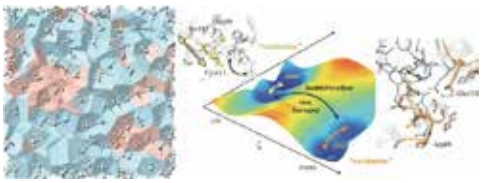

Figure 1. Snapshot of two-state model in supercooled water consisting of high- and low-density liquids (left) and schematic of 2D free energy surface for enzymatic reaction (right).

Selected Publications

- T. Yagasaki and S. Saito, *Annu. Rev. Phys. Chem.* **64**, 55–75 (2013), T. L. C. Jansen, S. Saito, J. Jeon and M. Cho, *J. Chem. Phys. (Perspective)* **150**, 100901 (17 pages) (2019), C. R. Baiz *et al.*, *Chem. Rev.* **120**, 7152–7218 (2020).
- K. Kim and S. Saito, *J. Chem. Phys. (Special Topic on Glass Transition)* **138**, 12A506 (12 pages) (2013).
- S. Saito, B. Bagchi and I. Ohmine, *J. Chem. Phys.* **149**, 124504 (8 pages) (2018), S. Saito and B. Bagchi, *J. Chem. Phys.* **150**, 054502 (14 pages) (2019), S. Saito, *J. Chem. Phys.* **160**, 194506 (13 pages) (2024).
- J. Ono, Y. Matsumura, T. Mori and S. Saito, *J. Phys. Chem. B (Perspective)* **128**, 20–32 (2024).
- S. Saito, M. Higashi and G. R. Fleming, *J. Phys. Chem. B* **123**, 9762–9772 (2019).

1. Flat-Bottom Elastic Network Model for Generating Improved Plausible Reaction Paths[1)]

Rapid generation of a plausible reaction path connecting a given reactant and product in advance is crucial for the efficient computation of precise reaction paths or transition states. We propose a computationally efficient potential energy based on the molecular structure to generate such paths. This potential energy has a flat bottom consisting of structures without atomic collisions while preserving nonreactive chemical bonds, bond angles, and partial planar structures. By combining this potential energy with the direct MaxFlux method, a recently developed reaction-path/transition-state search method, we can find the shortest plausible path passing within the bottom. Numerical results show that this combination yields lower energy paths compared to the paths obtained by the well-known image-dependent pair potential. We also theoretically investigate the differences between these two potential energies. The proposed potential energy and path generation routine are implemented in our Python version of the direct MaxFlux method, available on GitHub.

2. Development of Molecular Dynamics Parameters and Theoretical Analysis of Excitonic and Optical Properties in the Light-Harvesting Complex II[2)]

The light-harvesting complex II (LHCII) in green plants exhibits highly efficient excitation energy transfer (EET). A comprehensive understanding of the EET mechanism in LHCII requires quantum chemical, molecular dynamics (MD), and statistical mechanics calculations that can adequately describe pigment molecules in heterogeneous environments. Herein, we develop MD simulation parameters that accurately reproduce the quantum mechanical/molecular mechanical energies of both the ground and excited states of all chlorophyll (Chl) molecules in membrane embedded LHCII. The present simulations reveal that Chl *a* molecules reside in more inhomogeneous environments than Chl *b* molecules. We also find a narrow gap between the exciton energy levels of Chl *a* and Chl *b*. In addition, we investigate the nature of the exciton states of Chl molecules, such as delocalization, and analyze the optical spectra of LHCII, which align with experimental results. Thus, the MD simulation parameters developed in this study successfully reproduce the excitonic and optical properties of the Chl molecules in LHCII, validating their effectiveness.

3. Fast Diffusion of Water along Carbon Nanotube near the Wall[3)]

The diffusion of water in carbon nanotubes (CNTs) is debated, particularly whether it is faster near the CNT wall or at the center and how the temperature influences this effect. Using molecular dynamics (MD) simulations, we study radially resolved water diffusion in CNT(26,26) (3.57 nm diameter) over a wide temperature range. Diffusion along the CNT axis is significantly enhanced compared to that of bulk water, with the effect intensifying at lower temperatures. Supercooling further amplifies this enhancement following near-Arrhenius behavior. Confinement has a smaller impact on the rotational dynamics. By resolving water motion into radial layers, we find that both translational and rotational dynamics are higher near the CNT wall due to weakened hydrogen bonding. The presence of dangling O−H bonds reduces friction at the CNT−water interface. Revisiting an NMR study, we suggest that the high-intensity peak corresponds to central layers, aligning with our MD results and refining our insights into confined water dynamics.

4. Correlated Flat-Bottom Elastic Network Model for Improved Bond Rearrangement in Reaction Paths[4)]

This study introduces correlated flat-bottom elastic network model (CFB-ENM), an extension of our recently developed flat-bottom elastic network model (FB-ENM) for generating plausible reaction paths, *i.e.*, collision-free paths preserving nonreactive parts. While FB-ENM improved upon the widely used image-dependent pair potential (IDPP) by addressing unintended structural distortion and bond breaking, it still struggled with regulating the timing of series of bond breaking and formation. CFB-ENM overcomes this limitation by incorporating structure-based correlation terms. These terms impose constraints on pairs of atom pairs, ensuring immediate formation of new bonds after breaking of existing bonds. Using the direct MaxFlux method, we generated paths for 121 reactions involving main group elements and 35 reactions involving transition metals. We found that CFB-ENM significantly improves reaction paths compared to FB-ENM. CFB-ENM paths exhibited lower maximum DFT energies along the paths in most reactions, with nearly half showing significant energy reductions of several tens of kcal/mol. In the few cases where CFB-ENM yielded higher energy paths, most increases were below 10 kcal/mol. We also confirmed that CFB-ENM reduces computational costs in subsequent precise reaction path or transition state searches compared to FB-ENM. An implementation of CFB-ENM based on the Atomic Simulation Environment is available on GitHub for use in computational chemistry research.

References

1) S.-i. Koda and S. Saito, *J. Chem. Theory Comput.* **20**, 7176–7187 (2024).
2) Z. Zhu, M. Higashi and S. Saito, *J. Chem. Theory Comput.* **21**, 413–427 (2025).
3) G. R. Kahn, S. Saito and S. Daschakraborty, *J. Phys. Chem. B* **129**, 6561–6573 (2025).
4) S.-i. Koda and S. Saito, *J. Chem. Theory Comput.* **21**, 3513–3522 (2025).

Theoretical Studies of Functional Molecular Systems and Heterogeneous Catalysts

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2008 Professor, Institute for Molecular Science
Professor, The Graduate University for Advanced Studies
2012 Professor, Elements Strategy Initiative for Catalysts and Batteries (ESICB), Kyoto University (additional post, –2022)

Awards
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Keywords Quantum Chemistry, Photochemistry, Heterogeneous Catalysis

We develop the useful electronic structure theories and investigate the photochemistry and catalysis theoretically. Currently, we focus on the following research subjects.

(1) Inverse design and theory for complex electronic states

We are interested in improving the various functions of molecular systems. Inverse design approach can optimize the functions in the "functional space." Recently, we adopted the inverse design approach and succeeded in maximizing various photofunctions of the molecular aggregates and molecule-nanoparticle systems. We also work on developing electronic structure theories for complex electronic states such as CAP/SAC-CI method for locating metastable resonance states.

(2) Nanocluster and heterogeneous catalysts

We proceeded the national project of Element Strategy Initiatives for Catalysts and Batteries (ESICB) where we focused on the developments of the platinum-group metal (PGM) reduced or PGM-free catalysts. We also investigated the nanocluster and heterogeneous catalysts for the fuel cells and fine chemicals like Pt, PtCo and PtNi sub-nanoclusters for oxygen reduction reaction (ORR), Pd-Au alloy nanoparticle for hydrosilylation, Niobium oxide surface for direct synthesis of various amides and imides.

(3) Functions of *C*-centered Au(I) based clusters

We theoretically investigate the various functions of metal nanoclusters. In the recent project, we worked on *C*-centered Au(I) based clusters such as chiral induction of CAu^{I}_{6} cluster with monodentate *N*-heterocyclic carbene (NHC) ligands, intense emission of $CAu^{I}_{6}Ag^{I}_{n}$ (n = 2–4) and $CAu^{I}_{6}Cu^{I}_{2}$ clusters and its biological application, vapochromism of CAu^{I}_{6} cluster, and the generation of CAu^{I}_{5} cluster and its red-shifted PL as well as catalytic activity.

(4) Photofunctional materials: Perovskite solar cells and modified single-walled carbon nanotubes (SWCNTs)

Recently, we worked on the method to fabricate high-quality multi-junction Sn-Pb perovskite semiconductor films. We elucidated the mechanism of how the phenylalanine cation interacts with the constituent ions of perovskite and their composed species during the solution stage. We also have investigated the selective PL from modified SWCNTs which enhances their PLs with red-shifted peaks. Previously, we proposed the substitution rule using Clar-sextet theory. We achieved the control of near-IR PL, the selective E_{11}^{**} PL (~1,200 nm) by tether alkyl functionalization, and the PL in telecommunication wavelength (>1,300 nm) by perfluoroalkyl functionalization.

Selected Publications

- T. Shiraogawa, G. Dall'Osto, R. Cammi, M. Ehara and S. Corni, "Inverse Design of Molecule-Metal Nanoparticle Systems Interacting with light for the Desired Photophysical Properties," *Phys. Chem. Chem. Phys.* **24**, 22768 (2022).
- H. Miura, K. Imoto, H. Nishio, A. Junkaew, Y. Tsunesada, Y. Fukata, M. Ehara and T. Shishido, "Optimization of Metal-Support Cooperation for Boosting the Performance of Supported Gold Catalysts for Borylation of C–O and C–N Bonds," *J. Am. Chem. Soc.* **146**, 27528–27541 (2024).
- X.-L. Pei, P. Zhao, H. Ube, Z. Lei, M. Ehara and M. Shionoya, "Single-Gold Etching at the Hypercarbon Atom of *C*-Centred Hexagold(I) Clusters Protected by Chiral *N*-Heterocyclic Carbenes," *Nat. Commun.* **15**, 5024 (2024).
- S. Hu, J. Wang, P. Zhao, M. Ehara, R. A. J. Janssen, A. Wakamiya, H. J. Snaith *et al.*, "Steering Perovskite Precursor Solution for Multijunction Photovoltaics," *Nature* **639**, 93–101 (2025).

1. Developing Interface Structure Control for Tin-Containing Perovskite Semiconductors and Elucidation of Mechanism: Realization of High-Performance Multi-Junction Solar Cells[1)]

Multi-junction solar cells demonstrate superior performance, achieving photovoltaic conversion efficiencies that surpass the radiative limits of single-junction cells. Furthermore, developing high-performance Sn-Pb perovskite semiconductor films is of great importance for thin-film devices. We have developed a method to fabricate high-quality Sn-Pb perovskite semiconductor films by incorporating phenylalanine hydrochloride, a simple compound bearing both amino acid and carboxylic acid groups, into the precursor solutions. Through various spectroscopic measurements and theoretical calculations, we elucidated the mechanism of how the phenylalanine cation interacts with the constituent ions of perovskite and their composed species during the solution stages, providing a global improvement in the bulk and surface quality of the as-deposited films. Single-, double-, and triple-junction solar cells incorporating these high-quality Sn-Pb perovskite layers achieved remarkable open-circuit voltages of 0.91 V, 2.22 V, and 3.46 V, respectively, and power conversion efficiencies of 23.9%, 29.7% (certified value: 29.26%), and 28.7%. Additionally, triple-junction devices with an area of 1 cm^2 demonstrated power conversion efficiencies of up to 28.4% (certified value: 27.28%). Furthermore, for the first time, all-perovskite four-junction devices were fabricated, achieving an impressive open-circuit voltage of 4.94 V and power conversion efficiencies of up to 27.9%.

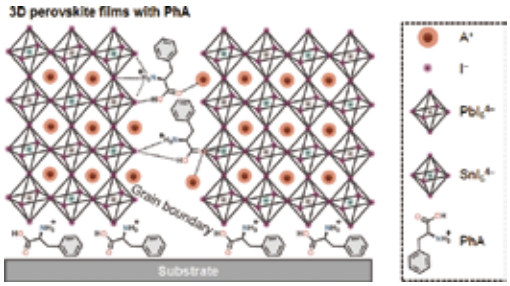

Figure 1. Structural modification at the perovskite bottom interface.

2. Oxidation of *para*-Substituted Benzyl Alcohols by $PdAu_{12}$ Cluster Catalysts: Effect of Pd Atom Doping[2)]

Single-atom doping of atomically size-controlled metal nanoclusters is useful for elucidating doping effects in catalysis. MAu_{12} (M = Au, Ir, Rh, Pt, Pd) nanoclusters were synthesized on a double metal hydroxide composed of Co and Ce. The catalytic activity and activation mechanism for benzyl alcohol oxidation were analysed through both experimental measurements and theoretical calculations. $PdAu_{12}$ exhibited 4.4 times the catalytic activity of Au_{13}, while other MAu_{12} catalysts (M = Ir, Rh, Pt) showed activity comparable to Au_{13}. Periodic DFT calculations based on slab model revealed that oxygen molecules are activated more efficiently on $PdAu_{12}$ than on Au_{13}, indicating that a different mechanism involving an activated oxygen molecule emerges with Pd single doping.

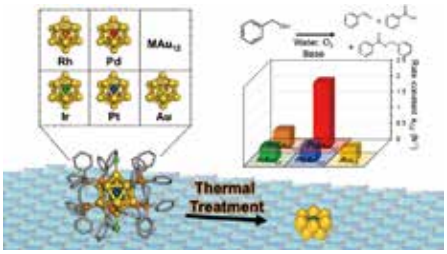

Figure 2. Supported size selective MAu_{12}/Co_3Ce catalyst for alcohol oxidation.

3. Control of Luminescence Wavelength in Modified Single-Walled Carbon Nanotubes Utilizing Steric Hindrance in Reductive Arylation[3)]

To control the luminescent properties of single-walled carbon nanotubes (SWCNTs), we have developed modified SWCNTs. In this study, emission wavelength control was achieved via reductive arylation using monosubstituted and disubstituted iodobenzene derivatives. Chemical modification with substituted iodobenzenes altered the functionalization depending on the position of the substituent on the aryl group, enabling control of both luminescence intensity and wavelength. Introducing a Me or MeO group at the 2-position and Me groups at the 3,5-positions of the phenyl ring increased the selectivity of E_{11}^{**} PL (~1230 nm) and E_{11}^{*} PL (~1100 nm), respectively. Theoretical calculations indicated that the effect of ortho-substituted groups on the relative stability of isomers is greater for diarylated SWCNTs than for hydroarylated ones. Experiments and theoretical calculations revealed that the substitution position on the benzene ring regulates the emission wavelength, influencing the favorable binding configuration of the SWCNT adduct, the relative stability of conformational isomers, and the emission wavelength.

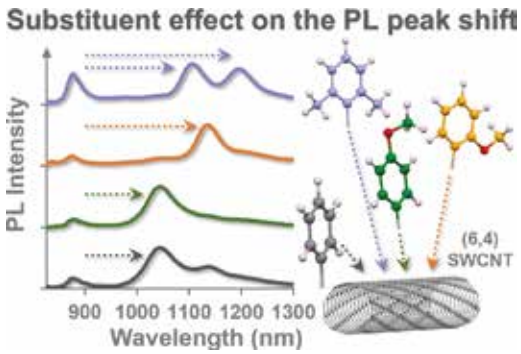

Figure 3. Control of photoluminescence of modified SWCNTs by steric hindrance in reductive arylation.

References

1) S. Hu, J. Wang, P. Zhao, M. Ehara, R. A. J. Janssen, A. Wakamiya, H. J. Snaith *et al*. *Nature* **639**, 93–101 (2025).
2) S. Masuda, H. Hirai, P. Zhao, S. Takano, M. Ehara and T. Tsukuda, *ACS Catal.* **14**, 17123–17131 (2024).
3) Y. Maeda, Y. Iguchi, P. Zhao, A. Suwa, Y. Taki, K. Kawada, M. Yamada, M. Ehara and M. Kako, *Chem. –Eur. J.* **31**, e202404529 (2025).

Molecular Dynamics Simulations of Disease-Related Biomolecules

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Keywords Molecular Dynamics Simulation, Protein, Amyloid

Biomolecules such as proteins and peptides have a complicated free-energy landscape with many local minima. The conventional canonical-ensemble molecular dynamics (MD) simulations tend to get trapped in a few of the local-minimum states. To overcome these difficulties, we have proposed new generalized-ensemble algorithms, such as the replica-permutation method. We apply these methods to proteins and peptides and try to predict the native structures of proteins, as in Figure 1.

We are also interested in disease-related biomolecules. For example, protein aggregates such as spherical substances called oligomers and acicular substances called amyloid fibrils (Figure 2) cause more than 30 kinds of diseases. Alzheimer's disease is thought to be caused by aggregated amyloid-β (Aβ) peptides. To overcome these diseases, it is essential to understand the aggregate genesis and disruption of Aβ peptides. We perform such MD simulations of oligomers and amyloid fibrils.

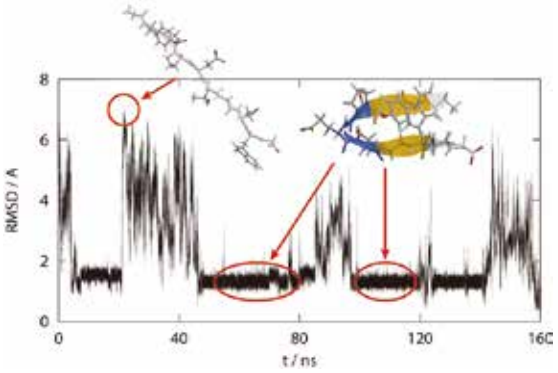

Figure 1. Time series of protein folding simulation.

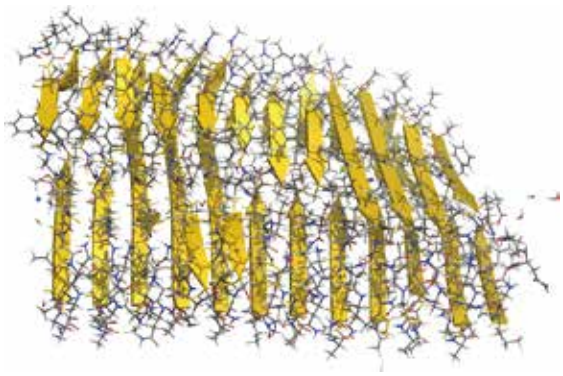

Figure 2. Snapshot of an Aβ amyloid fibril.

Selected Publications

- H. Okumura and S. G. Itoh, "Amyloid Fibril Disruption by Ultrasonic Cavitation: Nonequilibrium Molecular Dynamics Simulations," *J. Am. Chem. Soc.* **136**, 10549–10552 (2014).
- H. Okumura, S. G. Itoh, K. Nakamura and T. Kawasaki, "Role of Water Molecules in the Laser-Induced Disruption of Amyloid Fibrils Observed by Nonequilibrium Molecular Dynamics Simulations," *J. Phys. Chem. B* **125**, 4964–4976 (2021).
- S. Tanimoto, S. G. Itoh and H. Okumura, ""Bucket Brigade" Using Lysine Residues in RNA-Dependent RNA Polymerase of SARS-CoV-2," *Biophys. J.* **120**, 3615–3627 (2021).
- S. G. Itoh, M. Yagi-Utsumi, K. Kato and H. Okumura: "Key Residue for Aggregation of Amyloid-β Peptides," *ACS Chem. Neurosci.* **13**, 3139–3151 (2022).

1. Non-Equilibrium Molecular Dynamics Method to Generate a Poiseuille-Like Flow on a Lipid Bilayer

There are various flows inside and outside cells *in vivo*. It was shown recently that such flows enhance the protein aggregation. Non-equilibrium molecular dynamics (NEMD) simulation is a useful tool for understanding the effects of these flows on the dynamics of biomolecules. However, there was no NEMD simulation to handle a flow on a membrane surface. We thus proposed a NEMD method to generate a Poiseuille-like flow on a lipid bilayer.[1)] We extended the conventional equilibrium MD method to produce a flow by adding constant external force terms for the water molecules (Figure 3). Using the Lagrange multiplier method, the center of mass of the lipid bilayer is constrained so that the flow does not sweep away the lipid bilayer but the individual lipid molecules fluctuate. The temperature of the system is controlled properly in the solution and membrane using the Nosé–Hoover thermostat. We found that the flow between two lipid bilayers is slower than the analytical solution of the Navier-Stokes equations between rigid parallel plates due to fluctuations and deformation of the membrane (Figure 4). This method can be applied not only to a flow on lipid membranes but also to a flow on soft surfaces generally.

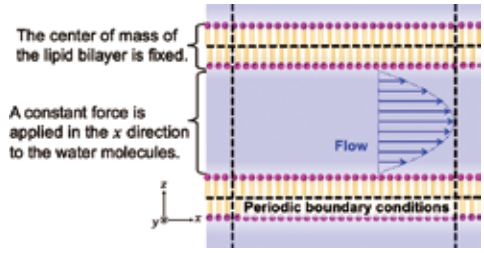

Figure 3. Schematic illustration of the method to generate a flow on bio-membranes.

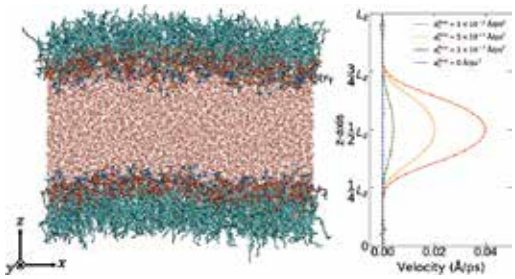

Figure 4. Snapshot during the NEMD simulation and flow velocity profile.

2. Why Do Histone Monomethylation and Dimethylation Cause a Significant Difference in Binding to LEDGF?

Lens epithelium-derived growth factor (LEDGF) is a chromatin-binding protein. It regulates gene transcription and is associated with AIDS and cancer. Its PWWP domain binds to histone H3 at K36 (H3K36). The binding affinity depends on H3K36 methylation. To investigate this dependency, we performed molecular dynamics simulations of the PWWP domain and histone fragments (Figure 5). We found not only hydrophobic interaction but also electrostatic interaction is important. The binding isn't maintained with nonmethylated and monomethylated H3K36 because the tips of these H3K36s form hydrogen bonds with water molecules, while dimethylated and trimethylated H3K36 form no such hydrogen bond, making this binding stable.

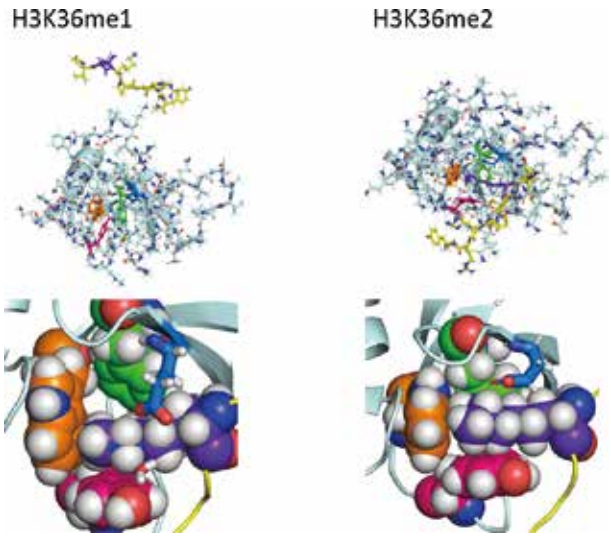

Figure 5. Typical binding structures of H3K36me1 and H3K36me2.

References

1) M. Otawa, S. G. Itoh and H. Okumura, *J. Chem. Theory Comput.* **20**, 10199–10208 (2024).
2) H. X. Suzuki, H. Okumura and S. G. Itoh, *J. Chem. Phys.* **162**, 185102 (8 pages) (2025).

Award

OKUMURA, Hisashi; Biophysics and Physicobiology Editors' Choice Award, The Biophysical Society of Japan (2024).

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Dynamics of Biomolecular Machines in Function Revealed by Theoretical Methods

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2016 Research Associate Professor, Institute for Molecular Science
2020 Associate Professor, Institute for Molecular Science
Associate Professor, The Graduate University for Advanced Studies

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Keywords Theoretical Biophysics, Biomolecular Machines, Molecular Simulation

Biomolecular machines, such as molecular motors and transporters in the cell, are known to change their structure when they function. For example, ATP synthase, which synthesizes ATP in mitochondria, is a molecular motor that uses chemical energy to rotate unidirectionally. Transporters, which transport substrate molecules across the cell membrane, perform substrate transport by changing their structure between inward-open and outward-open states relative to the membrane. We aim to elucidate the mechanisms of these elaborate and dynamic nanomachines created by nature at the atomic and molecular levels and to control their functions based on our findings.

We would like to understand the mechanisms of biomolecular machines by "seeing" the motion of biomolecular machines at the moment they function at the molecular level on a computer. However, this is not an easy task because biomolecular machines are huge molecules, and their functioning time scale is slow (for a molecular scale) at milliseconds or longer. Conventional atomistic molecular dynamics (MD) simulations cannot cover millisecond-long dynamics, especially for a large system like typical biomolecular machines. Therefore, we have developed and applied methods such as coarse-grained modeling and enhanced sampling to capture the motion at the moment of function.

We have been working on biomolecular motors such as ATP synthase. ATP synthase is a rotary motor that produces most of the ATP required in the cell. It is composed of two rotary motors: F_o and F_1. The F_o motor is embedded in the membrane and driven by a proton gradient, while the F_1 motor is driven by the ATP hydrolysis reaction. We clarified how the rotation of the F_1 motor is driven by a key chemical step, Pi release after the ATP hydrolysis reaction, by accelerating atomistic MD simulations with external forces.[1)]

Transporters are membrane proteins that transport their substrates across the membrane. We have studied a Na^+/H^+ antiporter, which exchanges sodium ions and protons inside and outside the cell. The ion transport process by the Na^+/H^+ antiporter was simulated in atomic detail with a transition path sampling technique to capture the moment of the ion transport. The simulations predicted the mutation that could speed up ion transport. The mutation was tested in experiments and shown to speed up the ion transport twice faster than the wild type. Therefore, we succeeded in controlling the function of the transporter based on the mechanism obtained from simulations by creating the faster transporter.[2)]

Selected Publications

- K. Okazaki and G. Hummer, "Elasticity, Friction, and Pathway of γ-Subunit Rotation in F_oF_1-ATP Synthase," *Proc. Natl. Acad. Sci. U.S.A.* **112**, 10720–10725 (2015).
- K. Okazaki, D. Wöhlert, J. Warnau, H. Jung, Ö. Yildiz, W. Kühlbrandt and G. Hummer, "Mechanism of the Electroneutral Sodium/Proton Antiporter PaNhaP from Transition-Path Shooting," *Nat. Commun.* **10**, 1742 (2019).
- R. Kobayashi, H. Ueno, K. Okazaki and H. Noji, "Molecular Mechanism on Forcible Ejection of ATPase Inhibitory Factor 1 from Mitochondrial ATP Synthase," *Nat. Commun.* **14**, 1682 (2023).

1. Mechanism of the Inhibitor Protein IF_1 for Mitochondrial ATP Synthase

ATPase inhibitory factor 1 (IF_1) regulates mitochondrial F_oF_1-ATP synthase by inserting into the rotor–stator interface and blocking F_1 rotation. Single-molecule experiments showed that rotation only in the ATP-synthesis direction ejects IF_1, but the atomic mechanism is unclear. Using all-atom MD simulations with torque applied on the γ subunit, we found that rotation proceeded further in the synthesis than hydrolysis direction. At 120° synthesis rotation, IF_1 contacts were disrupted, destabilizing its helices, and by 240° rotation, the β subunit pulled IF_1 outward. These stepwise changes appear key to IF_1 ejection. Simulations also revealed how hydrolytic rotation is nullified by steric clash between IF_1 and β_{TP}. We further discuss the proton motive force needed to release IF_1 inhibition.

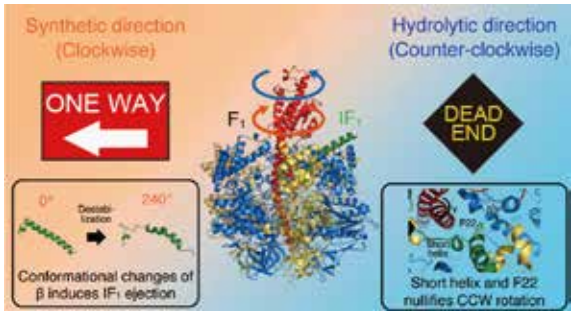

Figure 1. Rotation-direction-dependent mechanism of IF_1 inhibition for mitochondrial ATP synthase from atomistic molecular dynamics simulation.[3)]

2. Rotary Mechanism of the Prokaryotic V_o Motor Driven by Proton Motive Force

ATP synthases use the proton motive force (pmf) to rotate their c-ring and drive ATP synthesis. However, the mechanism of how pmf converts into c-ring rotation remains unclear. This study presents a 2.8 Å cryo-EM structure of the V_o domain of V/A-ATPase from *Thermus thermophilus*, revealing precise orientations of glutamate (Glu) residues in the c_{12}-ring with possible locations of water molecules that form the half channels for protons. MD simulations identified the channels and possible proton transfer pathway, and showed that protonation of specific Glu residues triggers unidirectional Brownian motion of the c12-ring towards ATP synthesis.[4)]

3. Integration of AlphaFold with MD Simulation

The computational cost of all-atom MD simulations for biomolecular machines is so high that direct simulation of the functional motions is impossible. We introduce a method that integrates AlphaFold with MD simulation to overcome this difficulty.[5)] This method first generates broad structures by AlphaFold with reduced MSA depth, including multiple stable conformations and intermediates. Then, MD simulations are conducted from these structures to cover the broad conformational space that is involved with the function. The method was tested with the transporter protein NarK. It successfully uncovers a missing conformational state and transition dynamics between stable states.

4. Machine Learning of Reaction Coordinates

It is a challenging task to identify reaction coordinates for biomolecular systems with many degrees of freedom. Unlike order parameters or collective variables, a reaction coordinate should describe the progress of a reaction between two metastable states. We have developed a machine learning method to identify reaction coordinates based on the committor function.[2,6)] We have applied a deep neural network (DNN) and Explainable Artificial Intelligence (XAI) for this problem.[6)] We also developed a hyperparameter tuning approach to this problem.[7)]

References

1) K. Okazaki and G. Hummer, *Proc. Natl. Acad. Sci. U. S. A.* **110**, 16468–16473 (2013).
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4) J. Kishikawa, Y. Nishida, A. Nakano, T. Kato, K. Mitsuoka, K. Okazaki and K. Yokoyama, *Nat. Commun.* **15**, 9883 (2024).
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7) K. Kawashima, T. Sato, K. Okazaki, K. Kim, N. Matubayasi and T. Mori, *APL Mach. Learn.* **3**, 016113 (2025).

Award

SEKI, Takehito; Young Presentation Award, 50th Meeting of Japan BioEnergetics Group (2024).

Visiting Professors

Visiting Professor
TSUCHIMOCHI, Takashi *(from Shibaura Institute of Technology)*

Theoretical and Computational Chemistry for Degenerate Electronic Structures

Our research focuses on quantum chemistry to compute the electronic structure of materials. We are particularly interested in chemical systems where electrons are strongly correlated, making them notoriously difficult to compute with traditional approaches due to either the inappropriate treatment of quantum entanglement or prohibitively large computational costs. To tackle this conundrum, we have proposed several methodologies based on symmetry-breaking of the underlying wave function as well as its restoration by means of symmetry-projection. While these methods primarily fall within the realm of wave function theory, we are integrating these concepts into the more affordable density functional theory. We have also been extensively exploring the potential of quantum computer to address such challenging electronic structures; recently, we have proposed a novel quantum-classical hybrid algorithm that mitigates the quantum measurement in optimizing the ground state energy. Finally, we actively collaborate with experimental groups to elucidate real chemical systems where quantum mechanical effects become important.

Visiting Professor
FUJII, Keisuke *(from The University of Osaka)*

Theoretical Research on the Fundamentals and Applications of Quantum Computers

Our research explores both theoretical foundations and applications of quantum computing. While recent advances have realized cloud-accessible devices with over 100 qubits, current noisy intermediate-scale quantum computers (NISQ) remain strongly affected by noise. We investigate how such devices can still be applied to meaningful tasks, such as machine learning and quantum many-body simulations, through noise mitigation. In parallel, we study architectures and physical systems for realizing large-scale fault-tolerant quantum computers (FTQC) with quantum error correction and estimate the resources required for practical problems. Recently, we have proposed new protocols for magic state distillation that significantly reduce FTQC resource requirements, and we are investigating how compiler-level optimizations can further reduce overhead.

Visiting Associate Professor
ABE, Minori *(from Tokyo University of Agriculture and Technology)*

Development of Relativistic Quantum Chemistry Software and Its Applications, and Generative AI Models for Chemistry

We have developed relativistic quantum chemistry software to compute molecular electronic structures involving heavy atoms. The CASPT2 method is employed in our program to treat multireference electron correlation effects, and relativistic effects are accurately incorporated by connecting to the DIRAC software. The software is publicly available on GitHub (https://github.com/RQC-HU/dirac_caspt2), and its application to the spectra of UO_2^{2+} has been published in the *Journal of Chemical Theory and Computation*.

In parallel, we have also developed generative machine learning models for chemical tasks based on the Bayesian Flow Network (ChemBFN). This model learns molecular structures from SMILES representations and generates new molecules in SMILES format. Furthermore, it can be fine-tuned for regression and classification tasks, enabling the generation of molecules with desired physical properties (N. Tao and M. Abe, *J. Chem. Inf. Model.* **65(3)**, 1178–1187 (2025)).

RESEARCH ACTIVITIES
Photo-Molecular Science

We study the interaction of atoms and molecules with optical fields with its possible applications to active control of atomic and molecular functionality and reactivity. We also develop novel light sources to promote those studies. Two research facilities, the Center for Mesoscopic Sciences and the UVSOR Synchrotron Facility, closely collaborate with the Department.

The core topics of the Department include attosecond coherent control for the development of ultrafast quantum computers and simulators, chiro-optical microscopy applied to nanomaterials, synchrotron-based spectroscopy of core-excited molecules and solid-state materials, vacuum-UV photochemistry, and the development of novel laser- and synchrotron-radiation sources.

Ultrafast Quantum Computer and Simulator

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Division of Photo-Molecular Science II

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1987 B. E. The University of Tokyo
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Professional Employment
1992 Research Associate, Tohoku University
2001 Associate Professor, Tohoku University
2003 Professor, Institute for Molecular Science
Professor, The Graduate University for Advanced Studies
2004 Visiting Professor, Tohoku University (–2005)
2007 Visiting Professor, Tokyo Institute of Technology (–2008)
2009 Visiting Professor, The University of Tokyo (–2011)
2012 Visiting Professor (Humboldt Awardee), Heidelberg University
2014 Visiting Professor, University of Strasbourg (–2016)

Awards
1998 Award by Research Foundation for Opto-Science and Technology
2007 JSPS Prize
2007 Japan Academy Medal
2008 Norman Hascoe Distinguished Lecturer, University of Connecticut, USA
2009 Fellow of the American Physical Society
2012 Humboldt Research Award (Germany)
2017 Hiroshi Takuma Memorial Prize of Matsuo Foundation
2018 Commendation for Science and Technology by the Minister of Education, Culture, Sports, Science and Technology of Japan
2021 Medal with Purple Ribbon (by His Majesty the Emperor of Japan)

Member
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TOMITA, Takafumi
Research Assistant Professor
MATSUBARA, Takuya
TAMURA, Hikaru
Post-Doctoral Fellow
CHAUHAN, Vikas Singh
JAUNET-LAHARY, Titouan
KUMAR, Pushpander
SRAKAEW, Kritsana
TIRUMALASETTY PANDURANGA, Mahesh
ANTHOINE-MILHOMME, Valentin
MAGRO, Valentin
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LORANCA CRUZ, Luisa Fernanda†
Visiting Scientist
BROSIG, Jule‡
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DENECKER, Tom
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KECIR, Omar
TANAKA, Aito
MAURUCUO URBINA, Jorge Antonio
WATANABE, Genki
ODAGAWA, Harumu
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Technical Support Staff
SUZUI, Mitsukazu
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TSURUTA, Shoko
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FUJIKAWA, Taketoshi
KAWAMOTO, Minako
MAKINO, Akane
INUKAI, Kazuhisa
IGAMI, Kento
NISHIOKA, Wakako
KOSHIDA, Yoko
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KUTARA, Yuriya
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OKADA, Mitsuya
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Keywords Quantum Simulation, Quantum Computing, Attosecond

It is observed in a double-slit experiment by Tonomura and coworkers that single electrons recorded as dots on a detector screen build up to show an interference pattern, which is delocalized over the screen.[1] This observation indicates that a delocalized wave function of an isolated electron interacts with the screen, which is composed of many nuclei and electrons interacting with each other, and becomes localized in space. This change, referred to as "collapse" in quantum theory, is often accepted as a discontinuous change, but a basic question arises: When and how the delocalized wave function becomes localized? Our objective is uncovering this mystery by observing the spatiotemporal evolution of a wave function delocalized over many particles interacting with each other. Having this objective in mind, we have developed coherent control with precisions on the picometer spatial and attosecond temporal scales. Now we apply this ultrafast and ultrahigh-precision coherent control to delocalized wave functions of macroscopic many-particle systems of an array of ultracold rubidium (Rb) Rydberg atoms, as depicted schematically in Figure 1 and named "ultrafast quantum simulator," envisaging the quantum-classical boundary connected smoothly.

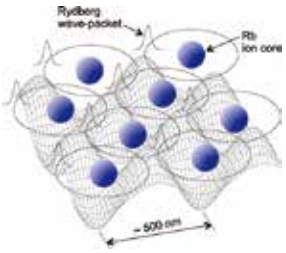

Figure 1. Metal-like quantum gas. A schematic of the many-body quantum simulator with ultracold Rydberg atoms, named "ultrafast quantum simulator," where electronic wave functions spatially overlap between neighboring atoms.[2]

Selected Publications

- H. Katsuki *et al.*, "Visualizing Picometric Quantum Ripples of Ultrafast Wave-Packet Interference," *Science* **311**, 1589–1592 (2006).
- H. Katsuki *et al.*, "Actively Tailored Spatiotemporal Images of Quantum Interference on the Picometer and Femtosecond Scales," *Phys. Rev. Lett.* **102**, 103602 (2009).
- K. Hosaka *et al.*, "Ultrafast Fourier Transform with a Femtosecond-Laser-Driven Molecule," *Phys. Rev. Lett.* **104**, 180501 (2010).
- H. Goto *et al.*, "Strong-Laser-Induced Quantum Interference," *Nat. Phys.* **7**, 383–385 (2011).
- H. Katsuki *et al.*, "All-Optical Control and Visualization of Ultrafast Two-Dimensional Atomic Motions in a Single Crystal of Bismuth," *Nat. Commun.* **4**, 2801 (2013).
- N. Takei *et al.*, "Direct Observation of Ultrafast Many-Body Electron Dynamics in an Ultracold Rydberg Gas," *Nat. Commun.* **7**, 13449 (2016).
- C. Liu *et al.*, "Attosecond Control of Restoration of Electronic Structure Symmetry," *Phys. Rev. Lett.* **121**, 173201 (2018).
- M. Mizoguchi *et al.*, "Ultrafast Creation of Overlapping Rydberg Electrons in an Atomic BEC and Mott-Insulator Lattice," *Phys. Rev. Lett.* **124**, 253201 (2020).
- Y. Chew *et al.*, "Ultrafast Energy Exchange between Two Single Rydberg Atoms on a Nanosecond Timescale," *Nat. Photonics* **16**, 724 (2022).
- V. Bharti *et al.*, "Picosecond-Scale Ultrafast Many-Body Dynamics in an Ultracold Rydberg-Excited Atomic Mott Insulator," *Phys. Rev. Lett.* **131**, 123201 (2023).
- V. Bharti *et al.*, "Strong Spin-Motion Coupling in the Ultrafast Dynamics of Rydberg Atoms," *Phys. Rev. Lett.* **133**, 093405 (2024).

1. Development of an "Ultrafast Quantum Simulator" by Optical Control with Precisions on the Attosecond Temporal and Submicron Spatial Scales[2–7)]

We develop a novel quantum simulator that can simulate quantum many-body dynamics for more than 1000 particles within one nanosecond, combining our two unique experimental resources: "coherent control with attosecond precision"[3)] and "a strongly correlated ultracold Rydberg gas."[4–6)]

We have completed a standard hardware of this ultrafast quantum simulator composed of an array of ultracold Rb atoms trapped in an optical lattice and excited to Rydberg levels with a coherent picosecond (ps) laser pulse.[5–7)] The broad bandwidth of the ps laser pulse has allowed us to excite the atoms in the neighboring lattice sites to Rydberg levels simultaneously for the first time. Recently in 2023, quantum magnetism has successfully been simulated with this standard hardware assembled with ~30,000 Rb atoms.[6)] Our novel scheme above has accelerated the simulation speed by three orders of magnitude compared to previous quantum simulators of magnetism. Moreover, we have succeeded in simulating the formation dynamics of "quantum entanglement," which is difficult to measure in actual magnetic materials, on the timescale of several hundred picoseconds.

Very recently in 2024 we have revealed the quantum entanglement between electronic and motional degrees of freedom of atoms in our "ultrafast quantum simulator," generated by the repulsive force due to the strong interaction between Rydberg atoms in the neighboring lattice sites.[7)] We have also proposed a new protocol including this repulsive force to introduce phonon motion into the quantum simulation.

We continue upgrading this ultrafast quantum simulators, generously supported by the Q-LEAP program of the MEXT of Japan.

2. Development of an Ultrafast Quantum Computer with Cold Atoms[8,10–13)]

We develop a novel quantum computer with two dimensional arrays of ultracold Rb atoms trapped in optical tweezers. These atomic qubits are manipulated with an ultrafast laser for the first time, leading to a completely new quantum computer we refer to as an "ultrafast quantum computer." With this ultrafast quantum computer, we succeeded in executing a controlled Z gate,[8)] accelerating a two-qubit gate (a fundamental arithmetic element essential for quantum computing) of cold-atom quantum computers by two orders of magnitude. It is also two orders of magnitude faster than the noise from the external environment and operating lasers, and thus can drastically reduce the noise effects. Moreover, this ultrafast two-qubit gate is faster than the fast two-qubit gate demonstrated recently by "Google Quantum AI" with superconducting qubits.[9)] We are currently improving its key underlying technologies with optical tweezers and operating lasers.[10–13)]

We continue upgrading this ultrafast quantum computers, generously supported by the Moonshot program of the Cabinet Office of Japan.

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8) Y. Chew *et al.*, *Nat. Photonics* **16**, 724 (2022). (Cover-Page Highlight)
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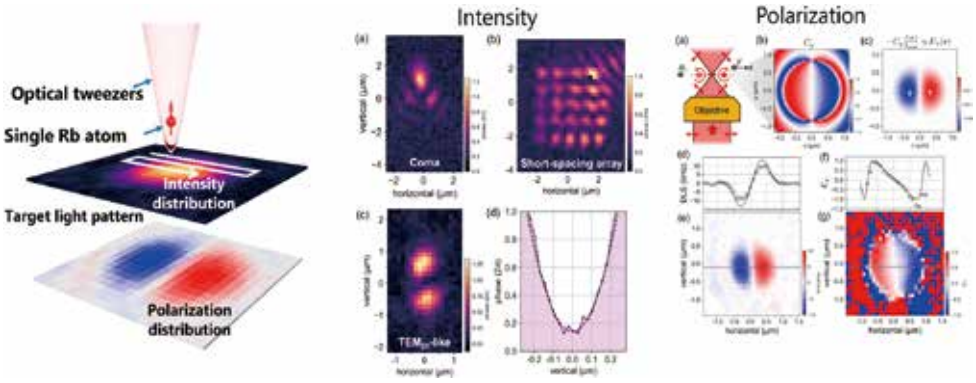

Figure 2. Atom Camera: Super-resolution scanning microscope of a light pattern with a single ultracold atom.[13)] This would be useful for super-resolution diagnosis of the spatial profiles of the intensity and polarization of optical tweezers and gate operation lasers.

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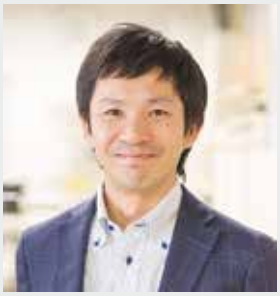
|| IMS International Internship Program

Electronic Property of Functional Low-Dimensional Material Systems

Department of Photo-Molecular Science
Division of Photo-Molecular Science III



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2004 Assistant Professor, Chiba University
2007 Associate Professor, Chiba University
2009 Visiting Associate Professor, Institute for Molecular Science
2013 Adjunct Lecturer, The Open University of Japan
2013 Visiting Associate Professor, Soochow University
2014 Professor, Institute for Molecular Science
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2019 Visiting Professor, Kyoto University, Hiroshima University
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Keywords Photoelectron Spectroscopy, Molecular Assemble, Electronic State

Functional low-dimensional material systems (LMS) such as oriented molecular assembles on the surface have recently attracted considerable attention both for fundamental research and device applications because of peculiar properties not found in bulk materials or small molecules. However, the mechanisms and the origin of various device characteristics are still under debate. Scientific discussions have been redundant because of long-standing beliefs that the electronic structure would be conserved as in an isolated molecule even for solid phases due to the weak van der Waals interaction. To reveal characteristics of the LMS, it is essential to investigate precisely the electronic structure at various interfaces, including organic–organic and organic–inorganic (metal/semiconductor) contacts. Recently we realized that the weak electronic interaction manifests itself as small intensity modulations of fine structures in photoelectron spectra, depending on the adsorption and aggregation conditions on the surface. Thanks to recent instrumentation improvements, we can assess hidden fine features in the electronic states, *e.g.* electron–phonon coupling, quasi-particle states, very small densities of gap states, narrow band dispersion, and dynamic electronic polarization. To elucidate what really impacts on the electronic states of the LMS as well as at the interface upon weak interaction, an evaluation of the wave-function spread of the electronic states is very important because the interface states are described as a delocalized molecular orbital state depending on the strength of weak electronic coupling (hybridization). Observing modifications of electron wave functions upon weak electronic coupling as well as strong electron–phonon coupling is a central issue on our agenda (Figure 1).

Figure 1. Overview of our agenda. A rich assortment of surface and interface structures of LMS to provide complicated spectral features of ultraviolet photoelectron spectroscopy.

Selected Publications

- Y. Nakayama, S. Kera and N. Ueno, *J. Mater. Chem. C* **8**, 9090–9132 (2020). [review]
- S. Kera, T. Hosokai and S. Duhm, *J. Phys. Soc. Jpn.* **87**, 061008 (7 pages) (2018). [review]
- J.-P. Yang, F. Bussolotti, S. Kera and N. Ueno, *J. Phys. D: Appl. Phys.* **50**, 423002 (45 pages) (2017). [review]
- S. Kera and N. Ueno, *J. Electron Spectrosc. Relat. Phenom.* **204**, 2–11 (2015). [review]

1. Enantiospecific Mirror-Imaged Growth in Overlayers of Enantiopure Helicene on Au(111) without Commensurability[1)]

Two-dimensional crystallization of chiral molecules on achiral crystal surfaces typically exhibits mirror-imaged growth, defined by the substrate's mirror plane and the lattices of each enantiomer. While various commensurate molecular overlayers have shown such growth, the possibility of achieving substrate-defined enantiospecific structures in non-commensurate chiral molecular overlayers remains elusive. Here, enantiopure thiadiazole-[9]helicene on Au(111) is shown to form overlayers without commensurability, exhibiting substrate-defined mirror-imaged growth (Figure 2). This study experimentally demonstrates that the rotational orientation locking without two-dimensional interface potential minima can support mirror-imaged growth, suggesting that it can serve as benchmark for enantiospecific growth in a broader range of chiral molecular systems. The well-defined chiral molecular system will be useful for studying the mechanisms of chirality-induced spin selectivity at the interface in the near future.

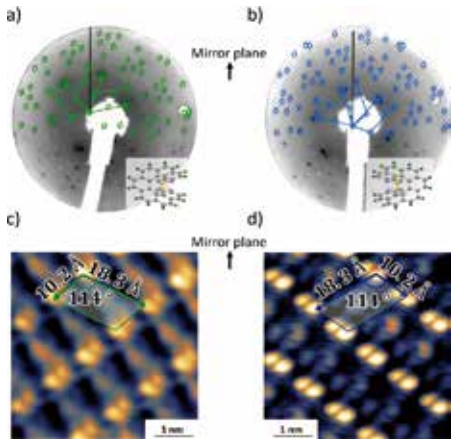

Figure 2. (a) and (b) are the distortion-corrected LEED images for (M)-TD[9]H and (P)-TD[9]H molecular layers on Au(111), observed at beam energies of 39.5 eV and 41.5 eV, respectively. (c) and (d) are STM images of (M)-TD[9]H and (P)-TD[9]H layers, respectively. The figure is after ref 1).

2. Fingerprinting Weak Electronic Interaction at a van der Waals Interface: Fano Signatures in Pentacene Monolayer on Graphite[2)]

The influence of van der Waals (vdW) interactions on the electronic structure at the interface between a pentacene monolayer and a graphite surface was investigated by using high-resolution angle-resolved photoelectron spectroscopy (ARPES) with synchrotron light sources. Upon cooling below 130 K, the pentacene molecules form a densely packed monolayer characterized by newly developed dispersive bands. These bands, observed using low-energy ARPES with photon energy varying from 7.2 to 8.5 eV, exhibit constant final state characteristics that overlap with nondispersive molecular orbital states (Figure 3). The results in variations for the photoemission intensity, both enhancement and suppressions the photoemission intensity, indicative of Fano resonance. Such resonance arises from the interaction between a discrete molecular state and a continuum state. The Fano profile analysis of spectral fine features reveals the wave-function connection by the broader spread in unoccupied states at the physisorbed interface. This discovery underscores the significant role of weak electronic coupling in shaping wave function connectivity, highlighted by the broader spread of unoccupied states. This spread serve as a spectral fingerprint for proving weak interactions at the vdW interface. The asymmetric parameter will provide quantifiable metrics for characterizing weak interactions, with further theoretical developments anticipated.

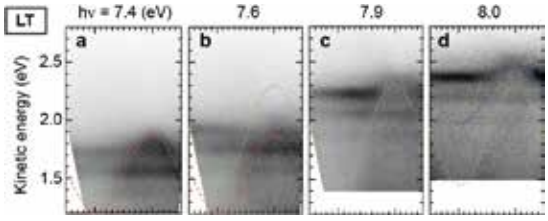

Figure 3. Photon energy dependence of the *E–k* map of pentacene on graphite (HOPG) recorded at LT (50 K for 8.0 eV and 14 K for 7.4, 7.6, and 7.9 eV) along with the fitting curves (POS: blue and red, NEG: green). The figure is after ref 2).

3. Other Activities in UVSOR

We have conducted beamline R&D and user supports in collaboration with other universities. Experiments using photoelectron momentum microscope are developing at BL6U.[3)] The perspectives required for future light-source facility have been discussed with communities.

References

1) F. Nishino, K. Fukutani, J. Brandhoff, M. Gruenewald, E. Fuerch, M. Schaal, F. Otto, D. Stelter, R. Forker, Z. Zhang, T. Hirose, T. Fritz and S. Kera, *Appl. Phys. Express* **18**, 015502 (2025).
2) Y. Hasegawa, T. Yamaguchi, M. Meissner, T. Ueba, F. Bussoloti, S. Ideta, K. Tanaka, S. Yanagisawa and S. Kera, *Phys. Rev. B* **112**, 085301 (2025).
3) K. Hagiwara, E. Nakamura, S. Makita, S. Suga, S. Tanaka, S. Kera and F. Matsui, *J. Synchrotron Radiat.* **31**, 540 (2024).

* IMS International Internship Program with Jena University

Light Source Developments by Using Relativistic Electron Beams

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Keywords Accelerator, Beam Physics, Synchrotron Radiation

UVSOR is a synchrotron light source providing low energy synchrotron light ranging from terahertz waves to the soft X-rays. Although it was constructed about 40 years ago, its performance is still in the world top level particularly among the low energy synchrotron light sources. This is the result of our continuous efforts on improving the machine. Our research group has been developing and introducing new accelerator technologies toward producing brighter synchrotron light with high stability, such as low emittance electron beam optics, novel insertion devices or state-of-the-art beam injection scheme. After two major upgrade projects, we now call our machine UVSOR-III. We have been developing novel light source technologies, such as free electron laser, coherent synchrotron radiation, structured light beams and laser Compton gamma-rays. We have been investigating beam physics which would be the basis of the future developments of the facility.

Figure 1. UVSOR-III Electron Storage Ring and Synchrotron Radiation Beamlines.

Selected Publications

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1. Light Source Technology Developments

We have been developing light source technologies at the UVSOR-III electron storage ring using a dedicated experimental station BL1U, which was constructed under the support of Quantum Beam Technology Program of JST/MEXT aiming to develop novel light sources and explore their applications. The BL1U is equipped with two undulators which constitute an optical klystron (Figure 2), a laser system which is synchronized with the accelerator beam and a dedicated beamline consisting of mirrors and a monochromator whose arrangement can be flexibly changed according to the types of the experiments (Figure 3).

In collaboration with Hiroshima Univ. and Nagoya Univ., we have succeeded in producing spatially structured synchrotron radiation such as vortex beam and vector beam. We are now exploring their applications.

We have been exploring the possibility utilizing the temporal structures of undulator radiation, in collaboration with Saga Light Source, Toyama Univ. and Hiroshima Univ. We have succeeded in the coherent controls of atoms and in observing ultrafast change of an electronic state of an atom by using radiation from two undulators arranged in tandem. We have demonstrated a state-of-the-art technology to observe ultrafast properties of synchrotron radiation, in collaboration with Toyota Technological Institute.

Figure 2. Twin Polarization-variable Undulators/Optical Klystron at UVSOR-III.

Figure 3. UVSOR BL1U experimental station for source development studies.

In these years, we are interested in the quantum nature of synchrotron radiation photons. We have established a technique to store only one electron in the synchrotron. We are working on experimental studies on photon emission from a single electron. Some of the results have been published as bachelor thesis and master thesis in Hiroshima Univ.

We have developed a laser Compton scattering gamma-ray source at BL1U, which is capable of producing ultrashort, monochromatic and energy-tunable gamma-rays. They are now opened for public use.

We have been continuing experimental studies on the origin of the homochirality of biomolecules using intense circularly polarized undulator radiation at BL1U, in collaboration with Yokohama National Univ., Hiroshima Univ. and NIFS. This year, we have started a new project on exploring novel experimental techniques based on chiral undulator radiation, including optical vortex and other chiral structured light.

2. Accelerator Technology Developments

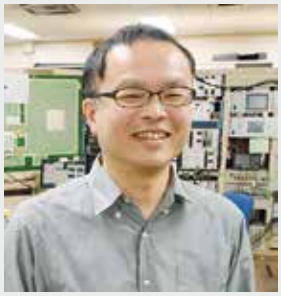
We carried out several upgrades on the UVSOR electron synchrotron since 2000. We designed a special beam optics intended to higher brightness. We developed necessary accelerator components, reconstructed the accelerator and commissioned it. We have commissioned six undulators successfully, three of which are variable polarization type and others in-vacuum type. Moreover, we have been continuously introducing new accelerator technologies such as the top-up operation in which the electron beam intensity is kept quasi-constant at a high beam current, 300mA, and the novel beam injection scheme with a pulsed sextupole magnet. As the result of all these efforts, now, the machine is one the brightest synchrotron light sources among the low energy machines below 1GeV in the world.

Currently, the storage ring is stably operated, however, the requirements from the users for the higher brightness is getting stronger, because new light sources and upgrade plans are being realized all over the world. We had seeked a possibility to reduce the emittance with the present magnet configuration. So far, we have found a few beam optics which would give lower emittance around 10 nm. However, they are not compatible with the operation of the narrow gap undulators. Then, we started a design study on a new light source facility. Currently we are focusing on designing a synchrotron with the electron energy of 1 GeV and the circumference of around 70 m. In parallel, we are designing a magnetic lattice which has same beam energy and circumference as the present machine but would give significantly lower emittance.

We are collaborating with Nagoya University, Hiroshima University and KEK Photon Factory to develop new accelerator technologies for the future plans of these facilities. Accelerator magnets based on permanent magnets are being developed, which would contribute to the power consumption saving. New pulsed multipole magnet is also being developed to realize a novel beam injection scheme.

Exploring a New Application of Synchrotron Radiation with Novel Light Source Technologies

UVSOR Synchrotron Facility
Division of Advanced Accelerator Research



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Keywords Synchrotron Radiation, Accelerator, Structured Light

UVSOR synchrotron at IMS is a compact low-energy synchrotron radiation facility which has been operating for more than 40 years. The light source performance is still in the word top level and continuous studies on the development of novel light source technologies have been conducted since the 1980s. From a viewpoint of exploring a new application of synchrotron radiation, UVSOR has advantages on the light source performance and the agility to immediately implement new concepts.

The waveform of electromagnetic radiation from an ultra-relativistic electron reflects the motion of the electron. This implies that, by controlling the electron motion in the magnetic field, one can control the properties of the radiation waveform in the nanometer or Angstrom scale. Our group has succeeded in generating the optical vortex beam which has helical phase plane and coherent double-pulse using insertion devices installed in the UVSOR synchrotron (Figure 1). The use of mutual coherence between the double-pulsed components enables time-domain interferometry experiments for controlling and monitoring the quantum state of matter using synchrotron radiation. Such an approach can be applied to the development of new spectroscopic and imaging methods using synchrotron radiation. We aim to develop novel measurement methods and their applications based on manipulating the motion of high-energy electrons in a synchrotron ring.

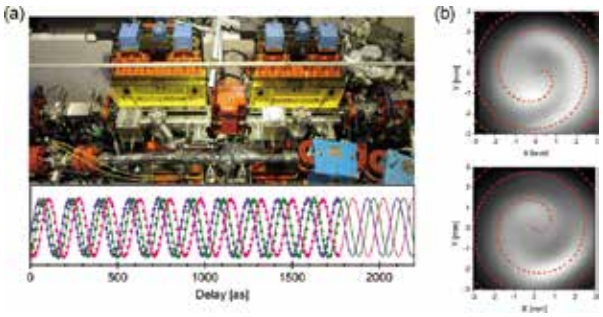

Figure 1. (a) Tandem-undulator system in the UVSOR-III synchrotron. Attosecond interference in photoexcitation of helium atoms is attached in the bottom panel. (b) Generation of optical vortex beam by synchrotron radiation.

Selected Publications

- T. Fuji, T. Kaneyasu, M. Fujimoto, Y. Okano, E. Salehi, M. Hosaka, Y. Takashima, A. Mano, Y. Hikosaka, S.-I. Wada and M. Katoh, "Spectral Phase Interferometry for Direct Electric-Field Reconstruction of Synchrotron Radiation," *Optica* **10**, 302 (2023).
- T. Kaneyasu, Y. Hikosaka, M. Fujimoto, H. Iwayama and M. Katoh, "Electron Wave Packet Interference in Atomic Inner-Shell Excitation," *Phys. Rev. Lett.* **126**, 113202 (2021).
- Y. Hikosaka, T. Kaneyasu, M. Fujimoto, H. Iwayama and M. Katoh, "Coherent Control in the Extreme Ultraviolet and Attosecond Regime by Synchrotron Radiation," *Nat. Commun.* **10**, 4988 (2019).
- T. Kaneyasu, Y. Hikosaka, M. Fujimoto, T. Konomi, M. Katoh, H. Iwayama and E. Shigemasa, "Limitations in Photoionization of Helium by an Extreme Ultraviolet Optical Vortex," *Phys. Rev. A* **95**, 023413 (2017).
- T. Kaneyasu, Y. Takabayashi, Y. Iwasaki and S. Koda, "Beam Lifetime Study Based on Momentum Acceptance Restriction by Movable Beam Scraper," *Nucl. Instrum. Methods Phys. Res., Sect. A* **694**, 107 (2012).

1. Attosecond Interferometry Experiments Using Synchrotron Radiation

Attosecond interferometry experiments have been conducted using the light source development beamline BL1U in UVSOR-III synchrotron (Figure 2).[1] In recent years, we have studied the interference phenomena between the photoelectron wave packets. The sequential interaction of an atom with a pair of coherent light pulses results in the production of a pair of photoelectron wave packets which interfere with each other during the propagation in a free space. The control and observation of photoelectron wave packet interference has been achieved so far by employing coherent pulse pairs generated by laser sources. In contrast, we have recently demonstrated that the phase coherent double pulses generated by a synchrotron light source can be utilized for the purpose of controlling the interference of photoelectron wave packets produced in the extreme ultraviolet wavelength range.[2]

Figure 3 presents the time-domain photoelectron interferogram associated with the photoionization of 5p electron in xenon atom. This interferogram is composed of photoelectron spectra acquired at various phase shifter delays. During the measurement, the central wavelength of linearly polarized radiation was set to approximately 40 nm and the kinetic energy of the photoelectron was determined using a hemispherical electron energy analyzer. The interferogram exhibits periodic modulation with a period of approximately 140 as, which corresponds to the photon frequency. The clear modulation of this interferogram indicates that the photoelectron wave packet interference can be precisely controlled by varying the time delay, which was calibrated by the frequency-domain interferometry.[3] Furthermore, the interferogram exhibits intensity modulation with a period of 3 fs. This effect can be attributed to the evolution of the spin–orbit wave packet produced in the Xe^+ ion, suggesting that the tandem undulator could be used to explore ultrafast quantum state dynamics with attosecond resolution.

Figure 2. Layout of the light source development beamline BL1U.

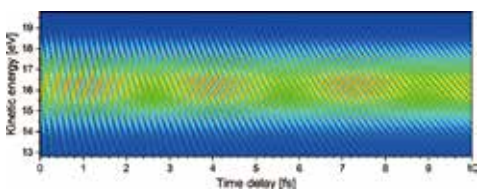

Figure 3. Time-domain photoelectron interferogram obtained for xenon 5p ionization.

2. Development of Atomic Fluorescence Polarimeter

Polarization represents one of the most significant characteristics of synchrotron radiation. The horizontally linear polarization of the radiation emitted from a bending magnet has been widely employed in various measurements for a long time. In addition, the rapid advancement of insertion devices in the 1990s has enabled arbitrary control of the polarization state of undulator radiation. However, the polarization state of the light changes according to the reflective properties of the beamline optics. Consequently, in order to ensure accurate measurements based on the polarization properties of synchrotron radiation, it is crucial to evaluate the polarization state of the light at the sample position.

To date, the synchrotron community has devoted considerable effort to the development of polarimeters for wavelengths shorter than those of vacuum ultraviolet (VUV) radiation. Simpler approach to measure the polarization of short wavelength light is to take advantage of the interaction of light with atoms and molecules in the gas phase. The use of a fluorescence polarimeter based on the conversion of VUV light into visible fluorescence light via atomic resonance allows the complete determination of the polarization state with a simple apparatus. In this study, the degree of linear polarization and the angle of inclination of the polarization axis of VUV light have been measured with a fluorescence polarimeter utilizing helium and neon atoms (Figure 4).[4] This study demonstrates that a fluorescence polarimeter can be used in conjunction with a variety of atoms and molecules and thus extends the range of wavelengths to which this method can be applied.

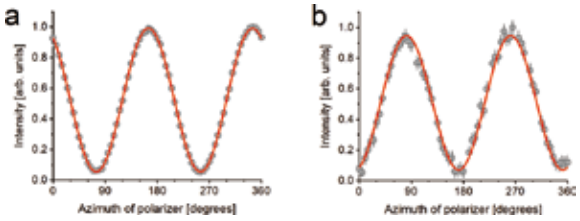

Figure 4. The fluorescence yield measured as a function of the polarizer angle for (a) helium and (b) neon atoms. The degree of linear polarization and angle of the polarization axis can be derived from the periodic modulation of the fluorescence yield.

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2) T. Kaneyasu, Y. Hikosaka, S. Wada, M. Fujimoto, H. Ota, H. Iwayama and M. Katoh, *Sci. Rep.* **13**, 6142 (2023).
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4) T. Kaneyasu, H. Takeda, K. Hosaka and J. Adachi, *J. Electron Spectrosc. Relat. Phenom.* **279**, 147488 (2024).

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Development and Utilization of Novel Quantum Beam Sources Using a High Energy Electron Beam

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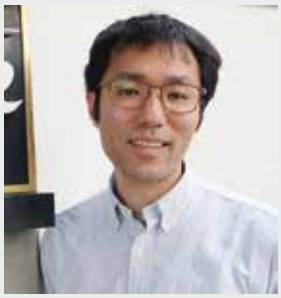

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Awards
2011 Nagoya University Outstanding Graduate Student Award
2012 Oral Presentation Award, The 9th Annual Meeting of Particle Accelerator Society of Japan
2012 Young Researcher Best Poster Award, 12th International Symposium on Radiation Physics
2013 Young Scientist Award of the Physical Society of Japan
2015 Young Researcher Best Presentation Award, Beam Physics Workshop 2015
2021 Outstanding Presentation Award, 64th Annual Meeting of the Japanese Society of Radiation Chemistry
2023 Young Scientist Award of the Japanese Positron Science Society

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Keywords Electron Beams, Synchrotron Radiation, Gamma-Rays

Our group develop new electromagnetic wave sources using a high energy electron beam. In the UVSOR-III electron storage ring at the Institute for Molecular Science, a 750-MeV electron beam can be generated. Electromagnetic waves in a wide frequency range from ultraviolet waves to gamma rays are emitted by interacting the electron beam with magnetic fileds and lasers.

Inverse Thomson (Compton) scattering is a method to generate a high energy gamma ray by the interaction between a high energy electron and a laser. We have developed ultra-short pulsed gamma rays with the pulse width of sub-ps to ps range by using 90-degree inverse Thomson scattering (Figure 1). This ultra-short pulsed gamma rays were applied to gamma-ray-induced positron annihilation pectroscopy (GiPAS). A positron is an excellent probe of atomic scale defects in solids and of free volumes in polymers at the sub-nm to nm scale. GiPAS enables defect analysis of a thick material in a few cm because positrons are generated throughout a bulk material via pair production.

Figure 1. Schematic illustration of 90-degree inverse Thomson scattering.

Selected Publications

- Y. Taira, M. Adachi, H. Zen, T. Tanikawa, N. Yamamoto, M. Hosaka, Y. Takashima, K. Soda and M. Katoh, "Generation of Energy-Tunable and Ultra-Short-Pulse Gamma Ray via Inverse Compton Scattering in an Electron Storage Ring," *Nucl. Instrum. Methods Phys. Res., Sect. A* **652**, 696 (2011).
- Y. Taira, T. Hayakawa and M. Katoh, "Gamma-Ray Vortices from Nonlinear Inverse Thomson Scattering of Circularly Polarized Light," *Sci. Rep.* **7**, 5018 (2017).
- Y. Taira, R. Yamamoto, K. Sugita, Y. Okano, T. Hirade, S. Namizaki, T. Ogawa and Y. Adachi, "Development of Gamma-Ray-Induced Positron Age-Momentum Correlation Measurement," *Rev. Sci. Instrum.* **93**, 113304 (2022).
- Y. Taira *et al.*, "Measurement of the Spatial Polarization Distribution of Circularly Polarized Gamma Rays Produced by Inverse Compton Scattering," *Phys. Rev. A* **107**, 063503 (2023).
- Y. Taira, Y. Yang, T. Shizuma and M. Omer, "Generation and Measurement of Gamma Rays with Axially Symmetric Polarization States via Compton Scattering," *Phys. Rev. Res.* **7**, 033130 (2025).

1. Gamma-Ray-Induced Positron Annihilation Spectroscopy (GiPAS)

In GiPAS, defect analysis is performed by measuring the energy spectrum and emission time distribution (positron lifetime spectrum) of annihilation gamma rays, which are generated when a positron annihilates with an electron inside material. Gamma-ray-induced positron annihilation lifetime spectroscopy (GiPALS) is a technique that measures the time difference distribution between a reference signal and a detector output of annihilation gamma rays. The reference signal is the output of a photodiode placed near the collision point between the electron beam and the laser, which detects the laser just before it generates gamma rays. A BaF_2 scintillator and a photomultiplier tube is utilized to detect the annihilation gamma rays. Two detectors are arranged at 180 degrees because two annihilation gamma rays are generated at 180-degree direction. A digital oscilloscope is used to store the waveforms of the photodiode and the BaF_2 detector, and calculate the time difference distribution. One digital oscilloscope for four BaF_2 detectors is used as a pair of detection systems. The annihilation gamma rays are generated to whole solid angle. Therefore, array detectors are effective to increase the count rate of the annihilation gamma rays and to reduce the measurement time. A detection system with eight detectors and two digital oscilloscopes was constructed. Time resolution is 140 ps in full width at half maximum, which is high despite the use of a 52-mm thick BaF_2 scintillator. A typical count rate is 20 cps.

Currently, user applications of GiPALS are underway at BL1U of UVSOR, and users from universities, research institutes, and private companies are using the system. Measurements of samples under special environments such as stress loading, high temperature, gas atmosphere, laser irradiation, hydrogenation, etc., which are difficult to measure with conventional methods using ^{22}Na, are being performed.

Meanwhile, we are also developing gamma-ray-induced spin-polarized positron annihilation spectroscopy using circularly polarized gamma rays. The spin-polarized positrons are generated from the circularly polarized gamma rays inside a sample. If the electron spins of a sample are ordered in a particular direction and the positrons are also spin-polarized, the Doppler broadening spectra of annihilation gamma rays and the positron lifetime will change. From this change, it is possible to obtain information about the electron spins around defects in magnetic materials. To demonstrate the principle of circularly polarized gamma-ray-induced spin-polarized positron annihilation spectroscopy, a pure iron sample is mounted between permanent magnets and the positron lifetime and Doppler broadening are measured. We have not been able to measure the difference in positron lifetime due to the helicity inversion of circularly polarized gamma rays, but we will continue research and development.

2. Spatial Polarization Measurement of Gamma-Rays Generated Using Polarized Lasers

Inverse Thomson/Compton scattering of a polarized laser by energetic electrons is an excellent method to generate polarized gamma rays. The development and use of linearly and circularly polarized gamma rays have been conducted. The polarization state of linearly and circularly polarized lasers is homogeneous across their cross sections. However, it is possible to produce lasers with spatially variant polarization states. An example is the axially symmetric polarization state, referred to as an axially symmetric polarized laser or a cylindrical vector beam. Although the polarization characteristics of gamma rays produced by linearly or circularly polarized lasers have been theoretically clarified, that of gamma rays generated by axially symmetric polarized lasers have not. If gamma rays with novel polarization characteristics can be generated, it is possible to develop new ways to use gamma rays.

A novel Compton polarimeter was constructed to measure the linear polarization of MeV gamma rays. Gamma rays are irradiated onto an iron target, and the azimuth distribution of scattered gamma rays is measured by seven NaI detectors to determine the polarization axis of the gamma rays. The gamma rays expand over a diameter of 10 mm. By installing a collimator with a diameter of 1 mm on the gamma ray beam axis and irradiating only the gamma rays that pass through it onto the target, it is possible to measure the polarization axis at that position. Moreover, by scanning the collimator in two dimensions, it is possible to measure the spatial polarization distribution of gamma rays. Figure 2 shows the spatial polarization distribution of inverse Compton scattered gamma rays measured for the first time using the developed polarimeter. We were able to demonstrate that the polarization axis changes depending on the position of the beam cross section in both horizontal and vertical polarization. Gamma rays generated using a circularly polarized laser showed that the outer polarization changed to linear polarization and that the polarization axis was oriented in the azimuth direction. Gamma rays generated using radially and azimuthally polarized lasers were found to possess random polarization near the central axis and azimuth polarization states on the outer region.

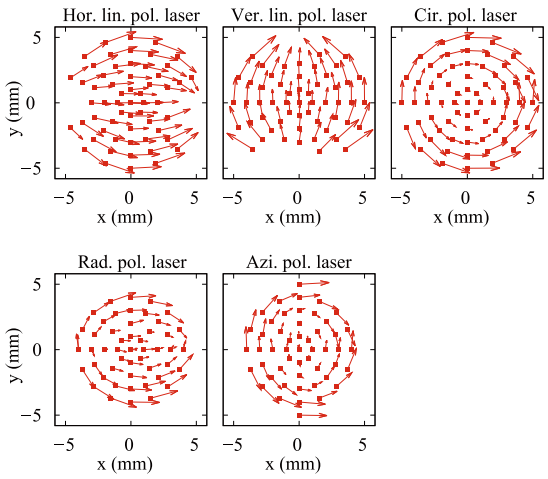
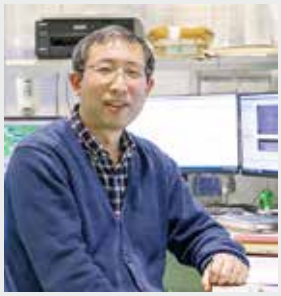


Figure 2. Measured spatial polarization distribution of gamma rays generated using five types of polarized lasers.

* CSC-IMS Scholarship Program

Symmetry Breaking in Crystal Microcosms Reflected in a Photoelectron Kaleidoscope

UVSOR Synchrotron Facility
Division of Advanced Solid State Physics



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2009 Young Scientist Award of the Physical Society of Japan
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Keywords Photoelectron Spectroscopy, Momentum Microscope, Electronic Spin Structure

The word "*kaleidoscope*" comes from the Greek "*kalos*," meaning beautiful, and "*eidos*," meaning shape or form. In a kaleidoscope, light repeatedly reflects off mirrors inside a tube, creating a beautiful pattern. The photoelectron angular distribution we study is similar to this kaleidoscope.

Photoelectron spectroscopy is a technique that uses photon to eject electrons from a solid. By analyzing the ejected electrons' energy and motion, we can determine the properties of the material. As the photoelectrons travel within a solid crystal, they form a complex angular distribution, much like the patterns in a kaleidoscope. This complex pattern holds astonishing information. The diffraction pattern of core-level photoelectrons reveals the local atomic arrangment of the specific element sites that make up the crystal, and the angular distribution of valence photoelectrons tells us about the fundamental electronic properties of the material.

We have developed a new analytical instrument, the photoelectron momentum microscope (PMM). PMM combines imaging-type photoelectron spectroscopy and microscopy techniques to visualize the electronic state (band dispersion, composition, and spin polarization) in reciprocal lattice space of a selected μm-sized area. We have constructed the world's first dual beamline (soft x-ray; SX and vacuum ultraviolet; VUV) PMM system at the IMS UVSOR synchrotron facility. Specifically, the "broken symmetry" in the kaleidoscopic patterns created by photoelectrons contains crucial information that determines the characteristics of a material.

Our research focuses on a range of intriguing phenomena, including twinning crystal growth, phase transitions, magnetism, and superconductivity. We are particularly fascinated by the interplay between domain boundaries and electronic properties, where the delicate balance between order formation and fluctuations creates a rich and complex environment. We are pioneering a new technique to unravel the mysteries of electronic properties within individual microcrystalline regions (Figure 1).

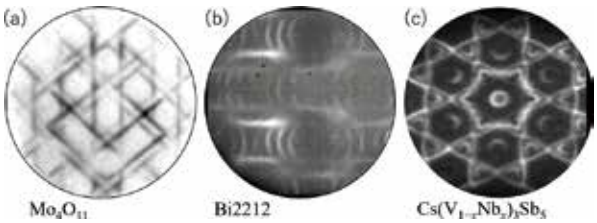

Figure 1. Photoelectron momentum distributions of Fermi surfaces from (a) a quasi-2D crystal, (b) a high-temperature superconducting copper oxide and (c) a Kagome-lattice superconductor.

Selected Publications

- T. Kobayashi, F. Matsui *et al.*, "Temperature-Dependent Electronic Structure of a Quasi-Two-Dimensional Conductor η-Mo_4O_{11}," *Sci. Rep.* **15**, 9034 (2025).
- K. Hagiwara, F. Matsui *et al.*, "Development of Dual-Beamline PMM for Valence Orbital Analysis," *J. Synchrotron Radiat.* **31**, 540 (2024).
- F. Matsui *et al.*, "Soft X-Ray PMM for Multimodal Valence Band Stereography," *Rev. Sci. Instrum.* **94**, 083701 (2023).
- T. Kato, F. Matsui *et al.*, "Fermiology and Origin of T_c Enhancement in a Kagome Superconductor $Cs(V_{1-x}Nb_x)_3Sb_5$," *Phys. Rev. Lett.* **129**, 206402 (2022).
- F. Matsui and S. Suga, "Coupling of k_z-dispersing π Band with Surface Localized States in Graphite," *Phys. Rev. B* **105**, 23526 (2022).

1. Photoelectron Feels the Broken Symmetry at the Surface

PMM can also map conduction band dispersion. The conduction band structure is imprinted on the energy-loss background of secondary electrons (SEs) that accompany the primary photoemission process. The interaction of these secondary electrons with the conduction band states reduces their emission intensity into the vacuum, creating a negative contrast pattern of the conduction band.[1,2] This is analogous to the negative photoelectron diffraction patterns seen in the angular distribution of energy-loss electrons accompanying core-level photoemission.[3] Consequently, a standard photoelectron spectroscopy setup, typically used for occupied states, can also visualize the unoccupied conduction band.

Figure 2(a) shows the overall valence band dispersion of graphite, where darker regions indicate a stronger photoelectron signal. We tuned the photon energy to 68 eV to match the bulk L symmetry point. By selectively detecting photoelectrons from a terrace with a single termination type, we confirmed a clear surface symmetry breaking (Figure 2(b)).[4]

Figure 2(c) displays the momentum-resolved kinetic energy distribution of SEs. The unoccupied band dispersion appears as a negative contrast due to the absorption of photoelectrons by the conduction band states. Figure 2(d) presents a series of angular patterns at various kinetic energies. A key finding is that while most patterns exhibit six-fold symmetry, those at kinetic energies around 20 eV show a three-fold symmetry. This suggests that as photoelectrons escape from the solid into the vacuum, they are influenced by the three-fold symmetric structure of the top surface of graphite.

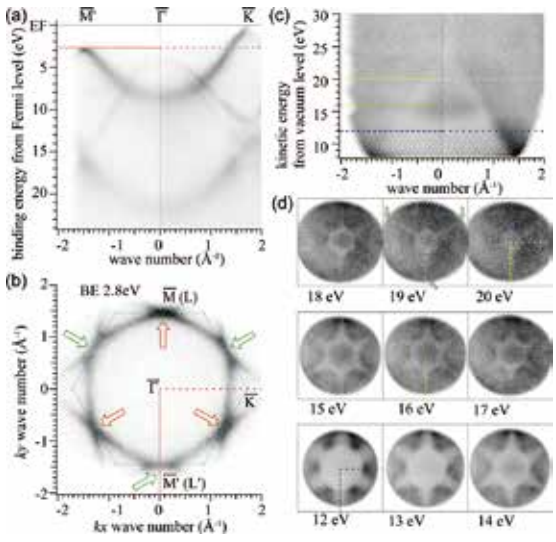

Figure 2. (a) The overall dispersion of the valence band of graphite. Dark areas correspond to larger photoelectron signals. (b) Momentum distribution indicated as a red line in (a). (c) The momentum resolved kinetic energy distribution of SE electrons. The conduction band signature appears as a lighter grey contrast. (d) A series of SE angle patterns at several kinetic energies. Note that at kinetic energies of 19 and 20 eV, the patterns appear as three-fold symmetric.

2. Spins, in Which Direction Are You Oriented?

That's the fundamental question at the heart of spin physics. Spin, a crucial quantum number, enriches the properties of materials, magnetism and superconductivity for instance. To truly understand those phenomena, we need to clarify not only their electronic structures but also the behavior of electron spins.

Spin-polarized photoelectron momentum microscopy (SP-PMM) is a powerful technique for detecting spin polarization in 2D real and reciprocal spaces. Its main advantage is efficiency, providing instant, spin-resolved snapshots of valence band structures. Our SP-PMM at the UVSOR synchrotron facility uses both grazing-incidence soft X-rays and normal-incidence vacuum ultraviolet light. A unique feature of our instrument is a spin rotator placed just before the spin detector, which allows for precise spin manipulation.

The Au(111) surface state is a classic example of spin–orbit coupling. The loss of bulk symmetry at the surface splits the band dispersion into two branches due to the Rashba effect (Figures 3(a), (b)). The in-plane spin components of these split bands are known to point in opposite directions, and observing this state is a common milestone in spin-polarized ARPES.

However, a review of the literature on the Au(111) Rashba state revealed a significant contradiction: The spin orientation of the outer bands is ambiguously assigned as either counter-clockwise (ccw) or clockwise (cw). This confusion has been made worse by numerous secondary publications.

To resolve this issue, we performed a case study on the Au(111) surface state using our SP-PMM. By carefully investigating our multichannel detection system, we were able to unambiguously determine the precise spin orientation of the Au(111) surface state (Figure 3(c)).[5]

Our PMM at the UVSOR synchrotron facility uses both grazing-incidence soft X-rays and normal-incidence vacuum ultraviolet (VUV) light with variable polarization. This normal-incidence setup is particularly useful for directly investigating the relationship between orbital angular momentum and transition matrix elements (Figure 3(d)).[6]

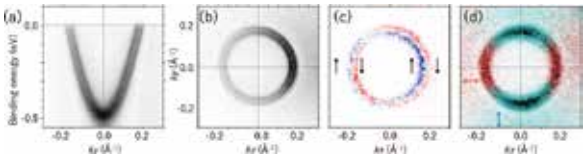

Figure 3. (a) The dispersion of the Au(111) surface state. (b) A cross-section of the surface state at the Fermi level. (c) The determined spin orientation of the surface state. (d) Intensity distributions excited by horizontal (magenta) and vertical (cyan) VUV polarization, respectively.

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5) F. Matsui *et al.*, *J. Phys. Soc. Jpn.* **94**, 114707 (2025).
6) K. Hagiwara *et al.*, *J. Synchrotron Radiat.* **31**, 540 (2024).

* carrying out graduate research on Cooperative Education Program of IMS with The University of Osaka

Angle-Resolved Photoemission Study on Strongly Correlated Electron Materials

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Keywords Strongly Correlated Electron System, Synchrotron Light, Photoemission

Strongly correlated electron materials have attracted more attentions in the last few decades because of their unusual and fascinating properties such as high-T_c superconductivity, giant magnetoresistance, heavy fermion and so on. Those unique properties can offer a route toward the next-generation devices. We investigate the mechanism of the physical properties as well as the electronic structure of those materials by using angle-resolved photoemission spectroscopy (ARPES). ARPES is a powerful experimental technique, directly measuring the energy (E) and momentum (k) relation, namely the band structure of solids. In the last quarter of a century, the energy resolution and angular resolution of ARPES have improved almost three order of magnitude better, which makes us possible to address the fine structure of the electronic strucature near the Fermi level: Superconducting gap, kink structure and so on. The main target materials of our group is high-T_c superconductors, such as cuprates and iron pnictides and use UVSOR-III as a strong light source.

Our group is also developing high-efficiency spin-resolved ARPES system. Spintronics is a rapidly emerging field of science and technology that will most likely have a significant impact on the future of all aspects of electronics as we continue to move into the 21st century. Understanding magnetism of surfaces, interfaces, and nanostructures is greatly important for realizing the spintronics which aims to control and use the function of spin as well as the charge of electrons. Spin-resolved ARPES is one of the most powerful experimental techniques to investigate the magnetic properties of such materials (Figure 1).

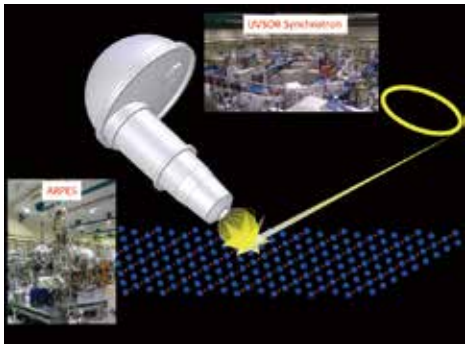

Figure 1.

Selected Publications

- K. Tanaka, W. S. Lee, D. H. Lu, A. Fujimori, T. Fujii, Risdiana, I. Terasaki, D. J. Scalapino, T. P. Devereaux, Z. Hussain and Z.-X. Shen, "Distinct Fermi-Momentum-Dependent Energy Gaps in Deeply Underdoped Bi2212," *Science* **314**, 1910–1913 (2006).
- W. S. Lee, I. M. Vishik, K. Tanaka, D. H. Lu, T. Sasagawa, N. Nagaosa, T. P. Devereaux, Z. Hussain and Z.-X. Shen, "Abrupt Onset of a Second Energy Gap at the Superconducting Transition of Underdoped Bi2212," *Nature* **450**, 81–84 (2007).
- K. Tanaka, N. Hieu, G. Vincini, T. Masui, S. Miyasaka, S. Tajima and T. Sasagawa, "Quantitative Comparison between Electronic Raman Scattering and Angle-Resolved Photoemission Spectra in $Bi_2Sr_2CaCu_2O_{8+\delta}$ Superconductors: Doping Dependence of Nodal and Antinodal Superconducting Gaps," *J. Phys. Soc. Jpn.* **88**, 044710 (2019).
- S. Ideta, N. Murai, M. Nakajima, R. Kajimto and K. Tanaka, "Experimental Investigation of the Suppressed Superconducting Gap and Double-Resonance Mode in $Ba_{1-x}K_xFe_2As_2$," *Phys. Rev. B* **100**, 235135 (7 pages) (2019).

1. Development of Spin-Resolved ARPES with Image-Spin Detection

Spintronics is an emerging field that aims to utilize the spin as well as the charge of electrons, and its progress is expected to strongly shape the future of electronics. To realize spin-based devices, it is crucial to understand the magnetism of surfaces, interfaces, and nanostructures at a fundamental level. Spin- and angle-resolved photoemission spectroscopy (spin-resolved ARPES) is one of the most powerful experimental methods for this purpose, because it can provide the full information of the electronic states—energy, momentum, and spin orientation. However, conventional Mott-type spin detectors suffer from an extremely low efficiency of about 10^{-4}, which has been a serious obstacle for decades. The development of very-low-energy-electron-diffraction (VLEED) detectors, with roughly 100 times higher efficiency, has made spin-resolved ARPES feasible in practice, yet most existing systems still use single-channel detection, where efficiency and angular resolution remain limited.

To overcome these limitations, our group reconstructed the BL5U beamline at UVSOR in 2017, creating a high-photon-flux and high-energy-resolution ARPES station. Building on this foundation, we initiated a long-term project to establish a next-generation spin-resolved ARPES system with multi-channel detection, which we call "image-spin" detection. The aim of this project is not only to improve detection efficiency and momentum resolution by factors of 100 and 10, respectively, but also to develop a platform that enables user-friendly and systematic spin-resolved measurements at synchrotron light sources. By pushing the limits of both efficiency and resolution, such a system can provide unprecedented opportunities for studying spin-dependent band structures, many-body interactions, and exotic electronic phases that cannot be accessed with conventional methods.

In 2024, we made substantial progress with the introduction of a spin manipulator combined with an ultra-bright electron gun. In our previous report, we demonstrated that this system could already achieve 100 times higher efficiency and 10 times better momentum resolution than conventional single-channel systems, but these improvements were restricted to one axis (the in-plane x-axis of the sample) and to a photon energy range of only 40–80 eV. Over the past year, careful optimization of the electron lens parameters allowed us to extend spin detection to two in-plane axes (x and y directions), as shown in Figures 2 and 3. At the same time, the usable photon energy range was expanded to 21–120 eV. This not only enables the study of a wider variety of materials, but also allows systematic comparisons across different excitation energies, which is particularly important for disentangling bulk and surface contributions in complex systems.

An additional improvement in 2024 was the refinement of the spin target handling. The magnetization procedure, which had previously required frequent manual intervention, was motorized to allow precise and reproducible control during experiments. This change enhanced the stability of the spin-resolved signals and improved the reliability of the data.

Our plan for FY2025 is to complete the lens calibration for the out-of-plane (z-axis) direction, so that spin polarization can be measured along all three spatial axes. Achieving this goal will make it possible to obtain the full spin information of electronic states in a truly three-dimensional manner, establishing a comprehensive framework for future spin-resolved studies at UVSOR.

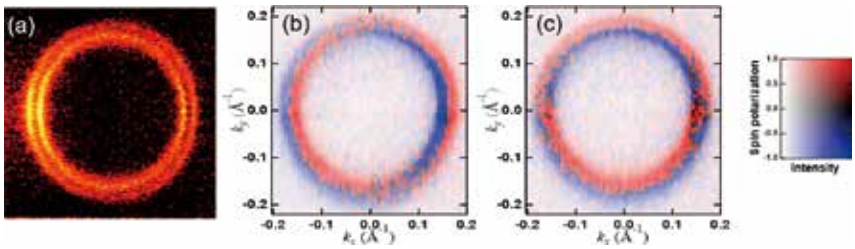

Figure 2. (a) Fermi surface image of Au(111) obtained using ordinary ARPES. Spin-resolved Fermi surface image of Au(111) with the spin detection axis aligned along the k_y (b) and k_x (c) directions.

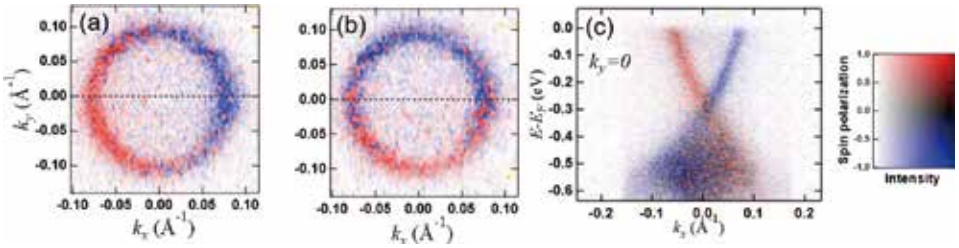

Figure 3. Spin-resolved Fermi surface images of the topological insulator Bi_2Se_3 with spin the detection axis aligned along the k_y (a) and k_x (b) directions. (c) Spin ARPES image along $k_y = 0$ in (a).

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Soft X-Ray Spectro-Microscopy and Scattering for Life Science—beyond Organelle Mapping

UVSOR Synchrotron Facility
Division of Advanced Photochemistry

ARAKI, Tohru
Senior Researcher

As a beamline scientist, I oversee the user science programs, in both academia and indsutry that utilize the BL4U-STXM (Scanning Transmission X-ray Microscopy) beamline at the UVSOR research facility. STXM is a form of X-ray absorption-based spectromicroscopy that provides label-free chemical mapping.

STXM is a specialized imaging technique that falls under the category of X-ray absorption-based spectromicroscopy. By measuring how different materials absorb X-rays at specific energies, STXM enables label-free chemical mapping, allowing researchers to visualize the distribution of various chemical components within biological and material samples without the need for dyes or stains. It has a wide range of applications in various fields, including energy materials, environmental and earth sciences, and industrial polymer studies. My current focus is on "beyond organelle mapping," which requires the advanced spectroscopy to identify the biomacromolecules. Shinohara *et al.* conducted a related study at the BL4U (*cells* 2019). The team presented the quantitative mapping of DNA, RNA, histones, and general proteins in mammalian cells, nuclei, and a chromosomes. This was achieved through the spectral fitting of the reference spectra. To accommodate a broader range of biological samples, including cells and tissues, it is essential to achieve higher chemical sensitivity and enhanced accuracy. "To establish this methodology, two key steps must be taken. First, a basic spectral interpretation of organelles must be conducted. Second, the sample preparation and specimen environment must be optimized. It is imperative to refrain from altering the samples and to preserve the native states of the cells, including the loss of metals or ions, throughout both the sample preparation and the data collection process, in order to prevent radiation damage." This is my statement from last year. However, due to technical difficulties and the need for a direct comparison between STXM and SEM, I have been working on the biological sample embedded in resin. The sample was ultra-thin sliced using a diamond knife to create a sample 100 nm thick for the STXM measurement. The bottom figures show the STXM results of *Ramazzottius varieornatus*, a tardigrade that is renowned for its anhydrobiotic capabilities, enabling it to survive in harsh, arid environments. The data was collected at the Carbon K-edge absorption for both active (hydrated) and inactive tardigrade samples. The experiment was conducted with the support of ExCELLS. My collaborators prepared the samples and conducted the SEM experiment. The spectra displayed in the Figure 1 correspond to the five significant components that were analyzed using principal component analysis and cluster analysis techniques of the active tardigrade. The following presentation offers a visual representation of the two component maps of C4 and C1 spectra for both active and inactive tardigrades. The distribution of the two components differs between two samples. To further elucidate these results, additional STXM data analysis and the scheduled immunoelectron microscopy experiment will be conducted.

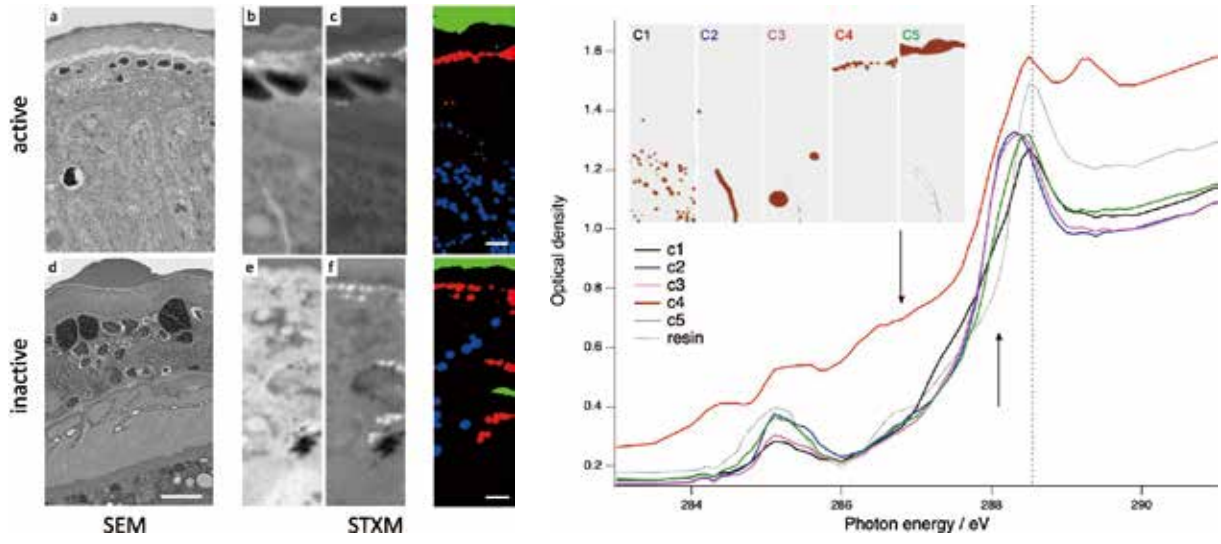


Figure 1. [left] SEM and STXM images of active (top) and inactive (bottom) tardigrade samples. (Scale bar 1 μm) RGB composite component map (red and blue: Two significant components, green: Resin). [right] 5 components map and the corresponding spectra of active tardigrade sample. (Two arrows indicate the photon energies used for the STXM images (b, e: 288.1 eV, c, f: 286.8 eV). The 5 significant components map is shown in C1–C5 images.)

Development of Resonant Soft X-Ray Scattering Spectroscopy for Photoresists

UVSOR Synchrotron Facility
Division of Advanced Photochemistry

IWAYAMA, Hiroshi
Senior Researcher

For further miniaturization of semiconductors, the era of EUV (13.5 nm) exposure has arrived, down from the 197 nm of the conventional ArF laser. This reduction in wavelength to less than one-tenth requires further thinning of the photosensitive materials (photoresists), leading to active development efforts of photoresist industry. Since the depth of focus decreases in proportion to the wavelength, EUV exposure requires a thickness of only a few tens of nanometers, compared to conventional photosensitive materials of around a few hundred nanometers. To preserve the 10-nm pattern, a thin base layer between the silicon substrate and photoresist is essential. The EUV exposure technology utilises a two-layer polymer film that is several tens of nanometers thick.

Resonant soft X-ray reflectivity is a technique that can determine the film thickness of different chemical species by utilizing the difference in X-ray resonance energy. We conducted experiments on a bilayer polymer film of PMMA (40 nm thick) and PVPh (70 nm thick). Figure 1 shows a schematic diagram of the sample.

The complex permittivity in the X-ray region is written as $(1-\delta(h\nu))-i(\beta(h\nu))$, where $(1-\delta)$ and β correspond to the refractive index and absorptivity, respectively. In the X-ray region, δ and β are much smaller than 1. Furthermore, δ and β are related by the Kramers-Kronig (KK) relation. Thus, $\beta(h\nu)$ is measured *via* the XAFS absorption spectrum. Figure 2 shows the refractive index δ calculated from each absorption spectrum using the KK transformation. Just as the pre-edge structure of the absorption spectrum differs depending on the molecular species, the refractive index δ also has a complex structure at the absorption edge that depends on the chemical species. Near the core absorption edge, selecting the resonance energy allows scattering contrast between chemically distinct species, even if their electron densities are nearly identical.

Figure 3 shows reflectivity measurements at both non-resonant and resonant energies. At non-resonant energy, a single period is observed, indicating a film thickness of 110 nm. The bilayer film appears as a single film. At resonant energy, a complex vibrational structure appears, reflecting the properties of a bilayer film. Details are still under analysis; according to these results, a method for analyzing multilayer polymer films using resonant soft X-ray reflection is being developed.

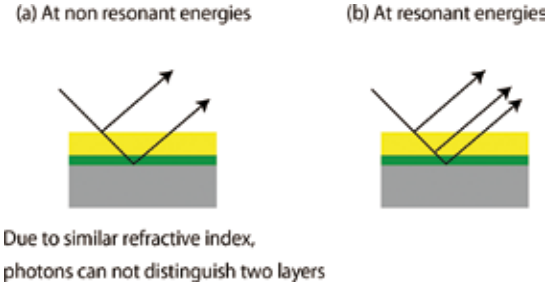


Figure 1. Schematic of (a) nonresonant and (b) resonant scattering of two polymer layers.

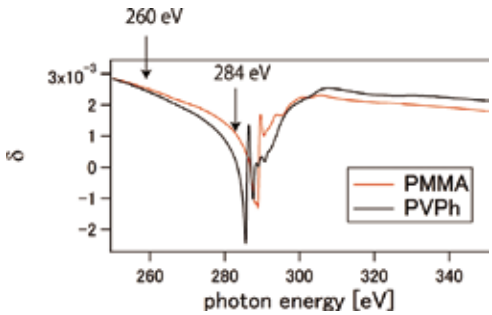


Figure 2. X-ray energy dependence of the refractive index δ of PMMA and PVPh polymers.

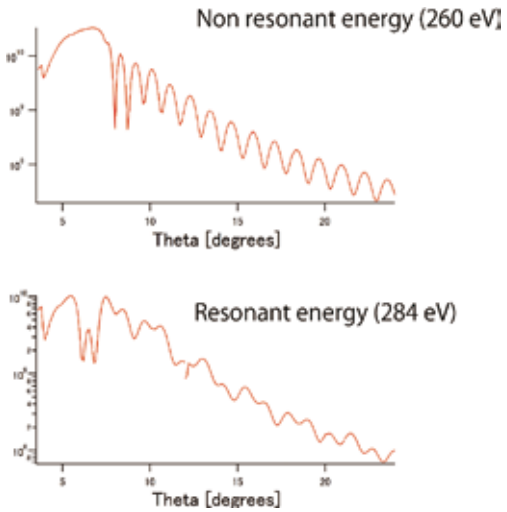
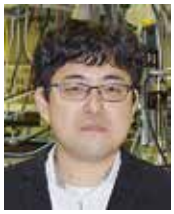


Figure 3. Reflectance spectra of (PMMA, PVPh) two-layer polymer film at off-resonance and resonant energies.

Soft X-Ray Absorption Spectroscopy for Observing Chemical Processes in Solution

Department of Photo-Molecular Science
Division of Photo-Molecular Science III



NAGASAKA, Masanari
Assistant Professor

Chemical processes in solutions were investigated using *operando* soft X-ray absorption spectroscopy (XAS) with different light elements.[1,2] In this year, the metal-ligand delocalization of metal porphyrin complexes was investigated from the ligand side,[3] and inner-shell calculations of large molecular systems were developed for polymers in solutions.[4]

1. Metal-Ligand Delocalization of Metal Porphyrin Complexes in Solutions

Metal-ligand delocalization of metal porphyrin complexes such as iron protoporphyrin IX was proved from the ligand side using N K-edge XAS.[3] The C=N π^* peaks of porphyrins are useful for discussing the central metal dependence of metal-ligand delocalization and the hydration structures of metal porphyrins in solutions.

2. Inner-Shell Calculations of Polymers in Solutions

Inner-shell spectra of poly(*N*-isopropylacrylamide) (PNIPAM) in solutions were calculated by extracting the 5-mer PNIPAM chains with terminated H atoms, including the second coordination shells of solvent molecules, from the snapshots of the molecular dynamics simulations.[4] The C=O π^* peaks of PNIPAM at the O K-edge reflected the structural changes of the polymer chains and the coordination of the C=O groups with solvent methanol and water molecules.

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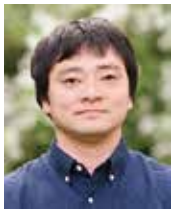
Visiting Professors

Visiting Professor
MATSUSHITA, Tomohiro *(from Nara Institute of Science and Technology)*

Development of Analysis Methods for Photoelectron Momentum Microscope

Following last year, we have continued the development of data analysis tools for the photoelectron momentum microscope introduced at UVSOR. This instrument is a highly powerful tool for observing the electronic structure of samples, including spin, by means of photoelectron spectroscopy. Using the first-principles calculation code OpenMX, we have enabled the calculation of photoelectron transition probabilities, so that the observed photoelectron intensities from the valence band can be analyzed. We have begun comparing the experimental results of twisted graphene obtained using the momentum microscope with theoretical calculations. In addition, we applied principal component analysis to the 1T-TaS_2 data obtained with this instrument, attempting to visualize the behavior of the phase transition. In this way, we are developing a framework that integrates first-principles calculations with information-theoretical approaches.



Visiting Associate Professor
SHIBUTA, Masahiro *(from Osaka Metropolitan University)*

Vibration-Resolved Unoccupied Molecular Orbitals by Two-Photon Photoemission Spectroscopy

Carrier-vibration couplings in organic thin films are important to understand the carrier mobilities in organic devices. So far, hole-vibration couplings have been studied, resolving fine structures of occupied orbitals using photoelectron spectroscopy. However, it was difficult to analyze electron–vibration couplings because we must analyze the unoccupied orbitals. Two-photon photoemission (2PPE) spectroscopy is a powerful method to observe unoccupied states with high resolution (20 meV), where a first photon injects an electron from a substrate into an adsorbed molecule, and the excited electron is extracted by a second photon. In fact, we have successfully resolved fine structures in the lowest unoccupied molecular orbital (LUMO)-derived peaks for small polyaromatic molecular films (*e.g.*, naphthalene, anthracene, phenanthrene) due to electron–vibration couplings. These results are opening the door to understand the electron mobility in the organic films. Furthermore, 2PPE can track the time-dependent behavior of the fine structures, which will unveil the energy modification and/or molecular motion of the excited state in the ultrafast regime.

RESEARCH ACTIVITIES
Materials Molecular Science

Extensive developments of new functional molecules and their assemblies are being conducted in three divisions of Electronic Structures, Electronic Properties, and Molecular Functions, and one division for visiting professors and associate professors, in an attempt to discover new phenomena and useful functions of molecular materials. The physical (electric, optical, thermal and magnetic) properties on new functional materials, the chemical properties like enzymes, catalysis and photochemistry, the exploitation of new spectroscopic methods for materials molecular science, and technological applications like batteries, photocatalysts, fuel cells, solar cells, and field effect transistors are investigated in this department.

Exploitation of Novel Spectroscopic Methods for Material and Surface Science

Department of Materials Molecular Science
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1994 Lecturer, The University of Tokyo
1996 Associate Professor, The University of Tokyo
2002 Professor, Institute for Molecular Science
Professor, The Graduate University for Advanced Studies

Member
Research Assistant Professor
KURAHASHI, Naoya
MAEJIMA, Naoyuki
Secretary
KURITA, Yoshiko

Keywords X-Ray Absorption Spectroscopy, Surface & Thin Film Magnetism, X-Ray Photoelectron Spectroscopy

For the developments of novel functional materials, it is quite important to exploit simultaneously new analytical methods based on advanced technology. Novel materials and devices often require spatial and/or time resolved analysis to optimize their qualities. In our group, we have been exploiting spectroscopic methods for material and surface science using mainly synchrotron radiation (SR) and partly lasers.

The first subject in our group is the spectroscopic analysis systems of magnetic thin films. In 2006, we successfully invented a novel magnetic nanoscope using ultraviolet magnetic circular dichroism (UVMCD) photoelectron emission microscopy (PEEM), which allows us to perform real-time and ultrafast magnetic imaging to investigate magnetic dynamics. We have also constructed *in situ* x-ray magnetic circular dichroism (XMCD) system using an ultrahigh vacuum superconducting magnet and a liq. He cryostat, which is installed at Beamline 4B of the IMS SR facility UVSOR-III. The apparatus is extensively open for public usage.

The second subject is the exploitation of ambient pressure hard x-ray photoelectron spectroscopy (AP-HAXPES) for polymer electrolyte fuel cells (PEFC) under working conditions. In 2017, we succeeded in real ambient pressure (10^5 Pa) HAXPES measurements for the first time in the world using Beamline 36XU of SPring-8. These works were supported by the NEDO Fuel Cell project. More recently, the apparatus moved to BL46XU and is used for more general chemical reactions on heterogeneous catalysts and electrochemical cells such as CO_2 reduction.

The third subject is applications of the x-ray absorption fine structure (XAFS) spectroscopy, soft x-ray emission spectroscopy, and angle-resolved ultraviolet photoelectron spectroscopy for functional materials. These investigations include femto- and picosecond time resolved XAFS measurements using x-ray free electron laser SACLA, for the investigations of the geometric structure of the photoexcited state of photocatalytic systems and the spin dynamics of magnetic materials. Conventional temperature dependent EXAFS spectroscopy has been conducted for a very long time to elucidate thermal and dynamic properties of functional alloy materials as negative thermal expansion alloys.

Selected Publications

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- T. Yokoyama and K. Eguchi, "Anharmonicity and Quantum Effects in Thermal Expansion of an Invar Alloy," *Phys. Rev. Lett.* **107**, 065901 (2011).
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- T. Koitaya, K. Yamamoto, T. Uruga and T. Yokoyama, "*Operando* Characterization of Copper–Zinc–Alumina Catalyst for Methanol Synthesis from Carbon Dioxide and Hydrogen by Ambient-Pressure Hard X-Ray Photoelectron Spectroscopy," *J. Phys. Chem. C* **127**, 13044–13054 (2023).
- Y. Uemura *et al.*, "Dynamics of Photoelectrons and Structural Changes of Tungsten Trioxide Observed by Femtosecond Transient XAFS," *Angew. Chem., Int. Ed.* **55**, 1364–1367 (2016).

1. Femtosecond Resonant X-Ray Emission Spectra of Photocatalyst WO_3[1)]

Tungsten trioxide WO_3 is one of the well-studied photocatalysts for the solar-assisted photochemical water splitting reaction. Previously we investigated femto- and picosecond time resolved x-ray absorption fine structure (XAFS) spectroscopy to reveal the local geometric and electronic structures of the metastable photoexcited states in WO_3, using synchrotron radiation from Photon Factory Advanced Ring and the x-ray free electron laser SACLA.[2–4)] The metastable photoexcited polaron state is found to exhibit more distorted W–O bonds with a reduced W valency compared to the ground state. In the present study, we have performed newly developed femtosecond high-energy-resolution fluorescence detection (HERFD) XAFS and resonant x-ray emission spectra (RXES) measurements for the femtosecond photoexcited state of the WO_3 catalyst using SACLA BL3 EH2.

Figure 1 shows the femtosecond time resolved W L_3-edge XAFS spectra with normal energy resolution. The HERFD-XAFS spectra were obtained from the RXES as given in Figure 2. By comparing Figures 1(a) and 1(c), the improvement of the energy resolution is quite clear, implying usefulness of the HERFD XAFS measurement. It is found that in the initial state of the visible-light photoexcitation (~100 fs), the W L_3 edge $W2p_{3/2} \rightarrow 5d$ absorption shifts to a lower energy side and the W 5d energy levels of the t_{2g} and e_g peaks are modulated due to the photoexcited electrons in the conduction band. The electronic state of the photoexcited W atoms is modified by 500 fs. The crystal field splitting (difference between the W 5d t_{2g} and e_g peak energies) shrinks by 500 fs, which indicates local structural changes around the W atoms due to the formation of the metastable polarons. Consequent schematic descriptions of the photoexcited electronic states are summarized in Figure 3.

HERFD-XAS and RXES provide more details about the early stage of the photoexcited states of WO_3. This work demonstrates that the detailed dynamics of 5d elements in the femtosecond range can be addressed with HERFD-XAS/RXES.

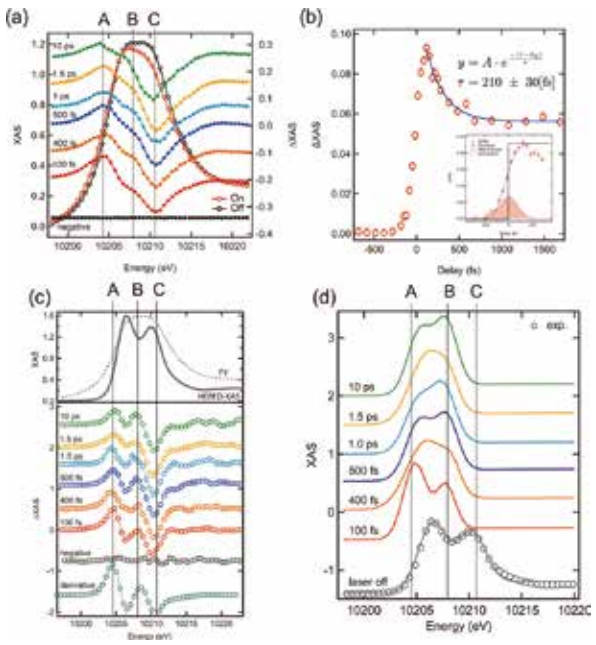

Figure 1. (a) Pump–probe normal energy resolution XAFS spectra and their first derivatives of WO_3 at different time delays. (b) The kinetic trace of XAFS at peak A in (a). (c) Pump–probe HERFD-XAFS and their first derivatives of WO_3 at the corresponding time delays to those in (a). The first derivative of the laser off spectrum is also given. (d) shows the reconstructed excited state spectra.

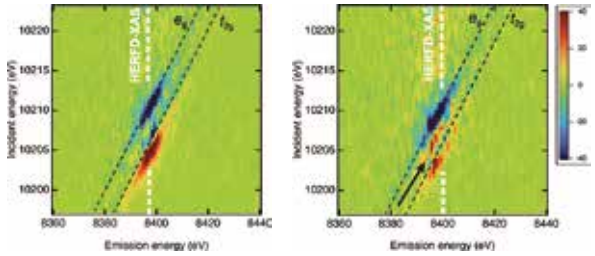

Figure 2. Typical examples of the pump–probe RXES at the delay time of 100 fs (left) and 10 ps (right). The white dash lines imply the energy to form HERFD-XAS in Figure 1(c).

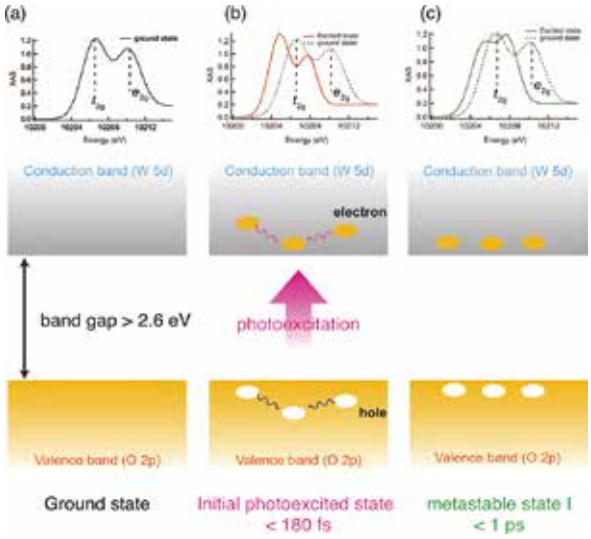

Figure 3. A sketch of proposed photoexcitation and relaxation mechanism: (a) the optical ground state, (b) the initial photoexcited state, (c) the metastable polaron state. After photoexcitation, electrons in the conduction band are delocalized. The HERFD-XAFS spectrum shifts in lower energies due to the presence of the electrons in the conduction band. In later delays in Figure 3(c), the electrons are localized, which is supported by the change of the spin–orbit coupling term for the multiplet calculations of W L_3 HERFD-XAFS.

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3) Y. Uemura *et al.*, *Angew. Chem., Int. Ed.* **255**, 1364 (2016). DOI: 10.1002/ange.201509252

4) D. Kido, Y. Uemura, Y. Wakisaka, A. Koide *et al.*, *Chem. Lett.* **51**, 1083 (2022). DOI: 10.1246/cl.220381

Exiotic Structures, Physicochemical Properties and Quantum Dynamics of Interfacial Water

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2018 CSJ Presentation Award 2018
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Keywords Surface & Interface Science, Nonlinear Optical Spectroscopy, Water Molecules

Interfacial water is ubiquitous in nature and plays crucial roles in a variety of disciplines, including physics, chemistry and biology. In such a symmetry-breaking system, not only adsorption geometry but also anisotropic molecular orientation (H-up/H-down configuration) is a key structural parameter that determines unique physicochemical properties of interfacial water systems. Nevertheless, orientation of water molecules, *i.e.* configuration of hydrogens, in the interfacial hydrogen-bond network is extremely hard to investigate with traditional experimental techniques such as electron diffraction, grazing X-ray scattering and even scanning prove microscopy, because hydrogen has only a single electron and responds extremely weakly to the probes of these techniques. Therefore, the determination of molecular orientation of interfacial water has been an experimental challenge.

We have used phase-sensitive sum-frequency generation spectroscopy for unveiling molecular orientation of interfacial water system. The remarkable feature of this technique is that $\mathrm{Im}\chi^{(2)}$ SFG spectra ($\chi^{(2)}$: The second-order nonlinear susceptibility) obtained by the heterodyne detection exhibit positive or negative sign for net orientation of OH with hydrogen pointing away (H-up) or toward substrate (H-down), respectively. Thus, the heterodyne-detected $\mathrm{Im}\chi^{(2)}$ SFG has a great advantage to direct observation of water orientation that cannot be investigated through other traditional experimental methods. With this sophisticated molecular spectroscopy technique, we have conducted a series of pioneering research on unique structures and physicochemical properties of hydrogen bonds of interfacial water molecules.

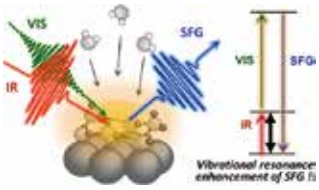

Figure 1. Infrared-visible sum-frequency-generation (SFG) spectroscopy of water molecules on solid surface.

Selected Publications

- T. Sugimoto *et al.*, "Orientational Ordering in Heteroepitaxial Water Ice on Metal Surfaces," *Phys. Chem. Chem. Phys.* **29**, 16435–17012 (2020). [review]
- H. Sato *et al.*, "Beyond Reduction Cocatalysts: Critical Role of Metal Cocatalysts in Photocatalytic Oxidation of Methane with Water," *Angew. Chem., Int. Ed.* **62**, e2023060 (2023).
- S. Takahashi *et al.*, "Broadband Tip-Enhanced Nonlinear Optical Response in a Plasmonic Nanocavity," *J. Phys. Chem. Lett.* **14**, 6919–6926 (2023).
- Z. Lin *et al.*, "Positive and Negative Impacts of Interfacial Hydrogen Bonds on Photocatalytic Hydrogen Evolution," *J. Am. Chem. Soc.* **146**, 22276–22283 (2024).
- H. Sato *et al.*, "Direct *operando* Identification of Reactive Electron Species Driving Photocatalytic Hydrogen Evolution on Metal-Loaded Oxides," *J. Am. Chem. Soc.* **146**, 24800–24807 (2024).
- A. Sakurai *et al.*, "Tip-Enhanced Sum Frequency Generation for Molecular Vibrational Nanospectroscopy," *Nano Lett.* **25**, 6390–6398 (2025).

1. Tip-Enhanced Sum Frequency Generation for Molecular Vibrational Nanospectroscopy[1)]

We achieved the first detection of vibrational sum-frequency generation (VSFG) signals from molecules at the nanometer scale by developing a tip-enhanced VSFG (TE-SFG) system. Conventional VSFG is a powerful tool for probing molecular structures and orientations at surfaces, but its spatial resolution is restricted by the diffraction limit, yielding ensemble-averaged responses from millions of molecules.

To break this barrier, we integrated femtosecond VSFG spectroscopy with scanning tunneling microscopy. By confining IR and near-IR pulses within the nanogap between a metallic substrate and an STM tip, we detected vibrational signals from molecules adsorbed on the surface. The signal emerged only in the tunneling regime and vanished when the tip–substrate distance exceeded 1 nm, demonstrating localization within ~1 nm. Characteristic vibrational modes of terminal methyl groups were clearly resolved, and analysis of the nonlinear susceptibility revealed their absolute orientation.

Electromagnetic simulations clarified that such extreme localization arises from two synergistic enhancement mechanisms: (i) the antenna effect, which enhances mid-IR absorption at the tip apex, and (ii) plasmonic resonance in the nanogap, which boosts the radiation efficiency of the visible VSFG signal.[2)] Together, these effects yield an enormous effective signal enhancement on the order of 10^{13}, enabling the near-field response from even a single molecule to dominate over far-field background contributions from ~10^8 molecules within a laser focal spot.

This achievement represents the first demonstration of molecular vibrational SFG detection at the nanometer scale. By uniting ultrafast vibrational spectroscopy with scanning probe microscopy, TE-SFG establishes a powerful platform for nonlinear optical nanospectroscopy. The method enables ultrahigh spatial resolution and single-molecule sensitivity, paving the way toward single-molecule ultrafast spectroscopy and molecular imaging beyond the diffraction limit. These capabilities hold strong promise for elucidating interfacial molecular processes in catalysis and materials science, offering a novel route for the rational design of advanced functional materials.

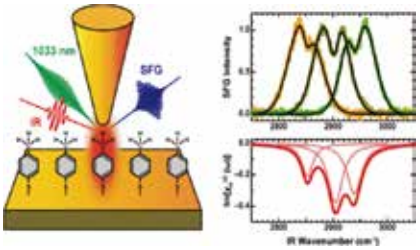

Figure 2. First successful demonstration of near-field tip-enhanced sum-frequency-generation vibrational nanospectroscopy of interfacial molecular systems.

2. Critical Impacts of Metal Cocatalysts on Oxidation Kinetics and Optimal Reaction Conditions of Photocatalytic Methane Reforming[3)]

Photocatalytic activation of methane, the main component of natural gas, is a key process for sustainable energy conversion. In this study, we clarified how metal cocatalysts critically regulate oxidation kinetics and determine optimal reaction conditions in photocatalytic methane reforming under ambient temperature.

Traditionally, noble metal cocatalysts supported on semiconductor photocatalysts have been viewed primarily as electron collectors that promote reduction reactions. Our recent paradigm-shifting work demonstrated, however, that metal cocatalysts can also act as efficient acceptors of photogenerated holes.[4)] Building on this concept, the present study provides the first direct evidence that cocatalyst loading drastically alters the methane pressure dependence of photocatalytic oxidation, shifting the optimal reaction regime to below ambient pressure.

Through systematic kinetic analysis, we revealed that this effect originates from molecular-level congestion of reactive intermediates during the oxidation process, with metal cocatalysts themselves functioning as active sites for oxidation. These findings overturn the conventional view that cocatalysts serve only reductive roles, highlighting their bidirectional contributions to both oxidation and reduction.

This work demonstrates that precise control of metal cocatalysts enables the microscopic design of surface reaction fields and optimization of reaction processes. By redefining the role of cocatalysts in photocatalysis, the study opens a pathway toward rational catalyst engineering for efficient and sustainable methane utilization.

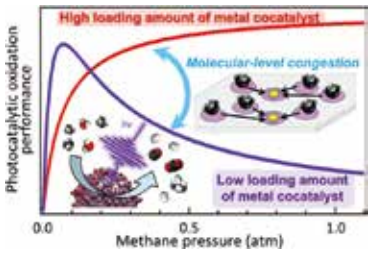

Figure 3. Photocatalytic oxidation kinetics and optimal pressure of methane vary significantly with the loading amount of metal cocatalysts. These variations are well described by kinetic analyses treating molecular-level congestion of oxidation intermediates.

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3) H. Sato and T. Sugimoto, *Chem. Commun.* **61**, 5942–5945 (2025).
4) H. Saito, H. Sato, T. Higashi and T. Sugimoto, *Angew. Chem., Int. Ed.* **62**, e2023060 (2023).

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Exploration of Novel Electronic/Ionic Physical Properties Using Inorganic Thin Films

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Keywords Inorganic Solid-State Chemistry, Surface-Interface Science, Solid-State Electrochemistry

Interface control is a critical issue in both electronic and electrochemical devices. Using thin-film technologies, our group constructs well-defined model interfaces and explore novel electronic and ionic properties.

For electronic devices, we focus on the synthesis and characterization of metastable metal hydrides. Non-equilibrium film growth processes and epitaxial growth techniques enable the realization of functionalities unattainable in bulk materials. By controlling the charge states of hydrogen in solids, we aim to achieve high-transition-temperature superconductivity and develop multifunctional switching devices driven by external fields such as light, heat, and electric fields.

For ionic devices, we are working to improve the performance of fluoride-ion secondary batteries toward high-capacity energy storage. Batteries consist of a cathode, electrolyte, and anode, and operate through the migration of carrier ions between electrodes across the electrolyte. In this process, the electrode–electrolyte interface, where dissimilar materials come into contact, often represents the bottleneck for ion transport. By fabricating model interfaces within thin-film battery and conducting quantitative evaluations, we establish strategies for controlling carrier-ion transport at interfaces.

In addition, to accelerate materials research we are working on the digital transformation (DX) of materials research, including laboratory automation. Conventionally, materials were carefully synthesized and optimized one by one to evaluate their electronic and ionic properties. In this context, we are introducing robots and AI technologies. The use of robots allows experiments to be conducted in extreme environments, such as inert gas atmospheres or X-ray irradiation conditions, where humans cannot enter. Our goal is to advance the automation of experiments and promote the coexistence of humans and robots in materials research.

Figure 1. (left): Multiple-field-induced functions of hydride-related materials. (right): Conceptual illustration of experiments combining artificial intelligence (AI) and robots.

Selected Publications

- Y. Komatsu, R. Shimizu *et al.*, "Repeatable Photoinduced Insulator-to-Metal Transition in Yttrium Oxyhydride Epitaxial Thin Films," *Chem. Mater.* **34**, 3616 (2022).
- K. Nishio, R. Shimizu *et al.*, "Immense Reduction in Interfacial Resistance between Sulfide Electrolyte and Positive Electrode," *ACS Appl. Mater. Interfaces* **14**, 34620 (2022).
- M. Haruta, R. Shimizu *et al.*, "Negligible "Negative Space-Charge Layer Effects" at Oxide-Electrolyte/Electrode Interfaces of Thin-Film Batteries," *Nano Lett.* **15**, 1498 (2015).
- R. Shimizu *et al.*, "Autonomous Materials Synthesis by Machine Learning and Robotics," *APL Mater.* **8**, 111110 (2020).
- S. Kobayashi, R. Shimizu *et al.*, "Autonomous Exploration of an Unexpected Electrode Material for Lithium Batteries," *ACS Mater. Lett.* **5**, 10 (2023).

1. Hydrogen Charge-State Control of Multi-Anion Hydrides

The charge state of hydrogen in solids depends on the electronegativity of its bonding partner and can exist as a proton (positively charged), atomic hydrogen (electrically neutral), or a hydride (negatively charged). In this study, we achieved control over protonic and hydridic states in thin-film materials with multi anions with oxygen and nitrogen.

In the calcium–nitrogen–hydrogen system ($Ca_xN_yH_z$), protonic CaNH (imide) and hydridic Ca_2NH (nitrride hydride) are known. However, no synthesis of these compounds in thin-film form had previously been reported, and no guidelines for their fabrication were available. Using reactive magnetron sputtering, we achieved the selective epitaxial growth of both CaNH and Ca_2NH thin films.

To elucidate the selective growth processes, we monitored plasma emission of atomic Ca (422 nm) during the sputtering process. This result revealed that the growth pathway is governed by the relative reaction probabilities of Ca with hydrogen and nitrogen: Under high hydrogen partial pressure, hydrogen reacts preferentially with Ca to form CaH_x, which subsequently converts into CaNH, whereas under low hydrogen partial pressure, hydrogenation and nitrogenation occur simultaneously in a single step to yield Ca_2NH.

Furthermore, by further reducing the hydrogen partial pressure, we successfully synthesized epitaxial thin films of the layered electride Ca_2N. These findings open up new opportunities for controlling physical properties and exploring novel functionalities across proton, hydride, and electride.

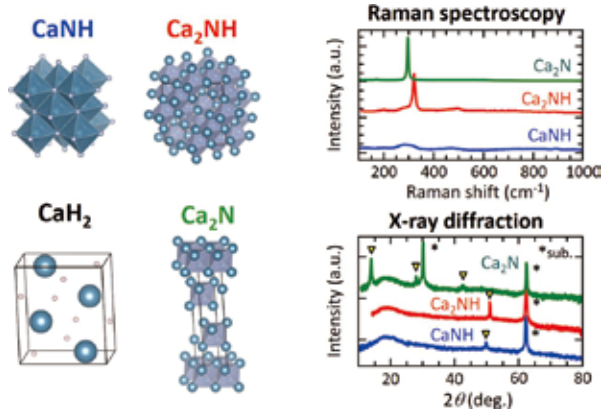

Figure 2. Selective growth of CaNH/Ca_2NH/Ca_2N epitaxial thin films.

2. Electrode/Electrolyte Interface Control of Fluoride Ion Batteries

To realize thin-film fluoride batteries, we fabricated and evaluated liquid-electrolyte cells using BiF_3 thin films as a cathode. When the BiF_3 thin-film electrode surface was directly immersed in the liquid electrolyte, the initial discharge capacity exceeded the theoretical value (~302 mAh g^{-1}), suggesting the occurrence of side reactions. Furthermore, the capacity retention decreased drastically upon cycling.

To address this issue, we applied interfacial control techniques established in Li-ion batteries[2] and introduced a chemically stable LaF_3 solid electrolyte buffer layer onto the BiF_3 electrode surface. As a result, side reactions were effectively suppressed, and the decline in capacity retention during cycling was suppressed. Future studies will focus on evaluations under non-exposure conditions by transferring the cells through vacuum and Ar atmospheres, thereby eliminating the influence of ambient moisture.

This study is collaboration with Dr. Taketoshi Minato of Instrument Center.

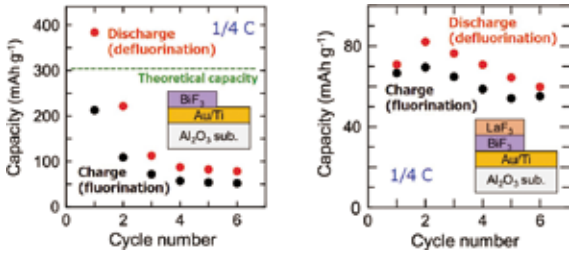

Figure 3. Cycle dependence of charge/discharge capacity. (Left) BiF_3 thin-film electrode in direct contact with liquid electrolyte; (Right) BiF_3 thin-film electrode covered with a LaF_3 solid-electrolyte buffer layer.

3. Format Standardization for Laboratory Automation

In advancing laboratory automation, the standardization of both hardware and software is essential. We have constructed a fully automated and autonomous system for inorganic thin-film synthesis and characterization. In recent years, we have also promoted the standardization of data format generated by automated measurement systems. Here, by employing the MaiML (Measurement, Analysis, Instrument Markup Language) framework—newly standardized as a JIS specification by the Japan Analytical Instruments Manufacturers' Association (JAIMA)—we established a scheme for data sharing on the cloud and successfully applied it to the optimization of synthesis conditions.[3]

At present, through collaborative research, we are extending such autonomous materials exploration systems to a variety of fields, including spintronics materials and hydrogen storage materials.

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3) K. Nishio, R. Shimizu *et al.*, *Digit. Discov.* **4**, 1734 (2025).

Nanostructure Fabrication, Optical Property Control, and Photonic Functionalization of Atomic-Layer Materials

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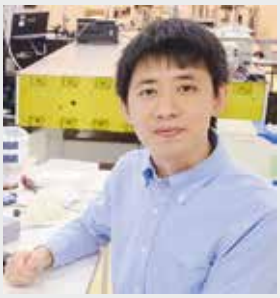

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Keywords Semiconductors, Two-Dimensional Materials, Photophysical Properties

Modern electronic devices are approaching their miniaturization limits, necessitating innovative solutions through the integration of optical and quantum effects. Our research group focuses on atomic layer materials, particularly transition metal dichalcogenides (TMDs), which exhibit remarkable optical properties due to their single-atom thickness.

These materials possess direct bandgaps with strong light–matter interactions and unique electronic properties stemming from their extreme two-dimensionality. By stacking different atomic layers through van der Waals forces, we can create artificial heterostructures. In these structures, excitons—bound pairs of electrons and holes generated by photoexcitation—become spatially confined within periodic moiré potentials.

Our team has successfully observed exciton localization phenomena in $WSe_2/MoSe_2$ heterostructures induced by moiré potentials. Through detailed investigations of interlayer exciton formation and their optical responses, including circular polarization characteristics and quantum coherence measurements, we continue to elucidate the quantum states of moiré excitons. Currently, we are advancing this research by developing nanofabrication techniques for atomic layer materials and precisely controlling light–matter interactions to explore novel optical phenomena and functionalities.

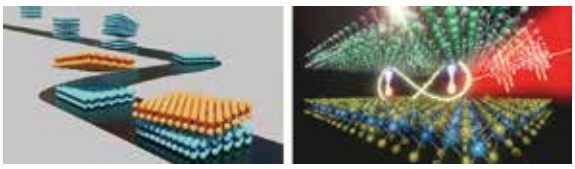

Figure 1. Left: Schematics of nanofabrication process for atomic-layer materials. Right: Visualization of quantum optical phenomena emerging from the engineered atomic-layer nanostructures.

Selected Publications

- H. Wang, H. Kim, D. Dong, K. Shinokita, K. Watanabe, T. Taniguchi and K. Matsuda, "Quantum Coherence and Interference of a Single Moiré Exciton in Nano-Fabricated Twisted Monolayer Semiconductor Heterobilayers," *Nat. Commun.* **15**, 4905 (2024).
- K. Shinokita, K. Watanabe, T. Taniguchi and K. Matsuda, "Valley Relaxation of the Moiré Excitons in a $WSe_2/MoSe_2$ Heterobilayer," *ACS Nano* **16**, 16862 (2022).
- K. Shinokita, Y. Miyauchi, K. Watanabe, T. Taniguchi and K. Matsuda, "Resonant Coupling of a Moiré Exciton to a Phonon in a $WSe_2/MoSe_2$ Heterobilayer," *Nano Lett.* **21**, 5938 (2021).
- K. Shinokita, X. Wang, Y. Miyauchi, K. Watanabe, T. Taniguchi and K. Matsuda, "Continuous Control and Enhancement of Excitonic Valley Polarization in Monolayer WSe_2 by Electrostatic Doping," *Adv. Funct. Mater.* **29**, 1900260 (2019).

1. Tailoring Exciton Dimensionality and Unveiling Prolonged Valley Polarization

Interlayer excitons (IXs) in twisted TMD heterostructures are a promising platform for novel optoelectronic devices. However, the moiré potential arising from the lattice mismatch often traps these IXs, forming zero-dimensional (0D) quantum emitters known as moiré excitons. While interesting for quantum optics, these localized states are less suitable for applications like photodiodes or solar cells, which benefit from mobile two-dimensional (2D) excitons.

To address this, we demonstrated a strategy to tune the dimensionality of IXs in a $MoSe_2/WSe_2$ heterostructure. By inserting an atomically thin hexagonal boron nitride (h-BN) layer as a spacer, we effectively modulated the moiré potential landscape, thereby transforming the trapped 0D moiré excitons into 2D IXs. The transition was unambiguously confirmed through systematic optical spectroscopy, which revealed a significant blue-shift in photoluminescence (PL) energy and a change from nonlinear saturation to linear power dependence of the PL intensity, a hallmark of the transition from a localized to a delocalized system. A remarkable feature of these engineered 2D IXs is their prolonged valley relaxation lifetime, which reaches up to 100 nanoseconds at low temperatures—orders of magnitude longer than the picosecond lifetimes typically observed in monolayer TMDs. This longevity is attributed to the suppression of the electron–hole exchange interaction, a dominant valley depolarization mechanism, which is weakened by the spatial separation of the electron and hole across the h-BN spacer. Our findings provide an effective strategy to tailor exciton dimensionality and harness the long valley lifetime of 2D IXs for future opto-valleytronic applications.

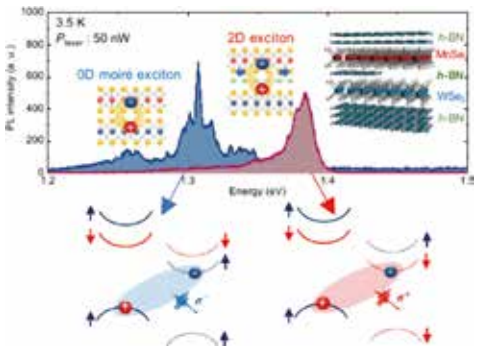

Figure 2. Dimensionality control and valley polarization of interlayer excitons in a $MoSe_2/WSe_2$ heterostructure. The insertion of an h-BN spacer layer (center schematic) transforms 0D moiré excitons with sharp emission peaks (blue spectrum) into 2D excitons with broad emission (red spectrum). These excitons exhibit a unique optical response to circularly polarized light (σ^+/σ^-, bottom schematic), enabling long-lived valley polarization.

2. Observation of Magnetically Switchable Nonlinear Photocurrents

The bulk photovoltaic effect (BPVE), which generates spontaneous photocurrents in non-centrosymmetric materials, offers a pathway to overcome the Shockley-Queisser efficiency limit of conventional solar cells. We investigated these nonlinear photoresponses in a vdW heterostructure that breaks both spatial inversion (P) and time-reversal (T) symmetry, composed of monolayer MoS_2 and the layered antiferromagnet $CrPS_4$. At the hetero-interface, the broken P-symmetry gives rise to a spontaneous photocurrent under illumination, which we identified as a shift current.

More strikingly, we discovered that this photocurrent is highly sensitive to the magnetic state of the $CrPS_4$ layer. The spontaneous photocurrent changed drastically below the Néel temperature of $CrPS_4$ (~40 K), where it transitions into an antiferromagnetic (AFM) phase. This phenomenon is attributed to the emergence of a "magnetic injection current," a distinct nonlinear photocurrent that arises in systems with broken T-symmetry and is superimposed on the existing shift current. We further demonstrated that the net photocurrent can be actively switched with an external magnetic field, which triggers distinct magnetic phase transitions in $CrPS_4$ (*e.g.*, from canted-AFM to ferromagnetic) and alters the contribution of the magnetic injection current. This work demonstrates a magnetic-field-controllable photovoltaic effect and opens a new avenue for "magneto-photovoltaics," a new class of devices that merge magnetism with solar energy conversion.

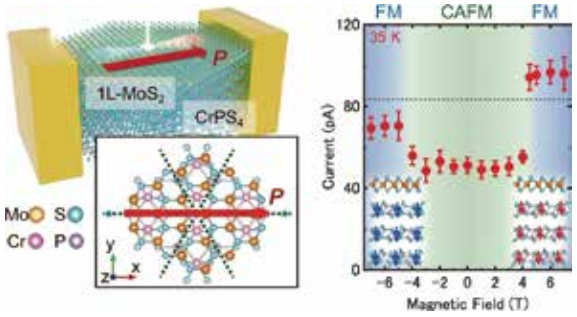

Figure 3. Magnetic field-switching of nonlinear photocurrent at a $MoS_2/CrPS_4$ hetero-interface with broken P- and T-symmetry. In the heterostructure (left schematic), a spontaneous photocurrent is observed. As the magnetic phase of the $CrPS_4$ layer is changed by an external magnetic field (right plot, from canted-AFM to ferromagnetic phase at 35 K), the photocurrent increases in a step-like manner, demonstrating active control of the optical response.

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Solid-State NMR for Molecular Science

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Keywords Solid State NMR, Biomolecules, Developments

In order to elucidate functions of molecules, characterization of the molecule is the first step. There is a variety of important molecules, which are insoluble in any solvents and functional at amorphous state. Solid-state NMR enables us to obtain a variety of information at atomic resolution without damage to molecules and significant restrictions. Thus, solid-state NMR is one of the essential tools for the characterizations of those molecules.

We have been working on methodology and hardware developments of solid-state NMR and their application to structural biology and materials science. We study characterizations of membrane proteins and peptides, organic materials, natural products and synthetic polymers. Characterization of those molecules based on solid-state NMR is underway through collaborations with several research groups.

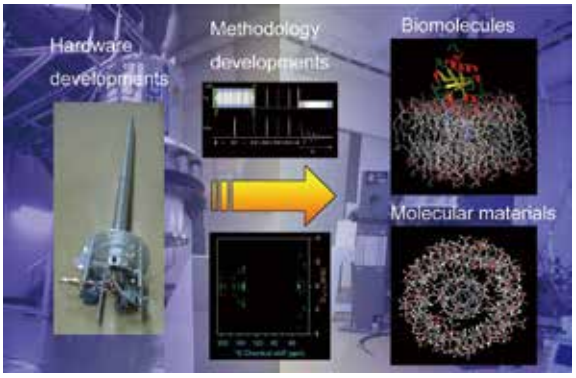

Figure 1. Outline of our studies.

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- M. Tanio and K. Nishimura, "Intramolecular Allosteric Interaction in the Phospholipase C-δ1 Pleckstrin Homology Domain," *Biochim. Biophys. Acta, Proteins Proteomics* **1834**, 1034–1043 (2013).
- T. Asakura, T. Ohata, S. Kametani, K. Okushita, K. Yazawa, Y. Nishiyama, K. Nishimura, A. Aoki, F. Suzuki, H. Kaji, A. Ulrich and M. Williamson, "Intermolecular Packing in B. Mori Silk Fibroin: Multinuclear NMR Study of the Model Peptide (Ala-Gly)15 Defines a Heterogeneous Antiparallel Antipolar Mode of Assembly in the Silk II Form," *Macromolecules* **48**, 28–36 (2015).
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- N. Ousaka, F. Mamiya, Y. Iwata, K. Nishimura and E. Yashima, "'Helix-in-Helix' Superstructure Formation through Encapsulation of Fullerene-Bound Helical Peptides within a Helical Poly(methyl methacrylate) Cavity," *Angew. Chem., Int. Ed.* **56**, 791–795 (2017).
- M. Yagi-Utsumi, S. G. Itoh, H. Okumura, K. Yanagisawa, K. Kato and K. Nishimura, "The Double-Layered Structure of Amyloid-β Assemblage on GM1-Containing Membranes Catalytically Promotes Fibrillization," *ACS Chem. Neurosci.* **14**, 2648–2657 (2023).

1. Developments of Solid-State-NMR Techniques

In rigid organic solids, it is not easy to achieve high resolution ^{1}H NMR spectra in solid-state NMR spectroscopy due to the presence of strong ^{1}H homonuclear dipolar couplings which broaden ^{1}H signals. Therefore, ^{1}H homonuclear dipolar couplings must be decoupled efficiently by applying either magic angle spinning (MAS) at sufficiently high speed larger than 60 kHz or MAS at moderate speed in combination with multiple pulses (MPs). MAS and MPs give perturbations to spatial and spin parts of ^{1}H homonuclear dipolar coupling Hamiltonian, respectively. Furthermore, by using significantly high power radio frequency field (RF), it is still possible to apply MPs under ultra-high speed MAS in which require to keep short cycle time of MPs respect to the MAS period to avoid interference of time averaging effect between spatial and spin parts of ^{1}H homonuclear dipolar coupling Hamiltonian. Even under ultra-high speed MAS, applications of MPs improve spectral resolution furthermore. Therefore, methodology developments of MPs is still one of important research topics. ^{1}H spectral resolution depends on both the efficiency of decoupling and chemical shift scaling factor of MPs. The former factor can be improved through design of MPs enabling the removal of high order correction terms. On the other hand, the latter factor also depends on the design of MPs and larger scaling factor contributes better spectral resolution.

In the last report, we have reported the developed new MP sequence enabling removal of high order correction terms with moderate sequence length to realize efficient ^{1}H homonuclear dipolar decoupling. In this time, we have developed similar but new MPs possessing larger chemical shift scaling factors over previous one. However, the new MPs have twice length of previous one. Therefore, those are suitable to the conventional MAS up to 40 kHz. Such new sequences were evaluated theoretically and their performances will be demonstrated soon.

We have also designed two different types of modules to achieve heteronuclear dipolar recoupling with homonuclear decoupling of irradiated nuclei. The detail of those experiments will be reported. Such new sequences were evaluated theoretically and their performances will be demonstrated soon.

2. Developments of Core Technologies for Solid-State NMR Probes

We have been working on developments of totally original solid-state NMR probes for a couple of years. The probe had been successfully built using originally designed parts except for a spinning module for 400MHz NMR. Then, we have been working on developments of original sample spinning modules for MAS solid-state NMR probes which are fully compatible with Bruker spectrometers and commercial sample tubes. The spinning modules have been designed to fit probes for narrow bore magnet with outer sleeve possessing 38 mm inner diameter. We started the design of a spinning module for a standard 4.0 mm sample tube. After several times of version up, our original spinning module significantly exceeded the spinning performance of the commercial one from Bruker.

The design and build of final version of the spinning module have been finished. Currently, it is under optimization of air bearing black to achieve sufficient stability of spinning at high spinning rate.

Furthermore, the design and build of final version of the original spinning module for 2.5mm sample tube have been finished and it is also optimization of air bearing black.

Currently, we are also working on the design and build of the original spinning module for 1.9 mm sample tube.

3. Characterization of Synthetic Molecules by Solid-State NMR[1)]

Solid-state NMR is one of the efficient techniques to characterize amorphous samples such as synthetic molecules. We have collaborated with many research groups for the characterization of new synthetic molecules using solid-state NMR at the past. During couple of years, we have been collaborated with Associate Prof. Segawa group in IMS for the characterization of their newly developed synthetic molecules which are categorized to covalent organic frameworks (COFs).

Finally, ^{13}C signal solid-state NMR signal assignments had been successfully achieved for two of the new molecules. The obtained results from solid-state NMR together with other experimental data from other experiments sufficiently prove the achievement of the target molecular form of COFs for those samples. This project is also on the way.

Reference

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Unveiling Complex Phenomena at Solid–Liquid Interfaces by Scanning Probe Microscopy

Instrument Center

MINATO, Taketoshi
Senior Researcher

The solid–liquid interface serves as a reaction field for a wide range of phenomena, including electro- chemical reactions, dissolution and crystallization, catalysis, and hydrophilicity.[1–3] Despite extensive research, many fundamental aspects of these interfaces remain poorly understood due to their complex and dynamic nature. Scanning probe microscopy (SPM) represents a rare and powerful technique that can directly access the solid–liquid interface, allowing for detailed analysis of geometric structures, mechanical properties, electronic properties, magnetic properties, and even reaction mechanisms with exceptionally high resolution and sensitivity. In our studies, we have applied SPM to investigate electrochemical reactions as well as the physical properties of ice–liquid interfaces, providing new insights into interfacial behavior at the nanoscale.

At the electrode–electrolyte interface in electrochemical systems, the spatial distribution of interfacial structures strongly influences reaction kinetics and mechanisms. However, conventional spectroscopic analyses often fail to provide precise information on local variations in the interfacial structure due to limitations in spatial resolution. To overcome this challenge, we employed force curve measurements using SPM to analyze the local interfacial structure. By examining the distance between plateaus in the force curves, we were able to characterize the distribution of interfacial species (Figure 1). Notably, we observed that changes in the potential of a gold electrode led to significant alterations in the distribution of ionic liquid structures at the interface. This approach demonstrates the potential for probing more complex electrochemical reactions and understanding how local structural changes influence reaction pathways.

In addition to electrochemical systems, we have investigated the interface between ice and liquids. While the physical properties of ice have been extensively studied under ultra-high-vacuum conditions, many ice-related phenomena in nature occur at the interface between ice and liquid. In collaboration with Professor Hiroshi Onishi (Kobe University and IMS), we developed an analytical system based on amplitude-modulation atomic force microscopy to study the interfacial state between ice and liquids. Using this system, we successfully characterized both the structural and mechanical properties of the interface between alcohols and ice.[4–5] To obtain even more detailed information, we further developed a frequency-modulation atomic force microscopy system capable of operating in sub-zero antifreeze liquids. This system was applied to investigate the interface between octanol and graphite, enabling the successful observation of interfacial structures.[6–7] We anticipate that this technique will be widely applicable to studying ice–liquid interfaces and other low-temperature interfacial systems.

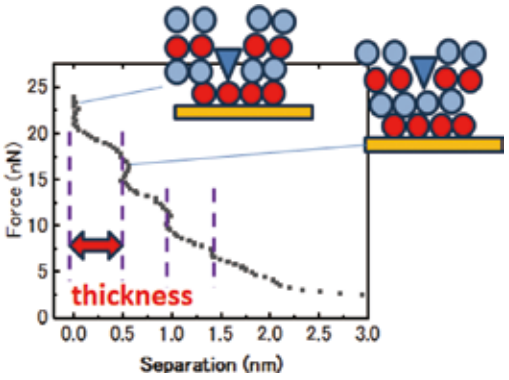

Figure 1. A typical force curve obtained at the interface between an ionic liquid and a gold electrode. The distances between the plateaus correspond to the thickness of the first layer of ionic species.

Our works highlight the importance of combining high-resolution force microscopy with carefully designed experimental systems to advance the understanding of complex interfacial phenomena across a broad range of materials and conditions.

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5) R. Yanagisawa, Kobe University Student Awards, Academic Division, Kobe University (2025).
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Visiting Professors

Visiting Professor
HAYAMI, Shinya *(from Kumamoto University)*

Molecular Spin Qubits in Spin Crossover Systems

Molecular magnetism is an attractive research area due to its interest as a quantum magnetism, such as single molecule magnets (SMMs) and molecular spin qubits (MSQs). We have attempted to control slow magnetic relaxation by using spin-crossover (SCO) compounds with controllable spin states and molecular distortions. Iron(III) SCO compounds ($S = 5/2 \leftrightarrow S = 1/2$) were prepared and investigated by single crystal analysis, magnetic susceptibility measurements, cw/pulsed electron paramagnetic resonance (EPR) and Mössbauer spectroscopy. The respective distortion parameters (Σ) are compared with those for previously reported SCO iron(III) compounds, and the distortion in HS state is larger than LS state. AC magnetic susceptibility has been also measured for the compounds at 2 K, and show frequency dependency. Pulsed EPR spectra were also measured in the LS state, T_m (coherence time) were estimated. These results are the first attempt to provide molecular design for the development of metal complexes with MSQ by using SCO compounds that can be tuned in the spin states and molecular distortions.

Visiting Associate Professor
MIURA, Hiroki *(from Tokyo Metropolitan University)*

Heterogeneous Catalysts for Sustainable Molecular Transformations

From the perspective of preventing global warming, it is essential to establish advanced carbon-circulation systems that utilize renewable resources such as biomass and waste plastics. Since biomass compounds and polyesters contain numerous C–O bonds, the development of efficient catalysts capable of transforming these bonds is crucial for establishing sustainable processes. Our group has focused on the unique catalysis of supported metal catalysts, in which metal nanoparticles and metal-oxide supports can work in cooperation to activate organic molecules. We recently demonstrated that the cooperation of gold nanoparticles and Lewis acid at the surface of metal oxides enabled highly efficient borylation of unactivated C–O bonds in alkyl esters and alkyl ethers. Furthermore, we found that the strong interaction between gold nanoparticles and organic radicals enabled radical silylation of unactivated C–O bonds in alkyl esters and alkyl ethers. These findings provide important guidelines for the design of highly active heterogeneous catalysts for sustainable molecular transformations.

Visiting Associate Professor
KAWASUGI, Yoshitaka *(from Toho University)*

Phase-Transition Devices Based on Molecular Strongly Correlated Electron Systems

Strongly correlated electron systems consisting of molecular materials are softer and have lower carrier densities than inorganic materials, making them highly sensitive to external fields such as strain and gate electric fields. We have fabricated phase-transition devices utilizing strain and electric fields in organic strongly correlated electron systems. Specifically, we employed bis(ethylenedithio) tetrathiafulvalene [BEDT-TTF] molecules. These devices exhibit a remarkable physical property change, transitioning from an insulator to a superconductor in response to external fields. Recently, we have focused on improving device performance through the fabrication of field-effect transistors using solid electrolyte gates. In solid electrolyte gate transistors, we have successfully observed a field-induced Mott transition where interacting “frozen” electrons dissolve into a conductive liquid state. We have also confirmed that solid electrolytes may possess superior carrier injection capabilities compared to ionic liquids, which are more prone to sample degradation.

RESEARCH ACTIVITIES

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 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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1982 B.S. Tokyo Institute of Technology
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1988 Postdoctoral Fellow, Georgia University
1989 Assistant Professor, Tokyo Institute of Technology
1994 Associate Professor, Japan Advanced Institute of Science and Technology
2002 Professor, Institute for Molecular Science
Professor, Okazaki Institute for Integrative Bioscience (–2018)
Professor, The Graduate University for Advanced Studies
2018 Professor, Exploratory Research Center on Life and Living Systems (ExCELLS)

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NOMURA, Junko
KAWAGUCHI, Ritsuko

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

- H. Matsuura, N. Sakai, S. Toma-Fukai, N. Muraki, K. Hayama, H. Kamikubo, S. Aono, Y. Kawano, M. Yamamoto and K. Hirata, "Elucidating Polymorphs of Crystal Structures with Intensity-Based Hierarchical Clustering Analysis on Multiple Diffraction Datasets," *Acta Crystallogr., Sect. D: Biol. Crystallogr.* **79**, 909–924 (2023).
- 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, 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 and Functional Analysis of Heme-Based Oxygen Sensor Protein HemAT

Aerotaxis is a typical biological signal transduction system that consists of a signal transducer protein (MCP), CheA, CheY, and other Che proteins. Signal transducer proteins, sometimes called as MCPs (methyl-accepting chemotoxis proteins), bind a repellant or attractant in their sensor domain. Many chemical and physical stimuli act as a repellant or attractant, among which molecular oxygen is a typical gaseous signaling molecule. HemAT is a MCP responsible for aerotaxis control, which consists of two domains, the sensor domain and the signaling domain. Though the sensor domain of HemAT shows structural homology to myoglobin, it has a different heme environmental structure in the distal heme pocket from myoglobin. In the case of myoglobin, a distal His forms a hydrogen bond with the heme-bound oxygen to stabilize the heme-oxygen complex. However, there is no distal His in HemAT, in which a Thr is involved in the formation of a hydrogen bonding network upon oxygen binding to HemAT.

HemAT forms HemAT/CheA/CheW complex, in which the intramolecular signal transduction takes place upon O_2 binding to HemAT. In this work, we have tried to determine the HemAT/CheA/CheW complex by cryo-electron microscopy (cryoEM) to understand the molecular mechanisms of O_2 sensing and signal transduction of HemAT and HemAT/CheA/CheW complex (Figure 1). We have carried out cryoEM single particle analysis to determine the structure of HemAT/CheA/CheW complex, which revealed that BsmHemAT, CheA, and CheW formed the complex in 2:1:1 ratio.

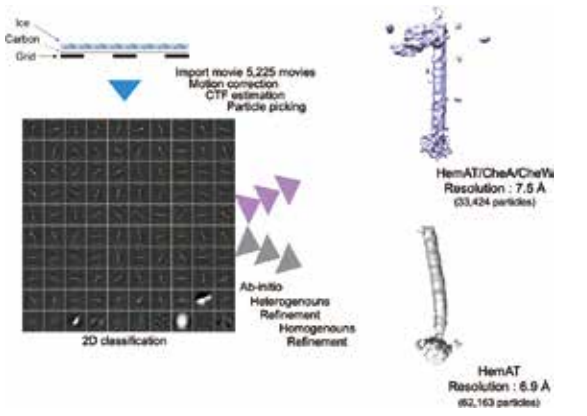

Figure 1. Structural determination of the HemAT/CheA/CheW complex by cryoEM.

2. CO Biosynthesis for the Construction of the Active Site in [NiFe]-Hydrogease

Hydrogenase, an enzyme that catalyzes the oxidation of hydrogen gas and the reduction of protons, plays a central role in hydrogen metabolism in bacteria and other microorganisms. Recently, it is also expected to be utilized as a catalyst for fuel cells. There are three types of hydrogenases classified based on the structure of their active centers: [NiFe]-, [FeFe]-, and [Fe]-hydrogenases. In all cases, carbon monoxide (CO) is coordinated to the Fe in the active center. While it is known that CO is biosynthesized through enzyme reactions, the molecular mechanism of CO generation has been unclear. In this work, the crystal structure of the enzyme HypX involved in CO biosynthesis used by [NiFe]-hydrogenase was determined. It was revealed that HypX synthesizes CO through a completely novel reaction. HypX consists of two domains (N-terminal domain and C-terminal domain), and within the molecule, there is a cavity spanning across these two domains. It was also found that coenzyme A (CoA) binds to the cavity on the C-terminal domain side.

Based on the obtained crystal structure, the following CO biosynthesis reaction mechanism was proposed: Two different chemical reactions occur in the N-terminal domain and the C-terminal domain of HypX. In the N-terminal domain, a formyl transfer reaction from formyl-tetrahydrofolate (formyl-THF), which is bound in the cavity of the N-terminal domain, to CoA takes place. During this process, CoA in the cavity adopts an extended linear conformation, and the -SH group at the end of CoA is positioned adjacent to the formyl group in formyl-THF. As a result of the formyl transfer reaction, formyl-CoA is generated as an intermediate. The generated formyl-CoA undergoes a significant conformational change within the cavity to position the formyl group at the end of the CoA molecule towards the enzyme active site in the C-terminal domain of HypX. In the C-terminal domain, the CO release reaction from formyl-CoA occurs, resulting in the production of CO and CoA.

The N-terminal domain of HypX is structurally homologous to the proteins that catalyze formyl-group transfer reaction with N^{10}-formyl-THF as a formyl-group donor such as the hydrolase domain of FDH, methionyl-t-RNA formyltransferase (FMT), and UDP-glucuronic acid dehydrogenase (ArnA). We also obtained HypX/THF complex by soaking HypX crystals with THF and solved its structure at a resolution of 2.1 Å. The THF binding sites are conserved among HypX, FDH, and ArnA (Figure 2), which supports the notion that N^{10}-formyl-THF is the substrate of HypX as is the case of FDH and ArnA.

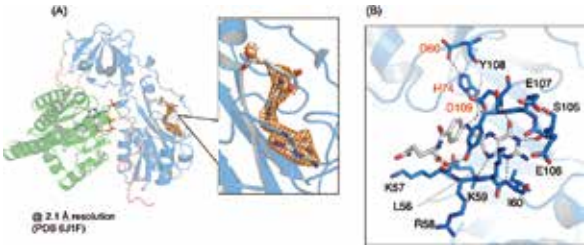

Figure 2. (A) Crystal structure of THF-bound HypX, in which the electron densities of THF is shown in orange mesh. (B) Closed-up view of THF binding site. Hydrogen bonding interactions are shown in dotted line. His74, Asp80, and Asp109 in HypX act as the catalytic triad to catalyze the formyl-group transfer from N^{10}-formyl-THF to CoA bound in HypX.

Dynamical Ordering of Biomolecular Systems for Creation of Integrated Functions

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2011 The 48th Baelz Prize

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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.

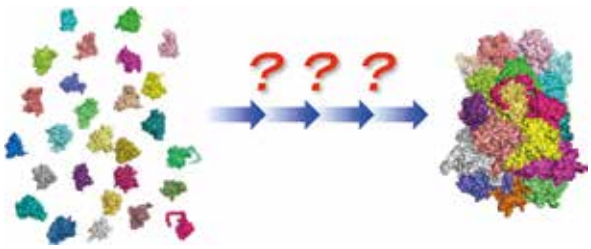

Figure 1. Formation of supramolecular machinery through dynamic assembly and disassembly of biomolecules.

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- K. Kato, S. Yanaka and H. Yagi, "Glycoprotein Preparation by Heterologous Expression," in *NMR of Glycoproteins*, J. Jiménez-Barbero and O.Millet, Eds., *Methods in Molecular Biology*, Humana; New York, **vol. 2961**, pp. 53–67 (2025).
- K. Kato, S. Yanaka and T. Yamaguchi, "The Synergy of Experimental and Computational Approaches for Visualizing Glycoprotein Dynamics: Exploring Order within the Apparent Disorder of Glycan Conformational Ensembles," *Curr. Opin. Struct. Biol.* **92**, 103049 (2025).
- K. Kato, S. Yanaka and H. Yagi, "Technical Basis for Nuclear Magnetic Resonance Approach for Glycoproteins," in *Experimental Approaches of NMR Spectroscopy II*, The Nuclear Magnetic Resonance Society of Japan, Ed., Springer Nature; Singapore, pp. 169–195 (2025).
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- D. Koga, S. Kusumi, H. Yagi and K. Kato, "Three-Dimensional Analysis of the Intracellular Architecture by Scanning Electron Microscopy," *Microscopy* **73**, 215–225 (2024).
- K. Kato and H. Yagi, "Current Status and Challenges in Structural Glycobiology," *Trends Carbohydr. Res.* **15**, 38–46 (2023).

1. Structural and Kinetic Modulation of Amyloid β Fibrils: Insights from Antibody Recognition and Familial Mutation

The dynamic interaction between amyloid β (Aβ) fibrils and antibodies during fibril elongation was investigated at the single molecule level.[1] Real-time observations revealed that Aβ fibril elongation alternates between an "elongation phase," in which two protofilaments grow in a staggered manner, and a "pause phase," during which growth temporarily halts. Notably, Aβ monomers were found to alternately attach to the two protofilaments during elongation, whereas growth paused when both protofilament tips became aligned. Furthermore, a monoclonal antibody 4396C selectively bound to fibril ends in this paused state, effectively suppressing further elongation. By integrating high-speed atomic force microscopy with molecular simulations, this study provided a detailed understanding of the dynamic assembly mechanism underlying Aβ fibril formation.

In parallel, we harnessed the unique microgravity environment aboard the International Space Station to elucidate, for the first time, the detailed structure of amyloid β fibrils bearing the Tottori-type familial mutation (D7N), a rare variant linked to Alzheimer's disease.[2] Under Earth gravity, Tottori-type Aβ40 predominantly forms amorphous aggregates, hindering structural analysis. In contrast, microgravity suppressed amorphous aggregation and promoted efficient fibril formation, enabling high-resolution cryo-electron microscopy (Figure 2). The resulting structures revealed a flexible, disordered N-terminal region, suggesting that the D7N mutation disrupts the stabilizing role of the N-terminus observed in wild-type Aβ fibrils. Under microgravity, the absence of convection and sedimentation limited off-pathway aggregation and facilitated the emergence of structurally convergent, high-quality fibrils.

These two perspectives jointly deepen our mechanistic understanding of Aβ fibril formation and offer new avenues for identifying therapeutic targets associated with Alzheimer's disease pathogenesis.

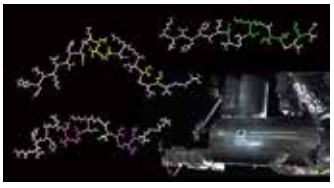

Figure 2. Fibril formation of the Aβ Tottori variant (D7N) was investigated under microgravity on the International Space Station.[2]

2. Decoding Glycan Dynamics and Engineering Precision in Glycoprotein Function

Glycans play vital roles in cellular recognition, immune signaling, and protein stability, yet their dynamic and heterogeneous structures remain difficult to characterize. We reported a series of studies that deepen our understanding of glycan conformational behavior, its influence on protein function, and its potential in glycoengineering and biopharmaceutical design.

To explore glycan dynamics, we developed an analytical framework integrating molecular dynamics (MD) simulations with NMR-guided constraints. Using nonlinear correlation metrics such as the Hilbert-Schmidt Independence Criterion and Maximal Information Coefficient, we uncovered hidden structural relationships beyond conventional intuition.[4] This data-driven approach reveals how glycan flexibility modulates protein interactions.

We next examined how glycosylation affects the structure and immune functions of human IgG antibodies.[5] Through isotope-assisted NMR and MD simulations, we analyzed four IgG1-Fc glycoforms differing in galactose and fucose content. Galactose residues acted as molecular "anchors" and "wedges," stabilizing the Fc domain and enhancing binding to Fcγ receptors and complement C1q (Figure 3). In contrast, the absence of core fucose altered dynamics of residues critical for ADCC, offering atomic-level insights for antibody optimization.

In parallel, we identified a 10-amino-acid "passport sequence" that enhances N-glycan maturation as well as secretion. When appended to therapeutic glycoproteins such as erythropoietin, the passport sequence is recognized by NUCB1, which resides near B4GALT1 in the Golgi and promotes its enzymatic activity. This facilitates N-glycan maturation and, in turn, enhances pharmacokinetics and therapeutic efficacy.[6]

Additional studies revealed temporal and sex-dependent N-glycosylation changes in rat serum[7] and unusual glycan structures in tardigrades,[8] underscoring the evolutionary diversity of glycosylation.

Together, these findings offer new strategies for precision glycoengineering and deepen our understanding of glycan-mediated regulation.

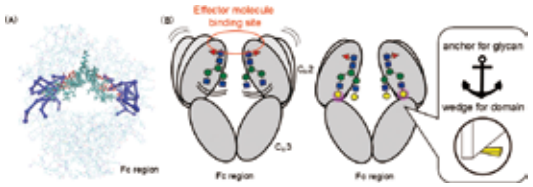

Figure 3. (A) Structural propagation pathways originating from galactose residues within the Fc-linked glycan. (B) Galactose residues (indicated by yellow circles) suppress glycan mobility by acting as molecular anchors, and constrain Fc domain dynamics by serving as molecular wedges—together enhancing the stability of the functional site and promoting effector molecule binding.[5]

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5) S. Yanaka *et al.*, *Proc. Natl. Acad. Sci. U. S. A.* **122**, e2505473122 (2025).
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Operation and Design Principles of Biological/Artificial Molecular Machines

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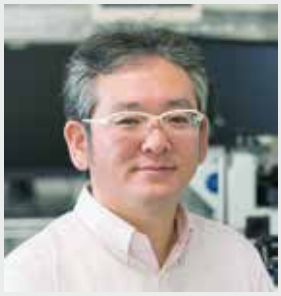

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Life is supported by protein molecular machines which show better performance than man-made machines. One representative of the protein molecular machines is molecular motors (Figure 1). Molecular motors show autonomous unidirectional motions using the energy of chemical reaction. We unveil operational principles of molecular motors with advanced single-molecule analysis. In addition, with protein engineering, we create non-natural/hybrid molecular motors to understand their design principles. Furthermore, we create DNA/RNA-based artificial molecular motors and motor systems that mimic and outperform biological ones.

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. Otomo, L. G. Hui Zhu, Y. Okuni, M. Yamamoto and R. Iino, "ATP Synthesis of *Enterococcus hirae* V-ATPase Driven by Sodium Motive Force," *J. Biol. Chem.* **301**, 108422 (2025).
- K. Suzuki, Y. Goto, A. Otomo, K. Shimizu, S. Abe, K. Moriyama, S. Yasuda, Y. Hashimoto, J. Kurushima, S. Mikuriya, F. L. Imai, N. Adachi, M. Kawasaki, Y. Sato, S. Ogasawara, S. Iwata, T. Senda, M. Ikeguchi, H. Tomita, R. Iino, T. Moriya and T. Murata, "Na^+-V-ATPase Inhibitor Curbs VRE Growth and Unveils Na^+ Pathway Structure," *Nat. Struct. Mol. Biol.* **32**, 450–458 (2025).
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1. ATP Synthesis of *Enterococcus hirae* V-ATPase Driven by Sodium Motive Force[1)]

V-ATPases generally function as ion pumps driven by ATP hydrolysis in the cell, but their capability of ATP synthesis remains largely unexplored. Here we show ATP synthesis of Na^+-transporting *Enterococcus hirae* V-ATPase (EhV_oV_1) driven by the electrochemical potential gradient of Na^+ across the membrane (sodium motive force, *smf*). We reconstituted EhV_oV_1 into liposome and performed a luciferin/luciferase-based assay to analyze ATP synthesis quantitatively. Our result demonstrates that EhV_oV_1 synthesizes ATP with a rate of 4.7 s^{-1} under high *smf* (269.3 mV). The Michaelis constants for ADP (21 μM) and inorganic phosphate (2.1 mM) in ATP synthesis reaction were comparable to those for ATP synthases, suggesting similar substrate affinities among rotary ATPases regardless of their physiological functions. Both components of *smf*, Na^+ concentration gradient across the membrane (ΔpNa) and membrane potential (Δψ), contributed to ATP synthesis. At the equilibrium points where *smf* and Gibbs free energy of ATP synthesis are balanced, EhV_oV_1 showed reversible reactions between ATP synthesis and hydrolysis (Figure 2). The obtained Na^+/ATP ratio (3.2 ± 0.4) closely matched the value expected from the structural symmetry ratio between EhV_o and EhV_1 (10/3 = 3.3), indicating tight coupling between ATP synthesis/hydrolysis and Na^+ transport. These results reveal the inherent functional reversibility of EhV_oV_1. We propose that the physiological function of EhV_oV_1 *in vivo* is determined by relatively small *smf* against large Gibbs free energy of ATP synthesis.

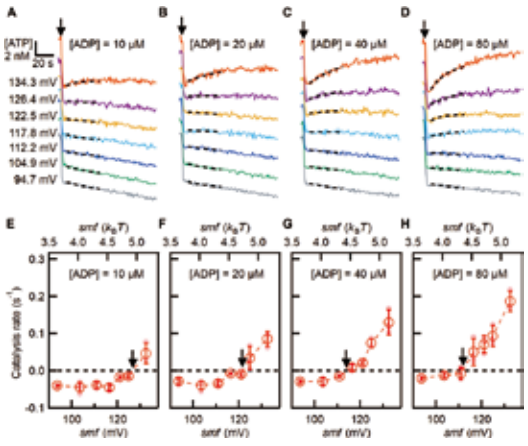

Figure 2. Determination of equilibrium points between ATP synthesis and hydrolysis. *A–D*, time courses of ATP synthesis and hydrolysis at different *smf* (93.5–132.6 mV). Reaction was initiated by adding proteoliposome as indicated by black arrow. The black dashed lines represent the fitting with a single exponential function for Δt = 35 s after the addition of PL. *E–H*, *smf* dependence of ATP synthesis and hydrolysis rates. Black arrows indicate equilibrium points obtained by linear fitting between two data points across the catalysis rate of zero. The reaction solution contains 25 nM ATP, 9.95 mM Pi, and ADP at 10 μM (*A* and *E*), 20 μM (*B* and *F*), 40 μM (*C* and *G*), and 80 μM (*D* and *H*), respectively.

2. Na^+-V-ATPase Inhibitor Curbs VRE Growth and Unveils Na^+ Pathway Structure[2)]

Vancomycin-resistant *Enterococcus faecium* (VRE) is a major cause of nosocomial infections, particularly endocarditis and sepsis. With the diminishing effectiveness of antibiotics against VRE, new antimicrobial agents are urgently needed. Our previous research demonstrated the crucial role of Na^+-transporting V-ATPase in *Enterococcus hirae* (EhV_oV_1) for growth under alkaline conditions. In this study, we identified a compound, V-161, from 70,600 compounds, which markedly inhibits EhV_oV_1 activity (Figure 3). V-161 not only inhibits VRE growth in alkaline conditions but also significantly suppresses VRE colonization in the mouse small intestine. Furthermore, we unveiled the high-resolution structure of the membrane V_o part due to V-161 binding. V-161 binds to the interface of the c-ring and a-subunit, constituting the Na^+ transport pathway in the membrane, thereby halting its rotation. This structural insight presents potential avenues for developing therapeutic agents for VRE treatment and elucidates the Na^+ transport pathway and mechanism.

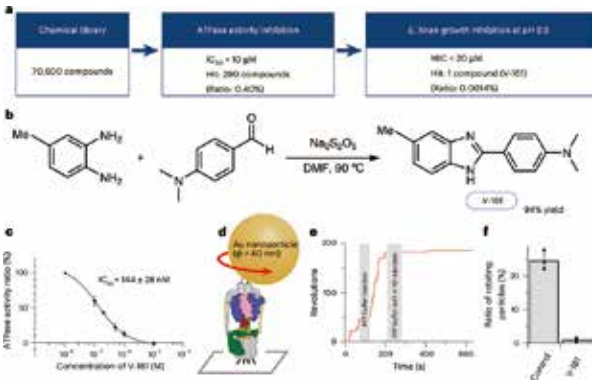

Figure 3. Schematic of screening process for EhV_oV_1 inhibitors. **b**, Chemical synthesis route of V-161. **c**, Inhibition of ATPase activity of EhV_oV_1 by V-161. Results are shown as mean ± s.e.m., derived from three separate experiments. **d**, Schematic of single-molecule rotation assay for EhV_oV_1. **e**, Rotation time course. After an initial 1 min of rotation recording, a buffer with 10 μM ATP was injected (indicated by the first gray square). After another several minutes of recording, a buffer containing both 2 μM V-161 and 10 μM ATP was injected (indicated by the second gray square). The recording speed was set to 50 frames per second. **f**, Ratio of rotating particles relative to the total particles attached to the glass surface. Results are shown as mean ± s.d., derived from three separate experiments.

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Biomolecular Science Based on In Situ Observation by Magnetic Resonance

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Keywords In-Cell NMR, Spin Life Science, Magnetic Resonance Measurements

Protein structures and dynamics are closely related to physiological functions, but are strongly affected by temperature, pH, ionic strength, pressure, and molecular crowding. Within cells, biomolecules are densely packed, and the intracellular space is compartmentalized by cytoskeletal structures and organelles. Furthermore, this environment is non-equilibrium, constantly adapting to external stimuli. To accurately understand protein function, it is therefore essential to investigate biomolecules in their native contexts. We apply magnetic resonance techniques—particularly in-cell NMR—to observe the atomic-level structures and dynamics of proteins directly in living cells, where they perform their natural roles. Our group also develops methodological innovations to improve sensitivity and resolution, expanding the scope of in-cell NMR. By correlating structural and dynamic information with cellular physiology, we aim to reveal the molecular basis of complex biological systems and establish a foundation for biomolecular science based on in situ magnetic resonance observation.

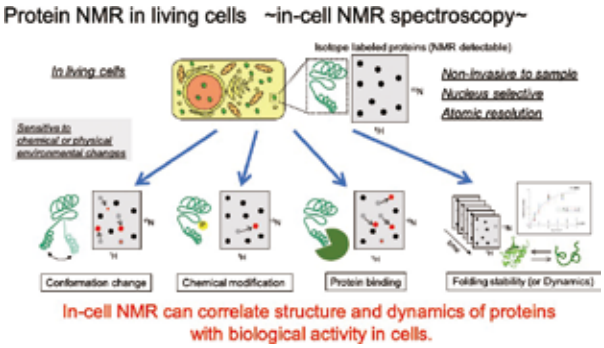

Figure 1. Overview of in-cell NMR spectroscopy.

Selected Publications

- M. Ikari, H. Yagi, T. Kasai, K. Inomata, M. Ito, K. Higuchi, N. Matsuda, Y. Ito and T. Kigawa., "Direct Observation of Membrane-Associated H-Ras in the Native Cellular Environment by In-Cell ^{19}F-NMR Spectroscopy," *JACS Au* **3**, 1658–1669 (2023).
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1. In-Cell NMR Analysis of Keap1-Nrf2 Interactions Enabled by Controlling Intracellular Degradation

We investigated the interaction between Nuclear factor erythroid 2-related factor 2 (Nrf2) and its regulator Keap1 in living mammalian cells using in-cell NMR spectroscopy. Nrf2 is a transcription factor that protects cells from oxidative stress by inducing antioxidant response genes, and its stability is tightly controlled by Keap1-mediated ubiquitination and proteasomal degradation. Dysregulation of this system is implicated in cancer, neurodegeneration, and other diseases.

A major challenge we faced was the rapid intracellular degradation of delivered ^{15}N-labeled Nrf2-Neh2, which hindered direct NMR observation. To overcome this, we optimized cell preparation conditions by applying proteasome inhibitors such as MG132 and bortezomib. This successfully stabilized Nrf2-Neh2 after electroporation into HeLa and other cell lines. By contrast, mutating ubiquitination sites (Nrf2-Neh2 R7) or deleting Keap1 alone did not prevent degradation, showing that proteasomal pathways beyond Keap1-dependent ubiquitination contribute significantly.

Using degradation-controlled conditions, we observed clear in-cell NMR spectra of Nrf2-Neh2, which provided atomic-level evidence of its interaction with endogenous Keap1. We detected strong signal attenuation around the DLG and ETGE motifs, confirming their role in binding. By comparing HeLa cells with A549 lung carcinoma cells harboring the Keap1 G333C mutation, we revealed that this mutation weakens binding in dilute solution but displays selective effects inside cells, particularly near the ETGE motif. This demonstrates that the intracellular environment modulates the consequences of disease-associated mutations in ways not apparent from in vitro experiments.

We further evaluated the small-molecule inhibitor KI696, a nanomolar-affinity binder of Keap1. In dilute solution, KI696 efficiently disrupted the Nrf2-Keap1 complex, restoring Nrf2-Neh2 signals. In living mouse embryonic fibroblast cells reconstituted with Keap1, KI696 also increased Nrf2-Neh2 signal intensity, though to a lesser degree than in vitro. These results highlight how molecular crowding and intracellular kinetics reduce inhibitor potency, underscoring the importance of evaluating drug action directly in the cellular context.

Our study also revealed that the Nrf2-Keap1 system in cells exhibits rapid association–dissociation dynamics, producing extensive NMR signal broadening not predicted by concentration ratios alone. We interpret this as ubiquitination-dependent cycling of Nrf2, even under proteasome inhibition, reflecting the highly dynamic nature of the intracellular environment.

Taken together, we established a robust methodology to overcome proteasome-mediated degradation, enabling in-cell NMR spectroscopy of unstable proteins. Applying this platform to the Nrf2-Keap1 system, we uncovered unique insights into binding dynamics, mutation effects, and inhibitor activity in living cells. These findings not only advance mechanistic understanding of Nrf2 regulation but also demonstrate the broad potential of in-cell NMR as a tool for probing protein–protein interactions and evaluating therapeutic compounds under physiologically relevant conditions.

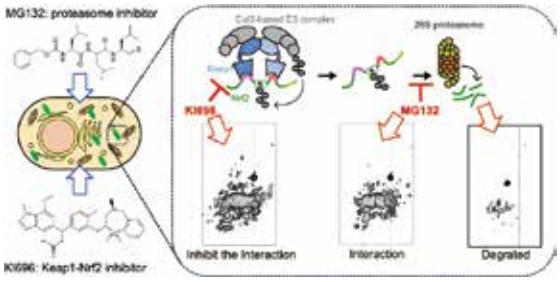

Figure 2. Schematic representation of Keap1-Nrf2 interactions in protein degradation-controlled mammalian cells.

2. In-Cell NMR Study of Protein Diffusion In Mammalian Cells

Protein diffusion in living cells is a crucial factor that determines localization, interactions, and functional regulation of biomolecules. Unlike dilute solution conditions, the intracellular environment is crowded and viscous, leading to significant restrictions on molecular mobility. To quantitatively characterize such behavior, we are developing an in-cell NMR platform that enables direct measurement of translational and rotational diffusion of proteins in mammalian cells.

As an initial step, we implemented fast, high-sensitivity NMR pulse sequences for intracellular diffusion measurements. Using ^{15}N-labeled ubiquitin mutants (L8A, I44A, V70A) introduced into HeLa cells, we successfully applied DOSY-SOFAST-HMQC experiments. Data acquisition was performed under optimized conditions, which enabled the detection of intracellular diffusion signals with sufficient sensitivity.

Diffusion analysis revealed a clear contrast between intracellular and dilute solution conditions. The translational diffusion coefficient was 2.18×10^{-10} m^2/s in buffer, but decreased to 4.96×10^{-11} m^2/s in HeLa cells—approximately a fourfold reduction. This result demonstrates that the dense intracellular milieu strongly impedes protein motion. Importantly, the ability to capture this quantitative difference confirms that our in-cell NMR setup is capable of monitoring protein dynamics under physiologically relevant conditions.

Looking forward, we plan to expand this model system to measure rotational diffusion in addition to translational motion. Rotational diffusion reflects molecular shape and local interactions and will complement the information gained from translational mobility. By integrating both, we aim to obtain a broader picture of protein dynamics across multiple timescales. In the coming year, we will refine our methodology and apply it to other protein systems, seeking to establish a versatile platform for in-cell structural biology.

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Development of Novel Catalytic Organic Transformations

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Keywords Transition Metal Catalysis, Green Chemistry, Photocatalysis

Our research interests lie in the development of catalytic reaction systems toward ideal SDGs-conscious (highly efficient, selective, green, safe, simple, *etc.*) organic molecular transformations. In particular, development of a wide variety of the heterogeneous in-water catalytic systems, continuous flow catalytic systems, and super active catalysts working at ppm-ppb loading levels, have been achieved. Furthermore, we have recently been studying on the novel photocatalysis where, for example, carbonyl groups underwent two successive single-electron reduction to generate carbinol anion species achieving electrophilic carbonyl substitution. Along this line, in 2024, we have developed a series of novel diazabenzacenaphthenium photocatalysts, denoted as ***N*-BAP**s, which promoted the unprecedented 4-electron photoreduction of esters to form the corresponding alcohols with visible LED light irradiation under aqueous conditions.

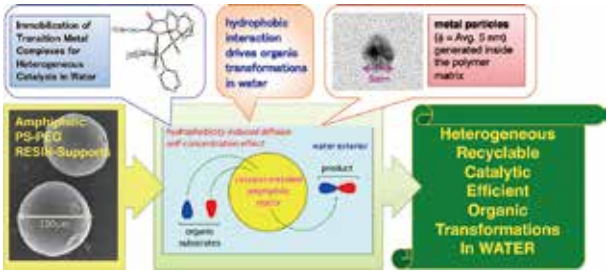

Figure 1. The typical concept of heterogeneous in-water catalyses using amphiphilic polymer-supported complex and nanoparticles catalysts.

Selected Publications

- S. Okumura, K. Torii and Y. Uozumi, "Electrophilic 1,4-Addition of Carbon Dioxide and Aldehydes to Enones," *Org. Lett.* **25**, 5226–5230 (2023).
- 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).
- 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).
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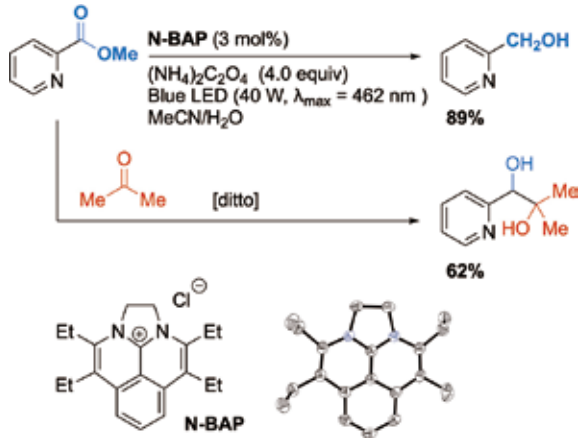
- G. Hamasaka, T. Muto and Y. Uozumi, "Molecular-Architecture-Based Administration of Catalysis in Water: Self-Assembly of an Amphiphilic Palladium Pincer Complex," *Angew. Chem., Int. Ed.* **50**, 4876–4878 (2011).
- Y. Uozumi, Y. Matsuura, T. Arakawa and Y. M. A. Yamada, "Asymmetric Suzuki-Miyaura Coupling in Water with a Chiral Palladium Catalyst Supported on Amphiphilic Resin," *Angew. Chem., Int. Ed.* **48**, 2708–2710 (2009).

1. Multielectron-Reduction with a Novel Photocatalyst *N*-BAP[1)]

In 2024, we have developed a novel diazabenzacenaphthenium photocatalyst ***N*-BAP** which was designed with a view to its use as a photocatalyst under visible-light irradiation in photoinduced multielectron-transfer reactions. Indeed, under visible-light irradiation, ***N*-BAP** promoted the four-electron reduction of esters, via the carbinol anion intermediates, to give the corresponding alcohols.[1a)] The intermediates, carbinol anions, also underwent a 1,2-addition to a second carbonyl compound, affording unsymmetric 1,2-diols. Furthermore, the ***N*-BAP**-catalyzed multielectron reduction is now applied to a variety of carbonyl compounds extensively.[1b)]



Scheme 1. Photocatalytic Reduction of Methyl Picolinate.

2. Silver-Mediated Homocoupling of Arylboronic Acids[2)]

We collaborated with Prof. Ohtaka's group at Osaka Institute of Technology to develop a homocoupling of arylboronic acids to form the corresponding biaryls. The coupling reaction proceeded with a catalytic amount of silver carbonate, where silver nanoparticles were generated to promote the reaction.

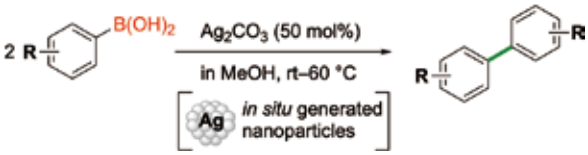
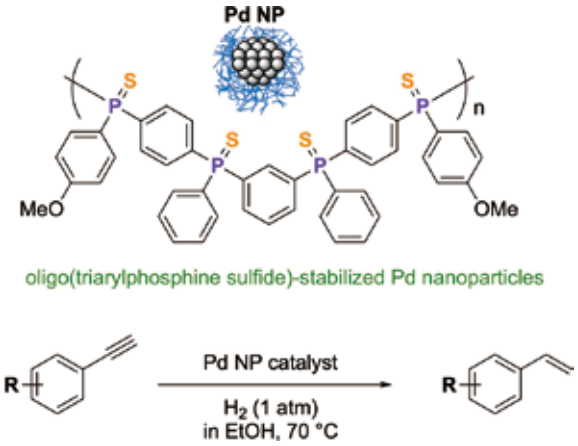


Figure 2.

TEM examination of the reaction mixture revealed that silver nanoparticles were generated in situ under the reaction conditions which should promoted the homocoupling reaction.

3. Oligo(Triarylphosphine Sulfide)s-Stabilized Pd Nanoparticles for Controlled Hydrogenation of Terminal Aryl Alkynes[3)]

In the development of high-performance metal nanoparticle (NP) catalysts, the exploration of new classes of multidentate organic stabilizers is crucial. Prof. Ohta and his co-workers at Ehime University and we have developed a series of structurally diverse oligo(triarylphosphine sulfide)s through the Pd-catalyzed P–C cross-coupling reactions of hydroxymethylphosphine sulfide derivatives with aryl halides. The oligomers were employed as stabilizing agents for Pd NP catalysts. These catalysts were characterized by TEM, EDS, and ICP-MS analyses to determine the average Pd particle size and the constituent elements on the catalyst. We evaluated their catalytic activity in the semihydrogenation of phenylacetylene to styrene in EtOH at 70 °C for 3 h under atmospheric pressure of H_2 with a catalyst loading of 0.5 mol% Pd. It was revealed that Pd NPs stabilized with oligo(triarylphosphine sulfide)s, featuring a high number of coordination sites and a combination of p-phenylene and m-phenylene linkers, exhibited high selectivity for styrene and low Pd leaching.



Scheme 2. Synthesis of oligo(triarylphosphine sulfide)s.

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Design and Synthesis of Organic Molecules for Catalysis

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Keywords Synthetic Chemistry, Molecular Catalyst, Augmented Intelligence

Our research aims to establish new principles for molecular catalysis and functional molecule discovery by integrating halogen-driven molecular design with digitalized synthesis frameworks. We have focused on two unique classes of halogen-based molecular systems. The first is *perfluorohalogenated arenes*, which exhibit unprecedented cooperative σ-hole and π-hole bonding interactions and provide new insights into organic materials. The second is *halenium complexes* featuring three-center-four-electron (3c4e) halogen bonds, which serve as strong and tunable non-metallic driving forces in catalysis. These studies highlight the potential of non-covalent halogen interactions to expand the chemical space of molecular catalysts and functional small molecules.

Furthermore, we are advancing the digitalization of organic synthesis through collaborations that combine *augmented intelligence* and *automated synthesis systems*. This approach allows accurate prediction of reaction outcomes under untested conditions, thereby accelerating the exploration of novel functional molecules. At the same time, our batch-type automated organic synthesis platform integrates reaction execution, purification, and analysis into a unified process, enabling Human-in-the-Loop collaboration between chemists and AI systems. Together, these approaches pave the way toward a new paradigm of "AI- and data-driven molecular discovery."

Selected Publications

- 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, 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).
- S. Oishi, T. Fujinami, Y. Masui, T. Suzuki, M. Kato, N. Ohtsuka and N. Momiyama, "Three-Center-Four-Electron Halogen Bond Enables Non-Metallic Complex Catalysis for Mukaiyama-Mannich-Type Reaction," *iScience* **25**, 105220 (2022).
- N. Ohtsuka, H. Ota, S. Sugiura, S. Kakinuma, H. Sugiyama, T. Suzuki and N. Momiyama, "Perfluorohalogenated Naphthalenes: Synthesis, Crystal Structure, and Intermolecular Interaction," *CrystEngComm* **26**, 767–772 (2024).

1. Design of Perfluorohalogenated Arenes

Halogens form attractive non-covalent interactions between terminal halogen atoms in compounds of the type R—X (X = Cl, Br, I) and Lewis bases. This non-covalent interaction is known as either halogen bonding or σ-hole bonding, which occurs when R is a highly electronegative substituent, such as perfluorinated alkyl or aryl substituents. Based on the electrophilic feature of the halogen atom, we have investigated perfluorohalogenated arenes, aimed at creating functional molecules.[1,2)]

Perfluorohalogenated naphthalenes (PFXNaPs) are unique small molecules with great potential to exhibit a new type of σ-hole and π-hole bonding, owing to the incorporation of multiple F atoms onto the naphthalene ring. We developed a synthetic protocol for PFXNaPs, conduct crystal engineering investigations, and explored the intermolecular interactions of PFXNaPs through π-hole and σ-hole bondings. We successfully synthesized PFXNaPs using Mg amide-mediated halogenation reactions of electron-deficient F_7 and F_6 naphthalenes, achieving good to excellent yields. Crystal structure analyses of 3,6-I_2F_6 naphthalene unveiled intermolecular π-hole stacking between two C atoms in the naphthalene ring, in cooperation with the σ-hole bonding of two I atoms. This mode of intermolecular interaction has not been classified in previous reports. Computational studies show that the π-hole bonding in PFXNaPs is substantially enhanced compared to corresponding benzene molecules without diminishing the σ-hole bonding. The unique stacked interaction in PFXNaPs is primarily governed by electrostatic interaction and dispersion correction energies, with the contribution of C···C contacts being 10 times greater than that in benzene analogs. The results enable further applications of PFXNaPs in the fields of perfluorohalogenated arenes and organic crystalline materials.[2)]

2. Design of Halenium Complexes

In the filed of perfluorohalogenated arenes, the two-center-two-electron (2c2e) bond is a key feature. Similarly, halogen(I), generally X^+ (X = I, Br, Cl), acts as a strong halogen bond donor site. In contrast to the 2c2e halogen bond, halogen(I) simultaneously interacts with two Lewis bases. This bond is recognized as a three-center-four-electron (3c4e) halogen bond. Importantly, successful examples have consistently required the use of stoichiometric amounts of 3c4e complexes. Despite the utility of the 3c4e halogen bond in synthetic chemistry, its potential for non-metallic complex catalysis had not been thoroughly investigated until our report.[3,4)]

We discovered that the 3c4e halogen bond can serve as a new driving force for catalysis. By integrating halogen(I) (X^+: I^+ or Br^+), the bis-pyridyl ligand *NN*, and a non-nucleophilic counter anion Y, we developed non-metallic complex catalysts, [*N*···X···*N*]Ys, that exhibited outstanding activity and facilitated the Mukaiyama–Mannich-type reaction of *N*-heteroaromatics with parts-per-million-level catalyst loading. NMR titration experiments, CSI-MS, computations, and UV-vis spectroscopic studies suggest that the robust catalytic activity of [*N*···X···*N*]Y can be attributed to the unique ability of the 3c4e X-bond to bind chloride: i) the covalent nature transforms the $[N\cdots X\cdots N]^+$ complexation to sp^2 CH as a hydrogen-bonding donor site, and ii) the noncovalent property allows for the dissociation of $[N\cdots X\cdots N]^+$ for the formation of $[Cl\cdots X\cdots Cl]^-$. This study introduces the application of 3c4e X-bonds in catalysis *via* halogen(I) complexes.[4)]

3. Digitalization of Organic Synthesis

Recent advances in our group have been directed toward the digitalization of organic synthesis. In collaboration with Professor Kazuhiro Takeda (Shizuoka University), we explored the use of generative machine learning with virtual variables (GMLV) to predict reaction outcomes under untested conditions. In particular, a predictive framework was developed for the deuteration of polyfluoroperylene (PFDPR), a promising luminescent material, based on small experimental datasets. By introducing virtual descriptors that capture the intrinsic relationships between reactants, the model achieved accurate estimation of reaction yields and provided mechanistic insights into reaction processes. This study highlights the potential of digitalized data and AI frameworks to accelerate the discovery of functional molecules.[5)]

Furthermore, we have developed a batch-type automated organic synthesis system. Unlike previously developed systems, our platform integrates reaction execution, work-up, purification, and analysis into a unified automated process. The system comprises modular equipment, including a multi-reaction station, robotic arms for liquid handling, automated purification, and mass spectrometry analysis. Importantly, it enables non-experts in organic synthesis to access a comprehensive experimental environment—"pushing a button does almost everything." This infrastructure provides a foundation for Human-in-the-Loop collaborations, where organic chemists and AI agents can work synergistically to accelerate reaction development and molecular discovery.[6)]

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3) S. Oishi, T. Fujinami, Y. Masui, T. Suzuki, M. Kato, N. Ohtsuka and N. Momiyama, *iScience* **25**, 105220 (2022).
4) S. Oishi, T. Fujinami, Y. Masui, T. Suzuki, M. Kato, N. Ohtsuka and N. Momiyama, *STAR Protocols* **4**, 102140 (2023).
5) K. Takeda, N. Ohtsuka, T. Suzuki and N. Momiyama, *Comput.-Aided Chem. Eng.* **53**, 2689 (2024).
6) Automated organic synthesis system: This platform was developed with support from the Institute for Molecular Science (IMS), Moonshot Goal 3 (Ushiku Project), and Transformative Research Areas (A) "Digitalization-driven Transformative Organic Synthesis (Digi-TOS)."

Design and Synthesis of Three-Dimensional Organic Structures

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2014 Akasaki Award
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 (Figure 1).

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 has 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.

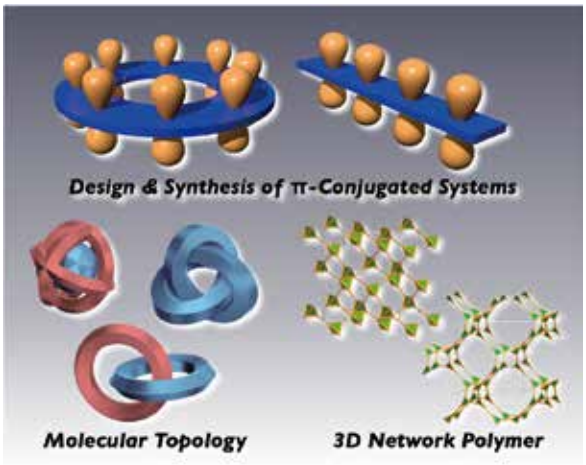


Figure 1. Design and synthesis of π-conjugated organic molecules (top); Development of novel molecular topology (bottom left); Construction of three-dimensional network polymers (bottom right).

Selected Publications

- M. Nagase, R. Yoshida, S. Nakano, T. Hirose and Y. Segawa, *Chem. Commum.* **61**, 11187–11190 (2025).
- K. Watanabe, H. Sugiyama and Y. Segawa, *CrystEngComm* **27**, 3552–3559 (2025).
- K. Watanabe, T. Toya, Y. Toyota, Y. Kobayashi, J. Usuba, Y. Hijikata, R. Matsuda, K. Nishimura, H. Sugiyama and Y. Segawa, *Chem. Commun.* **61**, 2822–2825 (2025).
- H. Sugiyama, K. Watanabe, C. Song, K. Murata and Y. Segawa, *Chem. Lett.* **53**, upae192 (2024).
- R. Yoshida, H. Sugiyama and Y. Segawa, *Chem. Lett.* **53**, upae048 (2024).
- S. Hirota, S. Nakano, H. Sugiyama and Y. Segawa, *Org. Lett.* **25**, 8062–8066 (2023).
- M. Nagase, S. Nakano and Y. Segawa, *Chem. Commun.* **59**, 11129–11132 (2023).
- Y. Segawa, *Chem* **9**, 2725–2727 (2023).
- Y. Segawa, *Bull. Chem. Soc. Jpn.* **95**, 1600–1610 (2022).

1. Twisted π-Conjugated Molecules Featuring 3D π–π Interactions in Solid States

Electronic devices based on organic materials are lightweight, flexible, and can display a wide variety of properties by subtle changes in molecular structure, making them promising environmentally friendly next-generation devices. Most organic electronic materials developed to date are made of planar molecules, so charge transport is confined to limited directions; as a result, devices require strict control of molecular orientation. The team wondered whether "twisting" molecules could yield a new material architecture in which charge carriers move easily in three dimensions.

We attached methyl groups to molecules containing multiple thiophene units, thereby synthesizing twisted molecules. X-ray crystallography confirmed the twisted geometry and revealed that, in the solid state, the molecules stack in a three-dimensional fashion. Computational analysis of charge-transport pathways predicted an aggregated structure in which holes can migrate in several directions. When the molecule was fabricated into an organic field-effect transistor, it exhibited a hole mobility of 1.85×10^{-4} cm^2 V^{-1} s^{-1}, experimentally confirming its behavior as an organic semiconductor.

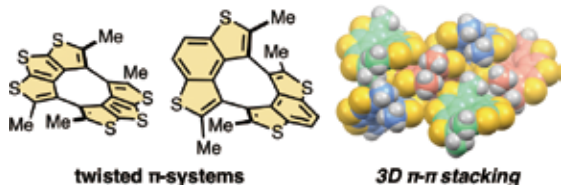


Figure 2. Structures of twisted π-conjugated molecules, and their 3D π–π stacking mode.

2. Diverse Clathrate Crystals Assembled from Weak Intermolecular Interactions

Tetracyanodihydrodipyrazinopyrazines with two mesityl (2,4,6-trimethylphenyl) groups formed clathrate crystals with 15 kinds of organic solvents. Two common types of host molecular networks were observed in the crystals. Theoretical calculations indicated that these host networks are constructed from π–π and CN–π interactions. As these intermolecular interactions are relatively weak, the host network can change flexibly in response to guest molecules. Guest-free crystals can be reversibly transformed into clathrate crystals through crystal-to-crystal phase transitions via the adsorption/desorption of solvent vapor.

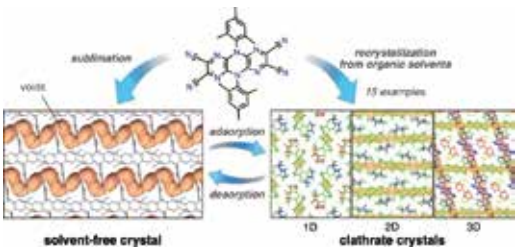


Figure 3. Solvent-free and clathrate crystals of tetracyanodihydrodipyrazinopyrazines.

3. Fully Fused 3D π-Conjugated Polymers Controlled by Steric Repulsion

The synthesis and characterization of fused aromatic networks composed of zinc tetrapyrazinoporphyrazines are reported. The steric repulsion of bulky substituents induced the formation of three-dimensional structures. Thus-obtained insoluble polymers adsorbed CO_2 and had near-infrared absorption indicating their porosity and extended π-conjugation.

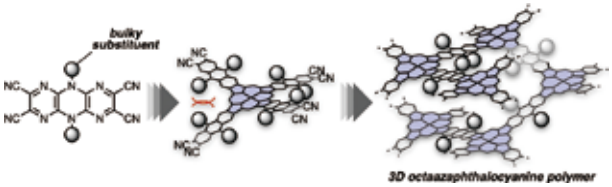


Figure 4. Synthesis of fully fused 3D π-conjugated polymers.

4. Structure Determination of π-Extended Tetraphenylenes by MicroED

The structure determination of large π-conjugated molecules using microcrystal electron diffraction (MicroED) was demonstrated. The poorly soluble solids of the tweezer-shaped molecules were subjected directly from the reaction vessel to MicroED to determine their structures and packing modes. This work validated the efficiency of MicroED in determining the structures of such compounds.

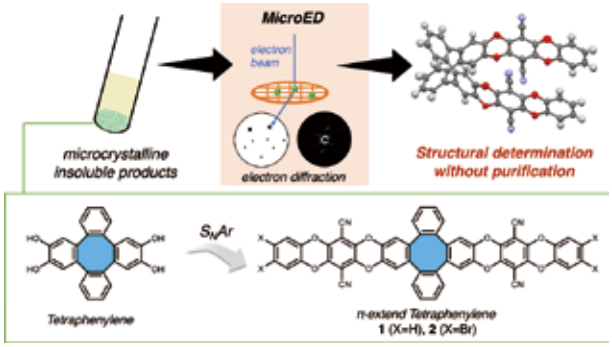


Figure 5. The synthesis and structure determination of π-extended tetraphenylene **1** and **2**.

References

1) M. Nagase, R. Yoshida, S. Nakano, T. Hirose and Y. Segawa, *Chem. Commum.* **61**, 11187–11190 (2025).
2) K. Watanabe, H. Sugiyama and Y. Segawa, *CrystEngComm* **27**, 3552–3559 (2025).
3) K. Watanabe, T. Toya, Y. Toyota, Y. Kobayashi, J. Usuba, Y. Hijikata, R. Matsuda, K. Nishimura, H. Sugiyama and Y. Segawa, *Chem. Commun.* **61**, 2822–2825 (2025).
4) H. Sugiyama, K. Watanabe, C. Song, K. Murata and Y. Segawa, *Chem. Lett.* **53**, upae192 (2024).

Visiting Professors

Visiting Professor
SATO, Sota *(from The University of Tokyo)*

Integrated Molecular Structure Analysis Through Industry-Academia Collaboration

Elucidating molecular structures is crucial in various fields of molecular science, regardless of academia or industry. In addition to NMR and mass spectrometry, X-ray/electron diffraction is a powerful analytical technique that can directly determine atomic positions, enabling clear determination of three-dimensional structures. We are actively pursuing the "crystalline sponge method" as one of core technologies, which eliminates the need for the crystallization process and completes sample preparation by simply soaking the target molecules into crystalline sponge. Recently, we achieved to reduce sample amount into only 3 ng using small-wedge synchrotron crystallography method. Furthermore, we are building collaborative relationships with numerous companies to promote research aimed at creating new industries. Also, we have been dedicated to fostering future talent who will support the scientific community in Japan and the world. We organized mock lectures and research experiences for junior high and high school students in collaboration with corporate researchers, aiming to nurture the next generation of scientists.

Visiting Professor
HAYASHI, Kumiko *(from The University of Tokyo)*

Interdisciplinary Research on Motor Proteins

Motor proteins move and carry out their functions by using the energy obtained from the hydrolysis of adenosine triphosphate (ATP). Our group has conducted research on motor proteins such as F_1-ATPase, a component of F_oF_1-ATP synthase that produces ATP in cells, and the kinesin motor KIF1A, which is responsible for axonal transport in neurons. To study these systems, we employ single-molecule experiments, cellular experiments, and theoretical analyses based on extreme-value statistics and nonequilibrium statistical mechanics. These approaches have enabled physical measurements of motor proteins under nonequilibrium conditions, which had been difficult to achieve with equilibrium statistical mechanics. At present, through collaborations with the National Institute of Information and Communications Technology (NICT) and the Institute for Molecular Science (IMS), we are pursuing the development of high-precision force measurements of these motor proteins using DNA origami technology. In the future, we aim to elucidate the in-cell mechanisms of motor protein motility through the development of this approach.

Visiting Associate Professor
SATO, Shinichi *(from Tohoku University)*

Development of Protein Labeling Methods and Applications to Chemical Proteomics

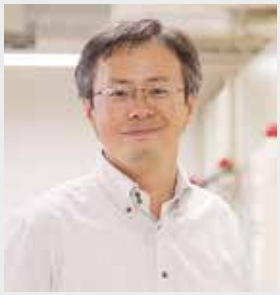
Our research tackles the fundamental challenge of understanding protein behavior in living systems through the development of organic chemistry-based tools. To address questions such as post-translational modifications, protein–protein interactions, and protein conformational changes that are difficult to investigate using biological methods alone, we have established unique chemical methodologies including protein labeling techniques that function specifically in nanometer-scale spaces within living systems, methods for detecting changes in amino acid residue (Tyr, His) exposure on protein surfaces, and technologies for selectively labeling aggregated proteins. By combining these novel chemical approaches with rapidly advancing proteomics techniques using mass spectrometry—capable of simultaneously analyzing thousands to tens of thousands of proteins in a single experiment—we aim to advance our understanding of biological phenomena, develop new manipulation technologies, and contribute to drug discovery applications.

RESEARCH ACTIVITIES
Research Center of Integrative Molecular Systems

The mission of CIMoS is to analyze molecular systems in nature to find the logic behind the sharing and control of information between the different spatiotemporal hierarchies, with the ultimate goal of creating novel molecular systems on the basis of these findings.

Biological Rhythm and Dynamics through Chemistry

Research Center of Integrative Molecular Systems
Division of Trans-Hierarchical Molecular Systems



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The Young Scientists' Prize
2007 Young Scientist Prize, The Biophysical Society of Japan
2006 SAS Young Scientist Prize, IUCr Commission on Small-angle Scattering
2002 The Protein Society Annual Poster Board Award

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Keywords Biological Rhythm, Circadian Clock, Cyanobacteria

Living organisms on Earth evolved over time to adapt to daily environmental alterations, and eventually acquired endogenous time-measuring (biological clock) systems. Various daily activities that we perform subconsciously are controlled by the biological clock systems sharing three characteristics. First, the autonomic rhythm repeats with an approximately 24-hour (circadian) cycle (self-sustainment). Second, the period is unaffected by temperature (temperature compensation). Third, the phase of the clock is synchronized with that of the outer world in response to external stimuli (synchronization). We seek to explain these three characteristics, and consider the biological clock system of cyanobacteria to be an ideal experimental model.

The major reason that cyanobacteria are considered to be the ideal experimental model is that the core oscillator that possesses the three characteristics of the clock can be easily reconstructed within a test tube. When mixing the three clock proteins KaiA, KaiB, and KaiC with ATP, the structure and enzyme activity of KaiC change rhythmically during a circadian cycle. Taking advantage of this test tube experiment, we used an approach combining biology, chemistry, and physics to elucidate the means by which the clock system extends from the cellular to atomic levels.

Among the three Kai proteins, KaiC is the core protein of the oscillator. In the presence of KaiA and KaiB, KaiC revelas the rhythm of autophosphorylation and dephosphorylation; however, the cycle of this rhythm depends on the ATPase activity of KaiC independent of KaiA or KaiB. For example, when the ATPase activity of KaiC doubles as a result of amino acid mutations, the frequencies of both the *in vitro* oscillator and the intracellular rhythm also double (the cycle period is reduced to half). This mysterious characteristic is called a transmural hierarchy, in which the cycle (frequency) and even the temperature compensation both *in vitro* and *in vivo* are greatly affected (controlled) by the function and structure of KaiC.

How are the circadian activities and temperature compensation features encoded in KaiC and then decoded from it to propagate rhythms at the cellular level? We are committed to better understanding biological clocks and other dynamic systems through the chemistry of circadian ***rhythm***, ***structure***, and evolutionary ***diversity***.

Selected Publications

- A. Mukaiyama, Y. Furuike, K. Ito-Miwa, Y. Onoue, K. Horiuchi, K. Kondo, E. Yamashita and S. Akiyama, *Nat. Commun.* **16**, 4541 (2025).
- Y. Furuike, Y. Onoue, S. Saito, T. Mori and S. Akiyama, *PNAS Nexus* **4**, pgaf136 (2025).
- Y. Furuike, A. Mukaiyama, S. Koda, D. Simon, D. Ouyang, K. Ito-Miwa, S. Saito, E. Yamashita, T. Nishiwaki, K. Terauchi, T. Kondo and S. Akiyama, *Proc. Natl. Acad. Sci. U. S. A.* **119**, e2119627119 (2022).
- Y. Furuike, A. Mukaiyama, D. Ouyang, K. Ito-Miwa, D. Simon, E. Yamashita, T. Kondo and S. Akiyama, *Sci. Adv.* **8**, eabm8990 (2022).
- J. Abe, T. B. Hiyama, A. Mukaiyama, S. Son, T. Mori, S. Saito, M. Osako, J. Wolanin, E. Yamashita, T. Kondo and S. Akiyama, *Science* **349**, 312–316 (2015).
- Y. Murayama, A. Mukaiyama, K. Imai, Y. Onoue, A. Tsunoda, A. Nohara, T. Ishida, Y. Maéda, T. Kondo and S. Akiyama, *EMBO J.* **30**, 68–78 (2011).

1. *Structure*: Reasons for Seeking Structure and Dynamics of Circadian Clock Components in Cyanobacteria[1–4)]

A great deal of effort has been devoted to characterizing structural changes in the clock proteins along the circadian reaction coordinate. However, little is known about the mechanism driving the circadian cycle, even for the simple cyanobacterial protein KaiC that has ATPase and dual phosphorylation sites in its N-terminal C1 and C-terminal C2 domains, respectively. Nearly all KaiC structures reported to date share a nearly identical structure, and they do not appear to be suggestive enough to explain the determinants of circadian period length and its temperature compensation. We are studying the structural and dynamical origins in KaiC using high-resolution x-ray crystallography,[1–4)] real-time fluorescence detection,[5)] and quasielastic neutron scattering.[6)]

2. *Rhythm*: Cross-Scale Analysis of Cyanobacterial Circadian Clock System[6–8)]

KaiC ATPase is of particular interest here, as it finely correlates to the frequencies of *in vivo* as well as *in vitro* oscillations and also it is temperature compensated. This unique property has inspired us to develop an ATPase-based screening[7)] for KaiC clock mutants giving short, long, and/or temperature-dependent periods.[8)] A developed HPLC system with a 4-channel temperature controller has reduced approximately 80% of time costs for the overall screening process (Figure 1). Using the developed device, we are screening a number of temperature-dependent mutants of KaiC.[6,7)]

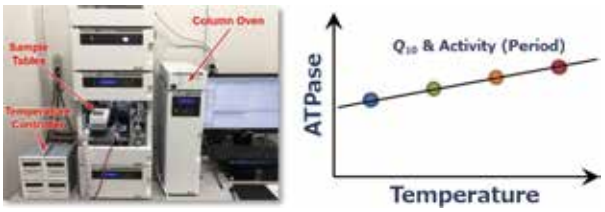

Figure 1. Development of a quick ATPase assay system.

3. Beyond Evolutionary *Diversity*[9)]

In the presence of KaiA and KaiB, the ATPase activity of KaiC oscillates on a 24-hour cycle. KaiC is not capable of maintaining a stable rhythm on its own, but its activity was observed to fluctuate with reduced amplitude over time (Figure 2A). We have identified a signal component that is similar to damped oscillation, and propose that it encodes the specific frequency, equivalent to a 24-hour cycle.

The habitats of cyanobacteria are diverse, so the space of their sequence is immense. Furthermore, some KaiA and KaiB genes are missing in several strains of cyanobacteria. This is understandable to some extent if KaiC possesses the specific frequency. Given this assumption, *what specific frequencies are possessed by KaiC homologues in other species and ancestral cyanobacteria?* (Figure 2B)

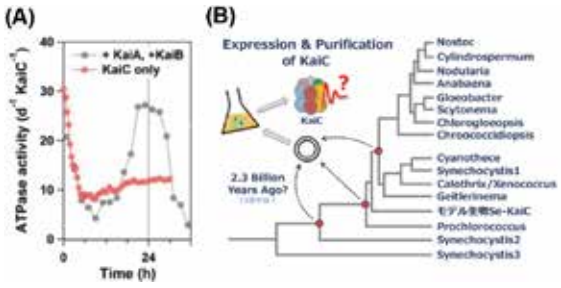

Figure 2. Damped oscillation of KaiC ATPase activity (**A**) and evolutionary diversity of cyanobacteria (**B**).

To address these questions, we restored the amino acid sequences of ancestral Kai proteins (Figure 2B) and studied their function (oscillation) and structures to determine the evolutionary origin of the self-sustained Kai-protein oscillators.[9)] Our results clearly demonstrate that the oldest Kai-protein oscillator emerges in the most recent common ancestor (MRCA) of cyanobacteria at approximately 2.2 Ga ago and is able to synchronize with temperature cycles of 18 h; this is shorter than the current rotation period of the Earth.

4. Bio-SAXS Activity in IMS[10)]

We have supported SAXS users so that they can complete experiments smoothly and publish their results.[10)]

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1) Y. Furuike, A. Mukaiyama, D. Ouyang, K. Ito-Miwa, D. Simon, E. Yamashita, T. Kondo and S. Akiyama, *Sci. Adv.* **8**, eabm8990 (2022).
2) Y. Furuike, A. Mukaiyama, S. Koda, D. Simon, D. Ouyang, K. Ito-Miwa, S. Saito, E. Yamashita, T. Nishiwaki-Ohkawa, K. Terauchi, T. Kondo and S. Akiyama, *Proc. Natl. Acad. Sci. U. S. A.* **119**, e2119627119 (2022).
3) Y. Furuike, E. Yamashita and S. Akiyama, *Biophys. Physicobiol.* **21**, e210001 (2024).
4) Y. Furuike, Y. Onoue, S. Saito, T. Mori and S. Akiyama, *PNAS Nexus* **4**, pgaf136 (2025).
5) A. Mukaiyama, Y. Furuike, E. Yamashita and S. Akiyama, *Biochem. J.* **479**, 1505–1515 (2022).
6) Y. Furuike, D. Ouyang, T. Tominaga, T. Matsuo, A. Mukaiyama, Y. Kawakita, S. Fujiwara and S. Akiyama, *Commun. Phys.* **5**, 75 (2022).
7) D. Ouyang, Y. Furuike, A. Mukaiyama, K. Ito-Miwa, T. Kondo and S. Akiyama, *Int. J. Mol. Sci.* **20**, 2789–2800 (2019)
8) D. Simon, A. Mukaiyama, Y. Furuike and S. Akiyama, *Biophys. Physicobiol.* **19**, e190008 (2022).
9) A. Mukaiyama, Y. Furuike, K. Ito-Miwa, Y. Onoue, K. Horiuchi, E. Yamashita and S. Akiyama, *Nat. Commun.* **16**, 4541 (2025).
10) T. Inobe, R. Sakaguchi, T. Obita, A. Mukaiyama, S. Koike, T. Yokoyama, M. Mizuguchi and S. Akiyama, *FEBS Lett.* **598**, 2292–2305 (2024).

* IMS International Internship Program

Elucidation of Function, Structure, and Dynamics of Condensed-Phase Molecular Systems by Advanced Ultrafast Laser Spectroscopy

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Awards
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2020 The Commendation for Science and Technology by the Minister of Education, Culture, Sports, Science and Technology
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Keywords Ultrafast Spectroscopy, Nonlinear Spectroscopy, Chemical Reaction Dynamics

We develop and apply advanced ultrafast laser spectroscopy based on state-of-the-art optical technology to study the chemical reaction dynamics of the condensed-phase molecules. In particular, we focus on exploiting unique methodologies based on few-cycle ultrashort pulses (*e.g.*, time-domain impulsive vibrational spectroscopy and multidimensional spectroscopy) and tracking molecular dynamics from electronic and structural viewpoints throughout the chemical reaction with exquisite temporal resolution. We also develop a novel methodology and light source to probe ultrafast dynamics of single molecules in the condensed phase at room temperature, with the aim to understand chemical reaction dynamics at the single-molecule level. Our particular interest rests on elucidating sophisticated molecular mechanisms that underlie the reactions of functional molecular systems such as proteins, molecular assemblies, and metal complexes. On the basis of new insights that can be gained from our advanced spectroscopic approaches, we aim to establish a new avenue for the study of chemical reaction dynamics.

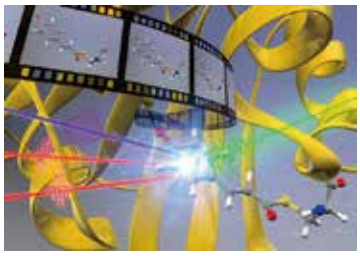

Figure 1. Schematic of the ultrafast nonlinear spectroscopy of complex molecules with few-cycle ultrashort pulses.

Selected Publications

- Y. Yoneda, T. Konishi, K. Suga, S. Saito and H. Kuramochi, "Excited-State Aromatization Drives Nonequilibrium Planarization Dynamics," *J. Am. Chem. Soc.* **147**, 12051 (2025).
- H. Kuramochi, T. Tsutsumi, K. Saita, Z. Wei, M. Osawa, P. Kumar, L. Liu, S. Takeuchi, T. Taketsugu and T. Tahara, "Ultrafast Raman Observation of the Perpendicular Intermediate Phantom State of Stilbene Photoisomerization," *Nat. Chem.* **16**, 22 (2024).
- Y. Yoneda and H. Kuramochi, "Room-Temperature Solution Fluorescence Excitation Correlation Spectroscopy," *J. Phys. Chem. Lett.* **15**, 8533 (2024).
- Y. Yoneda, and H. Kuramochi, "Rapid-Scan Resonant Two-Dimensional Impulsive Stimulated Raman Spectroscopy of Excited States," *J. Phys. Chem. A* **127**, 5276–5286 (2023).
- H. Kuramochi and T. Tahara, "Tracking Ultrafast Structural Dynamics by Time-Domain Raman Spectroscopy," *J. Am. Chem. Soc.* **143**, 9699–9717 (2021).
- H. Kuramochi, S. Takeuchi, K. Yonezawa, H. Kamikubo, M. Kataoka and T. Tahara, "Probing the Early Stages of Photoreception in Photoactive Yellow Protein with Ultrafast Time-Domain Raman Spectroscopy," *Nat. Chem.* **9**, 660–666 (2017).

1. Excited-State Aromatization Drives Non-Equilibrium Planarization Dynamics[1)]

Excited-state aromaticity is one of the most widely applied concepts in chemistry, often used as a rational guideline for predicting conformational changes in cyclic π-conjugated systems induced by photoexcitation. Yet, the details of the relationship between the corresponding photoinduced electronic and structural dynamics have remained unclear. In this work, we applied femtosecond transient absorption and time-resolved time-domain Raman spectroscopies to track a non-equilibrium planarization dynamics of cyclooctatetraene (COT) derivative associated with the excited-state aromaticity. In the femtosecond time-resolved Raman data, the bent-to-planar structural change was clearly captured as a continuous peak shift of the marker band, which was unambiguously identified with ^{13}C-labeling. Our findings show that the planarization occurs after a significant change in the electronic structure, suggesting that the system first becomes aromatic, followed by a conformational change. This work provides a unique framework for understanding the excited-state aromaticity from a dynamical aspect.

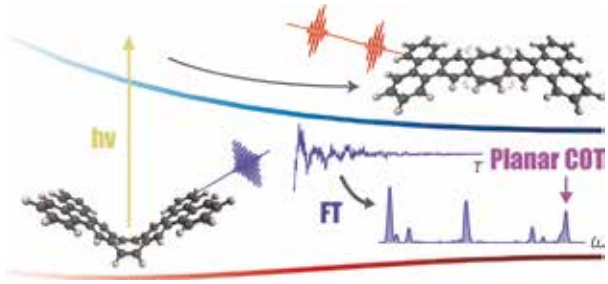

Figure 2. Schematic of time-domain Raman observation of the structural dynamics upon the onset of excited-state aromaticity.

2. Dynamic Excited-State Localization Induced by Jahn-Teller Distortion Observed by Coherent Vibrational Spectroscopy[2)]

Molecular symmetry is a central design element in functional materials, yet its dynamic modulation in the excited state and its consequences for optoelectronic properties remain largely unexplored, particularly in main-group p-block element complexes. We address this knowledge gap by investigating unique Al(III) dinuclear triple-helical complexes that combine high symmetry with twisted π-conjugated systems and achieve exceptional optical properties of unusually large Stokes shifts and high photoluminescence quantum yields. Using transient absorption spectroscopy with a 10 fs pump pulse, we detected coherent vibrational oscillations overlapped with transient absorption/stimulated emission signals. Analysis of the dephasing times of oscillatory signals revealed photoexcitation-triggered Jahn-Teller distortions in these high-symmetry p-block complexes, evidenced by a specifically short dephasing time constant of 410 fs associated with intraligand twisting vibrations. Our findings demonstrate that excited-state symmetry breaking, strongly coupled with intraligand twisting vibrations, is crucial in determining the remarkable photofunctional properties of large Stokes shifts and high photoluminescence quantum yields. This work elucidates the fundamental mechanisms underlying the performance of these Al(III) complexes and provides a conceptual framework for designing next-generation photofunctional materials by harnessing dynamic symmetry changes.

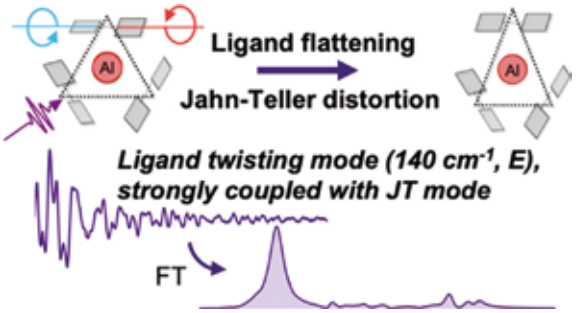

Figure 3. Schematic of the photoexcitation-triggered Jahn-Teller distortion in Al(III) dinuclear triple-helical complex.

3. Development of Two-Dimensional Fluorescence Excitation Correlation Spectroscopy

Polyatomic molecules in condensed phases undergo constant fluctuations in molecular structure and solvent environment. Fluorescence correlation spectroscopy (FCS) is advantageous in elucidating the fast fluctuation dynamics of freely diffusing molecules in solution, where a variety of chemical and biological processes occur. However, observing the fluctuation of diverse physical properties, such as electronic/vibrational spectra and ultrafast dynamics, still remains challenging. In this study, we developed fluorescence excitation cross-correlation spectroscopy for room-temperature solutions, which enables the study of spontaneous fluctuations in the excitation spectrum with microsecond time resolution. By employing Fourier transform spectroscopy with broadband femtosecond pulses and time-correlated single-photon counting, the method enables us to obtain an excitation wavelength-resolved fluorescence cross-correlation map in the microsecond to millisecond range, demonstrating the potential of this method to elucidate the transition between sub-ensembles in statistically equilibrium systems.

References

1) Y. Yoneda, T. Konishi, K. Suga, S. Saito and H. Kuramochi, *J. Am. Chem. Soc.* **147**, 12051 (2025).
2) T. Ehara, Y. Yoneda, T. Yoshida, T. Ogawa, Y. Konishi, T. Ono, A. Muranaka, H. Kuramochi, K. Miyata and K. Onda, *J. Am. Chem. Soc.* **147**, 26446 (2025).

Development of Designer Enzymes for Biomolecular Systems Engineering

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Keywords Artificial Metalloenzyme, Protein Engineering, Coordination Chemistry

Life processes are sustained by a complex network of interconnected biochemical reactions. There has been a growing interest in re-engineering these biochemical reaction networks, which has implications for synthesis of chemicals and medical applications. We believe that the integration of unnatural chemical reactions, not found in nature but developed by humans, into this biochemical reaction network will pave the way for new ventures, leading to the production of various high-value-added compounds and the development of novel drugs with unique modes of action. With this ultimate objective in mind, our group is focusing on designer enzymes that catalyze unnatural chemical transformations. We are conducting a comprehensive study on the development of designer enzymes, drawing on coordination chemistry, catalytic chemistry, and protein engineering, as well as the development of technologies for their delivery into cells and organisms.

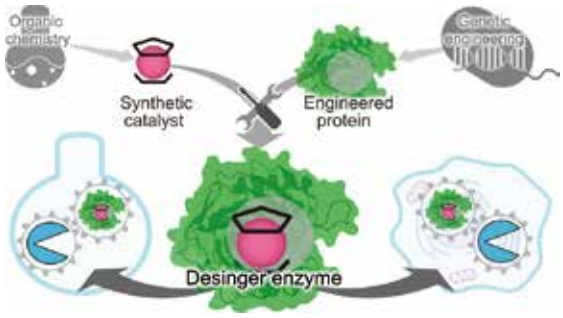

Figure 1. By combining synthetic catalysts developed through organic synthetic chemistry and proteins engineered through genetic optimization, we construct designer enzymes that possess non-natural functions. Using these designer enzymes, we aim to design chemical reaction networks within flasks and cells.

Selected Publications

- A. Ueno, F. Takida, T. Kita, T. Ishii, T. Himiyama, T. Mabuchi and Y. Okamoto, "A Cytokine-Based Designer Enzyme with an Abiological Multinuclear Metal Center Exhibits Intrinsic and Extrinsic Catalysis," *Nat. Commun.* **16**, 6781 (2025).
- Y. Okamoto, T. Mabuchi, K. Nakane, A. Ueno and S. Sato, "Switching Type I/Type II Reactions by Turning a Photoredox Catalyst into a Photo-Driven Artificial Metalloenzyme," *ACS Catal.* **13**, 4134–4141 (2023).
- H. J. Davis, D. Häussinger, T. R. Ward and Y. Okamoto, "A Visible-Light Promoted Amine Oxidation Catalyzed by a Cp* Ir Complex," *ChemCatChem* **12**, 4512–4516 (2020).
- Y. Okamoto, R. Kojima, F. Schwizer, E. Bartolami, T. Heinisch, S. Matile, M. Fussenegger and T. R. Ward, "A Cell-Penetrating Artificial Metalloenzyme Regulates a Gene Switch in a Designer Mammalian Cell," *Nat. Commun.* **9**, 1943 (2018).

1. Rational Design of a Synthetic Trinuclear Metal Complex Structures in a Protein Scaffold

Enzymes facilitate diverse chemical transformations in nature, with metal ions significantly expanding reaction capabilities. Examples include soluble methane monooxygenase (diiron enzyme for methane hydroxylation), nitrogenase (iron-molybdenum cofactor for nitrogen fixation), and photosystem II's oxygen-evolving complex (manganese-calcium cluster for water oxidation). In such metalloenzymes, protein scaffolds serve dual functions: Amino acid side chains act as ligands controlling metal ion reactivity, while defined internal spaces create reaction compartments enhancing rates and selectivity.

Designer metalloenzymes, created by incorporating synthetic molecules into proteins or constructing metal centers by using amino acid residues in protein, has proved the importance of reaction compartments by demonstrating enhanced reactivity and selectivity. However, using proteins as ligands lags behind their compartment applications due to difficulties in designing coordination chemistry at atomic levels. Designer mononuclear metalloenzyme development relies mainly on metal-substitution approaches and designing metal-binding site from scratch is further challenging. While some studies report construction of multinuclear metal centers using proteins and peptides as ligands, catalytically active examples remain limited with restricted scaffold variety.

Here, we successfully developed a designer enzyme containing a synthetic multinuclear metal complex structure by using proteins as the only coordination ligands.

As a model for grafting a multinuclear metal center into a protein scaffold, we have selected a synthetic trinuclear zinc complex (Figure 2a, b). This specific trinuclear zinc complex is a unique structural motif not typically found in natural enzymes. The choice of zinc ion was made due to its prevalence as one of the most abundant metal ions in biological systems.

For our study, we selected human macrophage migration inhibitory factor (MIF) as the scaffold protein because of its trimeric structure, which contains an internal pore suitable for hosting a synthetic trinuclear zinc complex structure (Figure 2c).

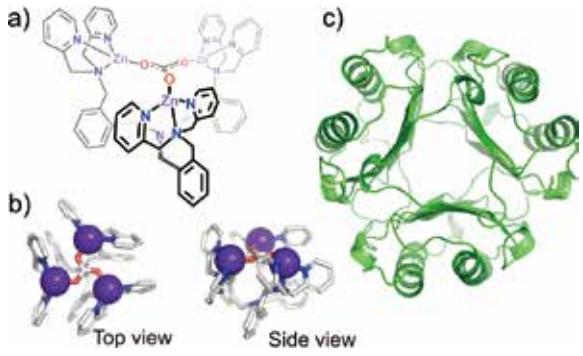

Figure 2. Building blocks used in this study. (a) Schematic and (b) crystal structures of the synthetic trinuclear zinc complex (CCDC 931956), and (c) crystal structure of human cytokine MIF (PDB code: 1MIF).

We have conducted a computational geometry search to identify suitable locations for placing histidine residues as ligands for the trinuclear zinc center. Subsequently, DFT calculations were performed to further refine the selection of candidate sites. As a result, we have prepared the identified variant, MIF(S61H/Y100H), along with an additional derivative, MIF(Y100H).

X-ray crystallography has verified the successful formation of the trinuclear zinc center in both MIF(S61H/Y100H) and MIF(Y100H) variants (Figure 3). The experimental structures align closely with the predictions from DFT calculations, illustrating the accuracy of our design strategy. Results from ITC analysis and DLS measurements confirm that the trimeric structures of the MIF variants are maintained in solution, with three zinc ions binding to the trimeric MIF variants.

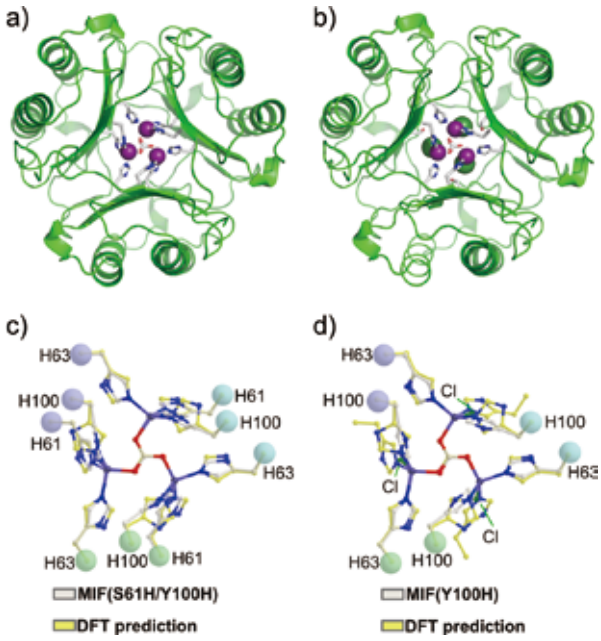

Figure 3. Crystal structures (a and b) of MIF(S61H/Y100H) (PDB code: 9JIZ; carbon: cyan) and MIF(Y100H) (PDB code: 9JJ0; carbon: cyan) in the presence of zinc ion. Superimposed images of the DFT-optimized trinuclear zinc center with (c) MIF(S61H/Y100H), and (d) MIF(Y100H) in the presence of zinc ion.

In the case of both MIF(S61H/Y100H) and MIF(Y100H) variants, hydrolytic activity was enhanced in the presence of zinc ions. This acceleration was not observed in the wild type MIF, indicating that the trinuclear zinc center plays a crucial role in catalysis. Interestingly, the trinuclear zinc center in the MIF(Y100H) variant exhibited higher activity compared to that in MIF(S61H/Y100H), achieving k_{cat}/K_M = 46.0 ± 0.4 M^{-1} s^{-1} at pH 7.9.

Reference

1) Ueno, F. Takida, T. Kita, T. Ishii, T. Himiyama, T. Mabuchi and Y. Okamoto, *Nat. Commun.* **16**, 6781 (2025).

Open up Future Electronics by Organic Molecules

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Keywords Organic Spintronics, Chirality, Organic Superconductor

Spintronics is a new ingredient of electronics in which a magnetic moment of an electron is utilized as an information carrier together with its charge. Spin-polarized current is one of the most important resources in spintronics, because it can drive devices such as ferromagnetic memory with spin angular momentum. In conventional spintronics, such a spin-polarized current is generated by passing a charge current through ferromagnetic metals. However, recently, researchers are finding other ways of spin-polarized current generation by using topological insulators and non-collinear antiferromagnets, which can sometimes be more efficient than those with ferromagnets.

Chiral molecules are attracting recent attention as a new source of spin-polarized current. Chirality-Induced Spin Selectivity (CISS) effect generates spin polarization parallel to or antiparallel to the electron's velocity depending on the handedness of the chiral molecule that is being passed through (Figure 1). Although the mechanism of CISS effect is still under debate, it seems to create spin-polarization higher than those of ferromagnets, which is surprisingly large when the small spin–orbit coupling energy of organic molecules is considered. In order to rationalize such a large effect, some microscopic hypotheses are proposed based on experimental results, whose proofs are being waited for. Our group is trying to unveil such mechanisms that drive CISS effect by using chiral crystalline materials.

The use of crystalline materials has several advantages. For example, one can employ theoretical framework with well-defined wave number of electrons. Another advantage is the size of the chiral material which allows direct attachment of detection electrodes in different positions. With these merits in mind, we are fabricating spintronic devices suitable for the CISS investigations.

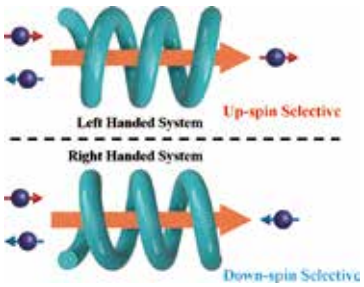

Figure 1. Conceptual schematic for CISS effect. P-helix molecule (lower panel) can transmit more electrons with spins antiparallel to the velocity (negative helicity electrons) than the other, while M-helix molecule (upper panel) favors transmission of electrons with parallel spin (positive helicity electrons).

Selected Publications

- R. Nakajima, D. Hirobe, G. Kawaguchi1, Y. Nabei1, T. Sato, T. Narushima, H. Okamoto and H. M. Yamamoto, *Nature* **613**, 479 (2023).
- Y. Nabei, D. Hirobe, Y. Shimamoto, K. Shiota, A. Inui, Y. Kousaka, Y. Togawa and H. M. Yamamoto, *Appl. Phys. Lett.* **117**, 052408 (2020).
- A. Inui, R. Aoki, Y. Nishiue, K. Shiota, Y. Kousaka, H. Shishido, D. Hirobe, M. Suda, J.-i. Ohe, J.-i. Kishine, H. M. Yamamoto and Y. Togawa, *Phys. Rev. Lett.* **124**, 166602 (2020).
- M. Suda, Y. Thathong, V. Promarak, H. Kojima, M. Nakamura, T. Shiraogawa, M. Ehara and H. M. Yamamoto, "Light-Driven Molecular Switch for Reconfigurable Spin Filters," *Nat. Commun.* **10**, 2455 (7 pages) (2019).

1. Spin Current Generation in a Chiral Organic Superconductor

Although *s*- and *d*-wave superconductors are in a spin singlet state at its ground state, a superconductor with broken mirror symmetry is expected to show spin triplet state when supercurrent is flowing, according to a theory developed by Edelstien.[1] This means spin polarization can be generated by applying supercurrent in a chiral superconductor. The magnetization direction that depends on the lattice symmetry has been recently calculated by group theory.[2] We have tested this idea by employing κ-(BEDT-TTF)$_2$Cu(NCS)$_2$ (hereafter, κ-NCS) which is an organic superconductor with chiral and polar crystal lattice. The space group of this crystal is $P2_1$, and its handedness is defined by the relative arrangement between the anionic Cu(NCS)$_2$ and cationic BEDT-TTF. This handedness can be experimentally determined by X-ray diffraction or circular dichroism (CD).

After confirming pure enantiomeric lattice system with CD microscope, a thin crystal of κ-NCS has been laminated onto a resin substrate with prepatterned gold and nickel electrodes. At temperature lower than superconducting T_c, an a.c. electrical excitation was applied to induce spin polarization (Figure 2). The spin polarization accumulated at the interface between κ-NCS and the magnetic electrode was detected as a built-up voltage that is dependent on the relative angle between the accumulated and ferromagnetic spins. We have compared the observed voltage with theoretical estimation and found that it exceeds the value predicted by Edelstein effect more than 1000 times. This surprising result suggests that there is a spin enhancement effect other than Edelstein effect, implying existence of an effect analogous to CISS for a chiral superconductor.

By measuring the angle dependency of this magneto–voltaic signal, the direction of accumulated spin could be determined. The observed spin polarization direction was dependent on the location of the detection electrode inside the crystal, and its arrangement was consistent with a magnetic monopole structure which has been hypothesized in a chiral molecule under non-equilibrium state with CISS effect. More specifically, the spin accumulation was forming an antiparallel pair on the upper and lower sides of the κ-NCS crystal. With a right-handed crystal, the accumulated spins showed outward spin pairs.

To our surprise, this spin accumulation could be observed in nonlocal measurements where the excitation and detection electrodes are separated by 600 μm. We have also fabricated a nonlocal detection device with a crystal possessing two chirality domains where right- and left-handed crystal structures are spatially separated. By exciting crystal domains at two different positions with opposite handednesses, we have observed a switching of antiparallel spin pairing mode from outward to inward. This corresponds to the sign reversal of magnetic monopole in the language of multipole expression.[3] An interesting point here is that the magnetic monopole is also breaking the mirror symmetry, and its sign is connected to the chirality of underlying crystal lattice, although the magnetic monopole is time-reversal-odd (*T*-odd chiral). Although this *T*-odd chirality is a metastable state and disappears at ground state, its relevance to the enantio-separation experiments in CISS effect is directly implied in this experiment. If one accepts the fact that a sign of such a metastable magnetic monopole at excitation can represent the sign of chirality (*T*-even electric toroidal monopole) in the lattice, both the large enhancement of spin polarization and the enantio-separation of chiral molecules at non-equilibrium state observed in CISS experiments can be naturally understood, because such a monopole can interact with magnetic substrate in a handedness-specific manner. Such an interaction will also provide a large exchange energy difference for each spin. In this sense, this experiment provides the first direct observation of antiparallel spin pair formation from coherent chiral system which seems to be connected to microscopic CISS mechanism. Although the Hamiltonians describing the chiral superconductor and chiral molecules are quite different, there are many common features such as singlet ground state, chiral lattice and quantum coherence over the entire body. Since the conversion from *T*-even spin current to *T*-odd spin accumulation requires time integration with an existence of spin reservoir, the spin carriers in chiral molecules and superconductors should be identified in future studies. We also expect emergence of superconducting spintronics once a sourcing of spin-polarized current in superconductor is established by chiral superconductors.
(BEDT-TTF = bis(ethylenedithio)tetrathiafulvalene)

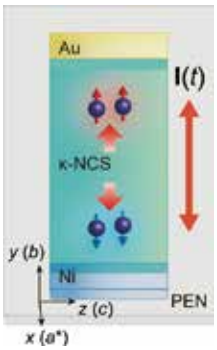

Figure 2. Device schematic for the detection of spin polarization in a chiral superconductor κ-NCS. By applying electrical current, electron spins are polarized along the current direction by CISS-like effect which can be detected as voltage across the κ-NCS/Ni interface. The amplitude of the signal is proportional to the accumulated spins at the interface.

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1) V. M. Edelstein, *Phys. Rev. B* **72**, 172501 (2005).
2) W.-Y. He and K. T. Law, *Phys. Rev. Res.* **2**, 012073(R) (2020).
3) J. Kishine, H. Kusunose and H. M. Yamamoto, *Isr. J. Chem.* **62**, e202200049 (2022).

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Design of Protein Functions Using Computational and Experimental Approaches

Research Center of Integrative Molecular Systems
Division of Trans-Hierarchical Molecular Systems

KOSUGI, Takahiro
Assistant Professor

Our research is to design a variety of protein functions using computational and experimental approaches. We try to (1) design enzymes from scratch and reveal the origin of the enzymatic activity, (2) control concerted functions by rationally engineering protein complexes and understand their mechanisms and (3) uncover roles of protein complexes in cells and control cellar functions by creating several customized proteins or protein complexes.

1. De Novo Design of ATPase

ATP hydrolysis plays pivotal roles in various proteins, including molecular motors and kinases. To elucidate the minimal structural requirements for ATP binding and hydrolysis, we computationally designed an ATPase from scratch, focusing the P-loop motif, a conserved phosphate-binding loop found in many naturally occurring ATPase.

Using computational design methods, we systematically explored an optimal topology that harbor the P-loop motif and facilitate binding to the adenine ring of ATP. Main-chain structures corresponding to the identified topology were generated, and amino acid sequences were designed to stabilize the main-chain structures and optimize ATP binding.

Biochemical assays for the designed proteins verified that one design was soluble, monomeric in solution, and exhibited ATP hydrolysis activity. Moreover, its crystal structure closely matched our design model and contained a P-loop motif with the typical features. We successfully demonstrated how to design a P-loop containing ATPase from scratch.

Reference

1) T. Kosugi, M. Tanabe and N. Koga, *Protein Sci.* **34**, e70132 (2025).

Award

KOSUGI, Takahiro; The Morino Foundation for Molecular Science (2025).

RESEARCH ACTIVITIES
Center for Mesoscopic Sciences

In the past few decades, great progress in experimental and theoretical methods to analyze structures, dynamics, and properties of single-component (or single hierarchical) molecules and nanomaterials has been made. Now we should also direct our attention to properties and functions of multi-hierarchical molecular systems. We develop innovative methods of measurements and analysis for molecular and materials systems to elucidate the processes that trigger the functions and reactions of the systems in the mesoscopic regime, that is the regime where micro and macroscopic properties influence each other.

Nano-Optical Imaging and Chiral Light-Matter Interaction in Nanomaterials

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1983 B.S. The University of Tokyo
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Professional Employment
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1990 Research Associate, The University of Tokyo
1993 Associate Professor, The University of Tokyo
2000 Professor, Institute for Molecular Science
Professor, The Graduate University for Advanced Studies

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Keywords Nano Optics, Plasmons, Chirality

Studies of local optical properties of molecular assemblies and materials are the keys to understanding nanoscale physical and chemical phenomena, and for construction of nanoscale functional devices. Optical microscopic methods, in particular nano-optical methods, such as scanning near-field optical microscopy (SNOM) which enables resolution beyond the diffraction limit of light, reveals essential characteristics of the materials and develop novel properties of them. Combination of microscopic techniques with various advanced spectroscopic methods may provide a methodology to analyze nanoscale functionalities and dynamics directly. We have constructed nano-optical (near-field and far-field) spectroscopic and microscopic measuring systems, for the studies on excited-state properties of nanomaterials, with the feasibilities of polarization dependence and nonlinear/time-resolved measurements. The developed apparatuses achieved nano-optical measurements of two-photon induced emission, femtosecond time-resolved signals, and chiro-optical properties (as typified by circular dichroism), in addition to conventional transmission, emission, and Raman-scattering. Based on these methods, we are investigating the characteristic spatial and temporal behavior of various metal-nanostructure systems and molecular assemblies. Typical examples are shown in Figure 1. We succeeded in visualizing wave functions of resonant plasmon modes in single noble metal nanoparticles, confined optical fields in noble metal nanoparticle assemblies, plasmon wave packet propagation dynamics, local chiro-optical properties of chiral and achiral metal nanostructures, and so forth. We also developed far-field high-precision circular dichroism microscope that facilitate chirality analysis of materials in a wide range of research areas. The information on nano-optical properties of the materials is also relevant to exploration of novel optical manipulation principles, which is another research topic of the research group.

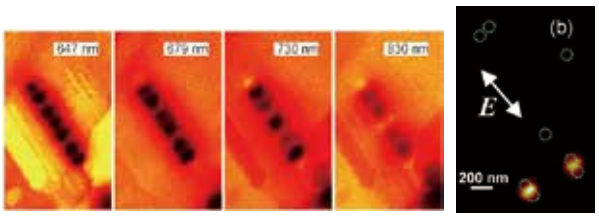

Figure 1. (Left four panels) Near-field transmission images of gold nanorod (20 nm^D × 510 nm^L). The wavelengths of observation were 647, 679, 730, and 830 nm from left to right. The spatial oscillating features were attributed to the square amplitudes of the resonant plasmonic wave functions. (Right) Near-field two-photon excitation image of dimers of spheric gold nanoparticles (diameter 100 nm) observed at 785 nm. The arrows indicates the incident light polarization. Dotted circles represent approximate positions of the particles.

Selected Publications

- H. Okamoto, "Local Optical Activity of Nano- to Microscale Materials and Plasmons," *J. Mater. Chem. C* **7**, 14771–14787 (2019).
- H. Okamoto, T. Narushima, Y. Nishiyama and K. Imura, "Local Optical Responses of Plasmon Resonance Visualized by Near-Field Optical Imaging," *Phys. Chem. Chem. Phys.* **17**, 6192–6206 (2015).
- H. Okamoto and K. Imura, "Visualizing the Optical Field Structures in Metal Nanostructures," *J. Phys. Chem. Lett.* **4**, 2230–2241 (2013).

1. Local Chiro-Optical Effects in Gold Nanostructures Investigated by Chiral Photoinduced Force Microscopy

Photoinduced force microscopy (PiFM) is an optical near-field imaging technique based on the technique of atomic force microscopy (AFM). By irradiating light on a system consisting of a sample and a probe tip, and detecting the force arising from interactions between the light-induced polarizations of the sample and the probe, PiFM enables the visualization of local optical near-fields with nanometer-scale resolution. By employing left-handed and right-handed circularly polarized light as the excitation source, the differential force signal measured between the two polarization states (referred to as chiral PiFM) is expected to reflect chiro-optical effects in the near field. We previously demonstrated the feasibility of this approach through experimental measurements using pseudo two-dimensional chiral metallic nanostructures.[1)]

In the present study, we extend this methodology to investigate the general applicability of chiral PiFM and to gain deeper insights into its measurement principles. To this end, we perform chiral PiFM measurements and analyses on a variety of gold nanostructures with different geometries. In the case of three-dimensional chiral gold nanoparticles, near-field signals that correlate with the handedness of the particles were observed. For achiral assembled particle systems, local chiro-optical responses were observed in the peripheral areas, exhibiting spatially oscillatory patterns with alternating positive and negative signals. In spherical nanoparticles, where no chiro-optical effect is theoretically expected under circularly polarized illumination, weak signals were still observed in the chiral PiFM measurements. The result suggests that such signals may arise from symmetry-breaking effects involving the probe tip itself, and further analysis is ongoing to elucidate the underlying mechanisms.

2. Development of Far-Field Circular Dichroism Microscopy

Circular dichroism (CD) spectroscopy is a powerful technique widely employed for the detection and characterization of materials chirality. However, in anisotropic samples, signals arising from linear dichroism and other polarization-dependent effects often interfere with CD measurements. Consequently, the application of conventional CD measurement techniques to microscopic imaging has faced significant challenges to ensure signal accuracy and precision. Only very few reports on CD-based microscopic imaging have been published. In a previous study, we developed a high-precision far-field CD microscope based on a novel circular polarization modulation method, which enabled CD microscopic imaging with sufficiently suppressed interference from linear polarization effects.[2)]

To apply CD imaging to a wider range of research, diagnostics, and so forth, it is desirable to reduce measurement time and to simplify the optical alignment procedures. The previously developed system required a certain level of expertise for optical alignment and typical measurement times on the order of several minutes per image, indicating a need for further development. In the present work, we propose a new approach to CD microscopy aimed at substantially reducing imaging time and improving ease of operation. As a result of one such attempt, we have succeeded in acquiring CD images at several frames per second, with a slight compromise in signal accuracy compared to the earlier system configuration. This improvement represents a significant step toward the realization of real-time or live CD imaging, which is expected to broaden the applicability of CD microscopy in both fundamental and applied research.

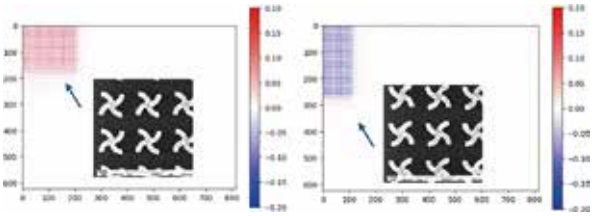

Figure 2. Examples of CD images of pinwheel-shaped gold nanostructure arrays. Red and blue parts indicate positive and negative CD signals.

3. Toward the Observation of Chirality-Induced Dynamics

In recent years, it has been reported that the irradiation of achiral plasmonic materials with circularly polarized light can induce the formation of chiral nanostructures through photochemical reactions. This process is believed to involve several key steps: The excitation of chiral plasmonic resonances on achiral structures under irradiation of circularly polarized light; generation of chiral local electromagnetic fields; the spatial arrangement and orientation of reactant molecules in response to these fields; and, finally, the photoexcitation (or thermal excitation) of the reactants followed by chemical reactions to form chiral nanostructures. To understand the mechanisms of the processes, we have constructed an experimental apparatus for time-resolved measurements of chiral optical responses. Using this setup, we are currently investigating the dynamics of chirality-induced optical responses in plasmonic materials.

References

1) J. Yamanishi, H.-Y. Ahn and H. Okamoto, *Nano Lett.* **23**, 9347 (2023).
2) T. Narushima and H. Okamoto, *Sci. Rep.* **6**, 35731 (2016).

Awards

YAMANISHI, Junsuke; 56th Excellent Presentation Award from Japan Society of Applied Physics (2024).
YAMANISHI, Junsuke; Nagoya University Ishida Prize (2025).
AHN, Hyo-Yong; Award for Promotion of the Most Excellent Young Researcher from Plasmonic Chemistry Research Group (2025).

Nano- and Atomic-Scale Spectroscopy

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2011 JSPS Research Fellow, Fritz-Haber Institute
2013 Group Leader, Fritz-Haber Institute
2021 Associate Professor, Institute for Molecular Science
Associate Professor, The Graduate University for Advanced Studies
2020 Guest Professor, Hokkaido University
2022 Guest Professor, Kyoto University

Awards
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2014 Morino Award for Molecular Science
2016 Gerhard Ertl Young Investigator Award
2020 Gaede Prize (German Physical Society)
2020 The Commendation for Science and Technology by the Minister of Education, Culture, Sports, Science and Technology
The Young Scientists' Award
2020 Heinrich Rohrer Medal (The Japan Society of Vacuum and Surface Science)

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Keywords Tip-Enhanced Near-Field Spectroscopy, Atomic-Scale Light–Matter Interactions, Nanomaterials Characterization

A detailed understanding of atomic-scale structures, properties, and dynamics is fundamentally important for the design of next-generation devices and optimization of material and energy conversion processes, including optoelectronics, solar cells, and catalysis. The rapid advancement of nanotechnology requires measurement techniques capable of directly observing phenomena with simultaneous high spatial and temporal resolution at the (sub)nanometer scale. Optical spectroscopy is a powerful and versatile tool for characterizing materials, but its spatial resolution is fundamentally limited by diffraction, restricting its ability to directly observe nanoscale systems. Near-field optics overcomes this limitation and enables optical characterization beyond the diffraction limit.

Our group has focused on developing and applying cutting-edge tip-enhanced near-field techniques in combination with laser spectroscopy, including nonlinear and ultrafast time-resolved techniques, to investigate photophysical and photochemical phenomena. Recently, we have demonstrated atomic-level sensitivity and spatial resolution using tip-enhanced Raman spectroscopy (TERS) and scanning near-field optical microscopy (SNOM) based on low-temperature scanning tunneling microscopy (STM) and atomic force microscopy (AFM). Furthermore, by integrating ultrashort pulsed lasers, we have shown that ultrafast coherent dynamics can be probed with atomic-scale resolution.

We are currently pushing the boundaries of atomic-scale spectroscopy with three key objectives: (1) extending its capabilities from the visible to the infrared region to investigate a broader range of materials and phenomena; (2) advancing nonlinear and time-resolved spectroscopic techniques; and (3) applying these methods to diverse low-dimensional systems to explore their unique optical properties.

Selected Publications

- B. Cirera *et al.*, "Joule Heating in Single-Molecule Point Contacts Studied by Tip-Enhanced Raman Spectroscopy," *ACS Nano* **16**, 16443 (2022).
- S. Liu *et al.*, "Nanoscale Coherent Phonon Spectroscopy," *Sci. Adv.* **8**, eabq5682 (2022).
- S. Liu *et al.*, "Inelastic Light Scattering in the Vicinity of a Single-Atom Quantum Point Contact in a Plasmonic Picocavity," *ACS Nano* **17**, 10172 (2023).
- J. Nishida *et al.*, "Sub-Tip-Radius Near-Field Interactions in Nano-FTIR Vibrational Spectroscopy on Single Proteins," *Nano Lett.* **24**, 836 (2024).
- Y. Wang *et al.*, "Ultrafast Nano-Imaging of Spatially Modulated Many-Body Dynamics in CVD-Grown Monolayer WS_2," *ACS Photonics* **12**, 207 (2024).
- A. Shiotari *et al.*, "Picocavity-Enhanced Raman Spectroscopy of Physisorbed H_2 and D_2 Molecules," *Phys. Rev. Lett.* **134**, 206901 (2025).
- A. Shiotari *et al.*, "Scattering Near-Field Optical Microscopy at 1-nm Resolution Using Ultralow Tip Oscillation Amplitudes," *Sci. Adv.* **11**, eadu1415 (2025).
- J. Nishida *et al.*, "Ultrafast Infrared Nano-Imaging of Local Electron–Hole Dynamics in CVD-Grown Single-Walled Carbon Nanotubes," *Sci. Adv.* **11**, eadv9584 (2025).

1. Atomic-Scale Optical Spectroscopy

Atomic-scale light–matter interactions are a frontier of optical nanoscience, providing opportunities not only for ultra-sensitive and ultra-high-resolution spectroscopy, but also for establishing picoscale optics and photonics. Recent studies have shown that extreme confinement of near fields occurs at atomic-scale protrusions on metal nanostructures, referred to as 'picocavity,' leading to unique optical phenomena. Using TERS, we demonstrated atomic-scale vibrational spectroscopy and revealed how picoscale structural changes affect Raman scattering.[1)]

While TERS has been applied to the study of organic molecules and atomically thin films, it has not yet been used to investigate small molecules such as hydrogen, oxygen, and water. Recently, we reported on TERS of H_2 and D_2 molecules physisorbed within a plasmonic picocavity at 10 K.[2)] The intense Raman peaks resulting from the rotational and vibrational transitions are observed at picoscale gap distances of the junction formed by an Ag tip and an Ag(111) surface, where a picocavity-enhanced field plays a crucial role. A significant redshift of the H–H stretch frequency is observed as the gap distance decreases, while the D–D stretch frequency is unaffected. Density functional theory, path-integral molecular dynamics, and quantum anharmonic vibrational energy calculations suggest that this non-trivial isotope effect is explained by a different molecular density between H_2 and D_2 on the surface. The capability to measure such small molecules holds great promise as a method for probing local structures and reactions that are involved in the elementary processes of heterogeneous catalysis.

In addition, single-molecule TERS has generally been limited to measurements on plasmonic substrates such as Au, Ag, or Cu surfaces. Recently, we have demonstrated that single-molecule TERS measurements are also feasible on a bulk silicon surface.[3)] This represents an important step toward expanding the applicability of TERS-based chemical analysis to a broader range of material systems and holds promise as a method for investigating atomic-scale structures in nanodevices.

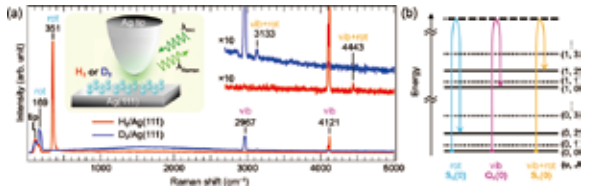

Figure 1. (a) TERS spectra of H_2 and D_2 confined within a picocavity. Raman peaks corresponding to rotational (rot), vibrational (vib), and combined vibrational–rotational (vib + rot) modes are clearly observed in each spectrum. (b) Schematic illustration of the rotational and vibrational energy level transitions of a hydrogen molecule, corresponding to the Raman peaks observed in (a).

2. Ultrafast Nano-Spectroscopy of Atomically-Confined Materials

Atomically confined materials, such as transition metal dichalcogenides (TMDs) and carbon nanotubes (CNTs), exhibit unique optoelectronic properties due to strong quantum confinement effects and are regarded as promising candidates for next-generation semiconductor materials. However, their properties are highly sensitive to local structures, such as defects, and interactions with the surrounding environment, owing to their extremely large surface-to-volume ratio. Recently, there has been growing interest in controlling their properties by stacking atomically thin layers to create moiré superlattices—nanoscale structural modulations that offer new degrees of freedom. These developments highlight the increasing importance of experimental techniques capable of simultaneously probing local structures and optical properties.

We have recently developed a highly sensitive ultrafast infrared SNOM, enabling real-time and real-space visualization of photoinduced dynamics in TMDs and CNTs.[4,5)] Figure 2 shows an example of photoexcited carrier dynamics in monolayer WS_2 grown by chemical vapor deposition (CVD) on a sapphire substrate. The near-field signal is stronger at the edges of the triangular domains, reflecting local variations in defect density within the WS_2. We also applied ultrafast nano-spectroscopy to directly observe exciton dynamics in CNTs grown on a sapphire substrate, capturing the generation and relaxation of electron–hole pairs confined within the one-dimensional structure at the nanoscale. These results demonstrate the capability of our technique to directly visualize spatial heterogeneity in ultrafast dynamics, arising from underlying local structures, which would otherwise be obscured in conventional, spatially averaged spectroscopic measurements. We are currently investigating ultrafast electron–phonon interactions in heterostructures composed of TMDs and hexagonal boron nitride, where ultrafast modulation of the photo-carrier and phonon polariton is observed.

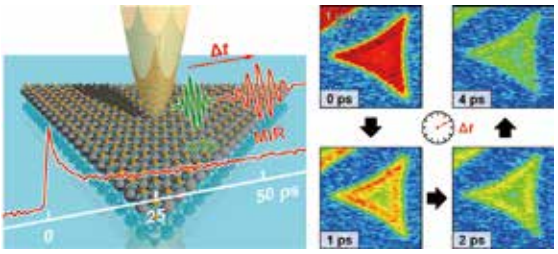

Figure 2. Ultrafast IR-SNOM imaging that visualizes spatially modulated photo-carrier dynamics within monolayer WS_2.

References

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2) A. Shiotari *et al.*, *Phys. Rev. Lett.* **134**, 206901 (2025).
3) B. Cirera *et al.*, *Phys. Chem. Chem. Phys.* **26**, 21325 (2024).
4) Y. Wang *et al.*, *ACS Photonics* **12**, 207 (2024).
5) J. Nishida *et al.*, *Sci. Adv.* **11**, eadv9584 (2025).

* IMS International Internship Program

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RESEARCH ACTIVITIES
Division of Advanced Molecular Science

The division consists of two sections. In the first one, scientists of the first water are invited as "distinguished professors," and the environment, in which they can devote themselves to their own research, is provided. The research in this section should be the last word in the field of molecular science.

In the second section, we invite researchers in the universities performing unique researches in the field of molecular science as cross-appointment faculty members, and provide the research environment to enable research activity with advanced facilities in IMS.

Second-Generation Crystalline Sponges: Structural Analysis of Medium-Sized Pharmaceutical Compounds

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1997 Associate Professor, Institute for Molecular Science
1999 Professor, Nagoya University
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2018 Distinguished Professor, Institute for Molecular Science
2019 Distinguished Professor, The University of Tokyo

Awards
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2000 Division Award of Chemical Society of Japan (Organic Chemistry)
2001 Tokyo Techno Forum 21 Gold Medal
2001 Japan IBM Award
2003 Nagoya Silver Medal
2004 Izatt-Christensen Award
2006 G. W. Wheland Award (Chicago University Lectureship Award)
2010 The Reona Esaki Award
2010 The JSCC Award
2011 3M Lectureship Award (University of British Columbia)
2012 Thomson Reuters Research Front Award 2012
2013 The Chemical Society of Japan (CSJ) Award
2013 Arthur C. Cope Scholar Award (ACS National Award)
2013 Merck-Karl Pfister Visiting Professorship (MIT Lectureship Award)
2014 ISNSCE 2014 Nanoprize
2014 Medal with Purple Ribbon
2014 Fred Basolo Medal (Northwestern University)
2018 Wolf Prize in Chemistry
2019 The Imperial Prize and the Japan Academy Prize
2020 The 73rd Chunichi Cultural Award
2020 Clarivate Citation Laureates (Chemistry)
2020 "Major Results" of Nanotechnology Platform, MEXT
2022 Le Grand Prix 2022 de la Fondation de la Maison de la Chimie
2023 Asahi Prize2023
2023 2022 Natta Award (Politecnico di Milano)
2024 Van't Hoff Award
2025 International Honorary Member of American Academy of Arts & Sciences

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Post-Doctoral Fellow
HE, Wei
Secretary
MASUDA, Michiko
NOGAWA, Kyoko

Keywords Self-Assembly, Nano-Space, Coordination Cages

The crystalline sponge (CS) method is a novel technique for X-ray diffraction analysis, in which a porous crystal absorbs and aligns target molecules, thereby eliminating the need for crystallization of the analyte. However, this approach faces significant challenges when analyzing large or highly polar molecules. We are developing a second-generation CS (2G-CS) method that employs coordination cages as CS, leveraging their exceptional guest-binding capability to overcome these limitations. This breakthrough method greatly expands the range of analyzable compounds, now including water-soluble molecules and large amphiphilic pharmaceutical compounds (MW > 1000). We anticipate this method will become a definitive technique for molecular structure determination in both academia and industry.

Selected Publications

- Y. Inokuma, S. Yoshioka, J. Ariyoshi, T. Arai, Y. Hitora, K. Takada, S. Matsunaga, K. Rissanen and M. Fujita, "X-Ray Analysis on the Nanogram to Microgram Scale Using Porous Complexes," *Nature* **495**, 461–466 (2013).
- M. Fujita, D. Oguro, M. Miyazawa, H. Oka, K. Yamaguchi and K. Ogura, "Self-Assembly of Ten Molecules into Nanometre-Sized Organic Host Frameworks," *Nature* **378**, 469–471 (1995).

1. Supramolecular Coordination Cages as Crystalline Sponges through a Symmetry Mismatch Strategy[1)]

The self-assembled octahedral M_6L_4 coordination cage **1** exhibits exceptional guest-binding abilities in solution. In the past thirty years, the rich host–guest chemistry of its host–guest complexes was thoroughly investigated and frequently elucidated through crystallographic studies. Motivated by these results, we aimed to convert this cage into a crystalline material that can enhance the current CS method.

Introducing large aromatic "sticker" anions **2** into the cage solution leads to the formation of high-quality crystals, driven by electrostatic interactions between the positively charged cage and the negatively charged anions. The symmetry mismatch between the T_d-symmetric cage and the D_{2h}-symmetric anions resulted in the production of crystals in a low-symmetry space group (P-1), preventing the disorder of guest molecules and leading to the formation of guest-accessible channels in the crystal.

This cage-immobilized crystals were examined for the CS method to determine the structure of guest molecules. Guest molecules can be introduced to the crystal either before or after the cage crystallization. Owing to the versatile molecular recognition with cage, analytes with molecular weights ranging from 200 to 1200 can be captured by the cage thus enabling their structural determination *via* X-ray diffraction analysis. Notably, various large amphiphilic molecules **3**–**6** with significant pharmaceutical interest were examined and successfully determined the molecular structures.

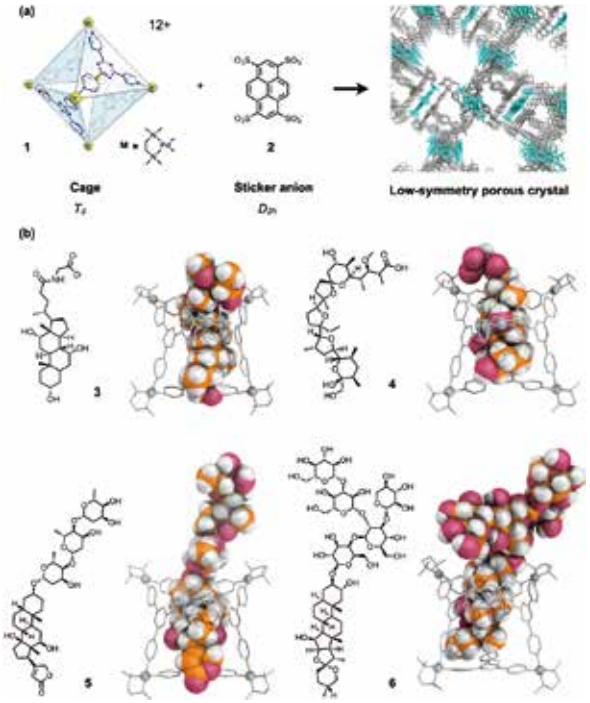

Figure 1. Coordination cages as crystalline sponges for structural analysis of medium-sized pharmaceutical compounds. (a) Symmetry-mismatched pair used for crystallization. (b) Crystal structures of amphiphilic molecules **3**–**6** encapsulated in cage-based crystals.

2. Host–Guest Chemistry in a Capillary Applied to the Facilitation of the Crystalline Sponge Method[2)]

Although conceptually elegant, the traditional CS method requires delicate handling and high experimental skill, limiting its broader applicability. Major challenges include handling trace amounts of analyte and simplifying the workflow.

We addressed these by employing glass capillaries—a convenient tool for transferring, mixing, and storing microvolumes of liquid. Our optimized protocol involves simply dipping the capillary into a series of bench-stable standard solutions. This process yields sponge crystals encapsulating the target molecule. The resulting in-capillary crystals are comparable in quality to those grown in flasks and can be directly analyzed within the capillary using standard laboratory X-ray diffractometers.

This miniaturized approach reduces the required sample amount from milligrams to micrograms and shortens the analysis time from weeks to days. As a result, the CS method is transformed from a specialized technique into a simple, broadly applicable tool suitable for any chemical laboratory, enabling on-site molecular detection and promoting broader adoption in both academia and industry.

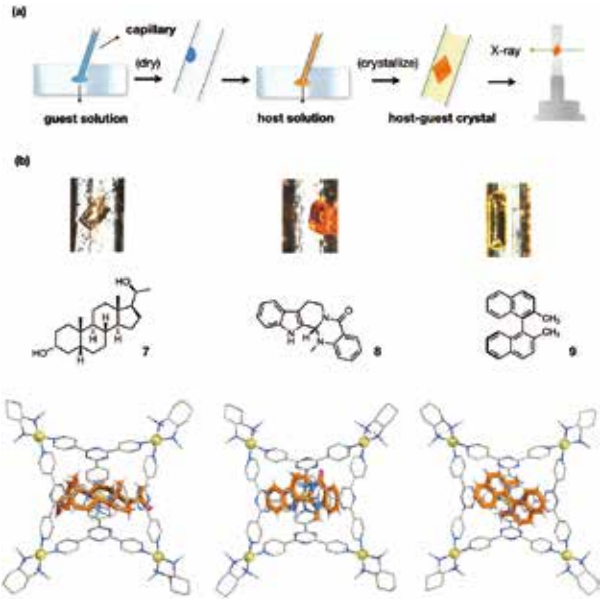

Figure 2. Highly practical CS analysis using glass capillaries. (a) Schematic illustration of the in-capillary workflow. (b) Photographs of guest-encapsulated crystals in capillaries, chemical structures, and X-ray structures of molecules **7**–**9**.

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Exploring Novel Physical Properties by Multi-Dimensional Spectroscopy

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Physical and chemical properties of solids, such as conductivity, magnetism, superconductivity, and chemical reactions, originate from microscopic electronic structure, lattice/molecular vibrations, and molecular movements based on quantum mechanics in materials and their interactions. By revealing the microscopic states and their evolution, we can learn about the origin of physical and chemical properties and hidden functionalities. Also, the microscopic information is helpful for the creation of novel functional properties. To visualize hidden microscopic information, we develop novel spectroscopic techniques using synchrotron radiation, high brilliant electron beams, and other so-called quantum beams. We have started a novel electron spectroscopy technique, Spin-Resolved resonant Electron-Energy-Loss Spectroscopy (SR-rEELS), with bulk-sensitive primary energies of 0.3–1.5 keV. At present, we combine it with a time- and angle-resolved technique, shown in Figure 1, to simultaneously observe both the changing electronic structure and collective excitations and the lattice and magnetic structure relaxation. Based on the obtained information on electronic structures, we aim to develop novel physical properties of new materials.

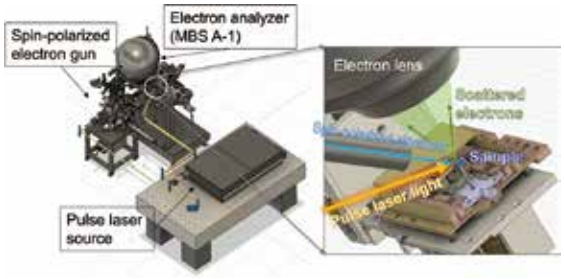

Figure 1. Time-, Spin-, and Angle-Resolved resonant Electron-Energy-Loss Spectroscopy (tSAR-rEELS) apparatus, which our group is now developing. The apparatus comprises a high-brilliant spin-polarized electron gun, a photoelectron spectrometer, and a femtosecond pulse laser with an optical parametric amplifier.

Selected Publications

- T. Nakamura, H. Sugihara, Y. Chen, R. Yukawa, Y. Ohtsubo, K. Tanaka, M. Kitamura, H. Kumigashira and S. Kimura, "Two-Dimensional Heavy Fermion in Monoatomic-Layer Kondo Lattice $YbCu_2$," *Nat. Commun.* **14**, 7850 (7 pages) (2023).
- Y. Ohtsubo, T. Nakaya, T. Nakamura, P. Le Fèrve, F. Bertran, F. Iga and S. Kimura, "Breakdown of Bulk-Projected Isotropy in Surface Electronic States of Topological Kondo Insulator $SmB_6(001)$," *Nat. Commun.* **13**, 5600 (7 pages) (2022).
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- K. Hagiwara, Y. Ohtsubo, M. Matsunami, S. Ideta, K. Tanaka, H. Miyazaki, J. E. Rault, P. Le Fèvre, F. Bertran, A. Taleb-Ibrahimi, R. Yukawa, M. Kobayashi, K. Horiba, H. Kumigashira, K. Sumida, T. Okuda, F. Iga and S. Kimura, "Surface Kondo Effect and Non-Trivial Metallic State of the Kondo Insulator YbB_{12}," *Nat. Commun.* **7**, 12690 (7 pages) (2016).

1. Current- and Photo-Induced Phase Transition on Black Samarium Monosulfide[1,2)]

A strongly correlated insulator, samarium mono-sulfide (SmS), is well-known to present a pressure-induced insulator-to-metal transition (IMT) with the color change from black to golden-yellow. Recently, it has also shown current-induced IMT (CIMT) with negative resistance. To clarify the origin of the CIMT of SmS and also the relation to the pressure-induced IMT, the electronic structure change has been investigated by optical reflectivity and angle-integrated photoelectron spectra by applying an electric current. At lower temperatures than about 100 K, where the nonlinear *V–I* curve has been observed, the carrier density rapidly increases, accompanied by decreasing relaxation time of carriers with increasing current. Then, the direct gap size increases, and the mean valence changes from Sm^{2+}-dominant SmS to the mixed-valent one with increasing current. These results suggest that the CIMT originates from increasing the Sm 4*f*–5*d* hybridization intensity induced by the applied current.

One scenario for the pressure-induced IMT of SmS is exciton condensations with decreasing energy gap by pressure. To investigate the role of the excitons, optical reflectivity, Sm 3*d* x-ray absorption spectroscopy (XAS), and x-ray diffraction (XRD) with the creation of excitons by photoexcitation (PE) are reported. In the pump–probe reflectivity measurement, following a huge reflectivity change of about 22%, three different relaxation times with a vibration component were observed. The fast component with the relaxation time (τ) of less than 1 ps is due to the excitation and relaxation of electrons into the conduction band, and the slowest one with $\tau >$ several 100 ps originates from the appearance of the photo-induced (PI) state. The components with $\tau \sim 10$ ps and vibration originate from the appearance of the PI state and the interference between the reflection lights at the sample surface and the boundary between the black-insulating and PI states, suggesting that the electronic structure of the PI phase is different from that of the black insulating state. XAS spectra indicate that the Sm mean valence is shifted from the Sm^{2+} dominant to the intermediate between Sm^{2+} and Sm^{3+} by PE, but did not change to that of the golden metallic phase across the IMT, consistent with the reflectivity data. The XRD result after PE shows that the PI state has much less lattice contraction than the golden metallic phase. These results suggest that the IMT cannot be achieved solely by creating excitons after PE but requires other effects, such as a lattice contraction. The photo-induced phase transition and the golden metallic phase are schematically explained in Figure 2.

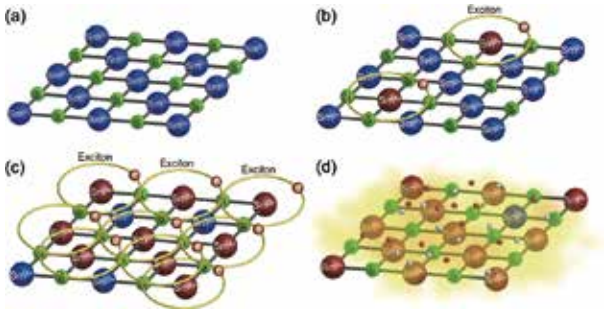

Figure 2. Schematic figure of the photo-induced phase transition along the excitonic instability picture. (a) The black insulating phase. (b) After the photoexcitation (PE) by several pulses irradiated to the sample, 4*f* electrons are excited and become excitons. The created excitons are isolated and localized at the original sites. The electronic structure and optical constants are slightly changed, but the lattice constant is identical before the PE. (c) After many laser pulses PE with a pile-up effect, many excitons are created but still isolated. The valence transition becomes visible by XAS because of many Sm^{3+} states. (d) The golden metallic phase, where excitons are condensed, and the state becomes metallic.

2. Light-Field-Driven Non-Ohmic Current Generation by an Intense THz Pulse in a Weyl Semimetal[3)]

In recent years, coherent electrons driven by light fields have attracted significant interest in exploring novel material phases and functionalities. However, observing coherent light-field-driven electron dynamics in solids is challenging because the electrons are scattered within several tens of femtoseconds in ordinary materials, and the coherence between light and electrons is disturbed. This study presents the light-field-driven dynamics by applying a THz pulse (~1 ps) to the Weyl semimetal $Co_3Sn_2S_2$, which has a relatively long coherent time to pico-seconds. As the electric-field intensity of the irradiating THz pulse was increased, the reflected/emitted THz wave changed from being similar to the incident THz wave to an asymmetric electric field. This asymmetric electric field emission suggests the generation of non-Ohmic direct current *via* coherent acceleration, and the fact that its intensity dependence is proportional to the square of the electric field suggests electronic excitation by the Landau–Zener transition, a characteristic of the light-field picture.

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Operando Molecular Science in Liquid–Solid Interfaces of Finite Thickness

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Keywords Reactions at Interfaces, Catalysis, Energy-Related Chemistry

We are proud of our internationally compatible studies of liquid–solid interfaces; photocatalysts for artificial photosynthesis, lubricants for smooth tribology, and ice in antifreeze liquids. Characterization with advanced AFM, time-resolved ATR-IR spectroscopy, soft X-ray absorption and microelectrode-based amperometry are being developed. We look forward to collaborating with researchers in academic and industrial organizations to unravel the science behind material conversion and energy dissipation at liquid–solid interfaces.

A new era of molecular science will be revealed at liquid–solid interfaces of finite thickness (Figure 1). The molecular interface is the site of reaction where molecules of interest collide or interact with other molecules. We need to observe individual molecules there. On the other hand, the molecular interface is connected to the liquid and solid. Materials and energy come from/to the two condensed phases, since functional interfaces are always open to the environment. Operando characterization is absolutely necessary to study the interface in its working state.

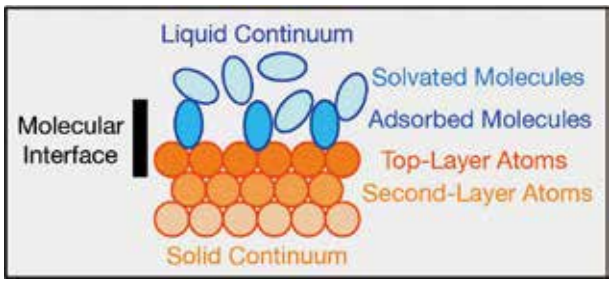

Figure 1. Liquid–Solid Interface of Finite Thickness.

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- Y.-H. Chew, N. Saijo, Y. Kumabe, T. Tachikawa and H. Onishi, "Unravelling the Influence of Major Seawater Salt Ions on the Photogenerated Charge Carriers in a Sr-Doped $NaTaO_3$ Photocatalyst *via* ATR-FTIR," *J. Phys. Chem. C* **129**, 3531–3538 (2025).
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1. Atomic Force Microscopy (AFM) in Sub-Zero Antifreeze Liquid

Ice in nature is surrounded by liquid most of the time, and therefore it is key to understand how ice and liquid interact. Atomic force microscopy is widely used for topographic imaging and force sensing at liquid–solid interfaces. Operation in antifreeze liquids has been examined at temperatures below the freezing point of water, although most AFM research in liquid is conducted in water at room temperatures. In our recent study,[1] the topographic imaging in the amplitude-modulation mode and force curves in the contact mode were examined on ice films under antifreeze liquid, using a Dimension XR Icon Nano Electrochemical microscope (Bruker).

In the present study,[2] a Shimadzu microscope (SPM-8100FM) capable of imaging and force spectroscopy in the frequency-modulation mode was utilized for probing graphite in 1-octanol ($C_8H_{17}OH$) liquid at temperatures as low as −15 °C. The topography of octanol molecules adsorbed on graphite was resolved, and octanol molecules in the liquid phase exhibited flat layers over graphite as evidenced in force spectroscopy. These results underlined the viability of frequency-modulation atomic force microscopy (FM-AFM) in sub-zero temperature liquids.

The resonance oscillation of the cantilever was mechanically excited with a piezo-actuator. In octanol liquid at RT, the resonant frequency of the cantilevers (f_0) was 100–140 kHz, with the quality factor of resonance ranging from 2 to 4. The oscillation amplitude was regulated at a preset amplitude in topographic imaging. When a conservative force was applied to the tip, the resonance frequency of the cantilever oscillation shifted accordingly. The topography of the object was traced by regulating the frequency shift (Δf) at a predefined setpoint. Figure 2 illustrates the topographic images observed at 27 and −11 °C.

In the images, linear stripes were recognized with trenches between the stripes. The edges of the stripes were presented brighter than the middle. This appearance is consistent to what proposed in earlier studies; the alcohol molecules are paired *via* hydrogen bonding when adsorbed on graphite, and the paired molecules exhibit stripes that are epitaxial to the graphite lattice.

To visualize the local density distribution of octanol liquid, the resonantly oscillating cantilever was scanned vertically from the bulk octanol to the graphite surface. During one such vertical scan, the frequency shift was recorded as a function of vertical coordinate, thereby obtaining one Δf–distance curve. Upon reaching a predetermined Δf threshold, signifying tip-to-solid contact, the cantilever was retracted into octanol by 4–5 nm. Subsequent to this retraction, the cantilever was shifted in the horizontal direction, and an additional vertical scan was conducted. A total of 1024 vertical scans were systematically acquired to construct a Δf map on a plane perpendicular to the graphite surface.

Figure 3 shows two Δf maps observed at 27 °C and −6 °C. The maps are associated with the distribution of the octanol-induced force on the AFM tip apex. Bright color in the Δf maps represent positive frequency shift. The brightest region at the bottom of each map represents the boundary between the liquid and solid. The repulsive force on the tip exhibited a rapid increase when the tip penetrated deeper into this region, signifying tip-to-solid contact. Hence, the envelope of the brightest region delineates the topography of the physisorbed octanol monolayer on graphite.

The frequency shift exhibited an uneven distribution in the proximity of the surface. Alternating dark and bright layers appeared in the maps, suggesting that the surface was covered by five or six liquid octanol layers. The vertical distance between the layers was 0.5 and 0.6 nm at 27 °C and −6 °C, respectively. The octanol liquid layers were suggested to be separated by this distance. The liquid-induced force pushing or pulling the tip apex is contingent on the local liquid density, though force–density relation is not straightforward. Subsequent examination of continuous scanning within a temperature range of −14 °C to 30 °C revealed no substantial structural variation, despite the lowest temperature was close to the freezing point of octanol.

Part of this research was supported by the Advanced Materials Research Infrastructure Project of the Ministry of Education, Culture, Sports, Science and Technology of Japan (JPMXP1224MS0005) and conducted at the Institute for Molecular Science, National Institutes of Natural Sciences. Financial support by JSPS KAKENHI (grant number 23H05448) is acknowledged.

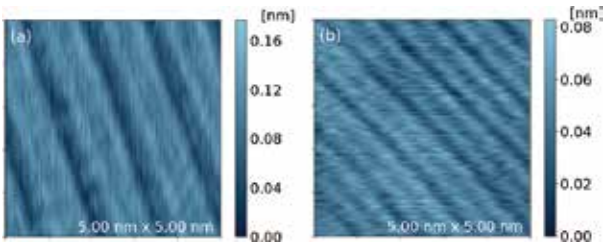

Figure 2. Topographic images of 1-octanol physisorbed on graphite captured at (a) 27 and (b) −11 °C.

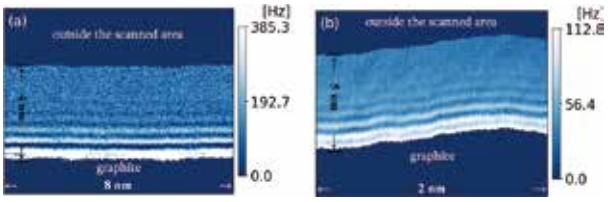

Figure 3. 1-Octanol liquid over a graphite wafer at (a) 27 and (b) −6 °C. The frequency-shift of the cantilever resonance oscillation (Δf) was mapped on a plane that was perpendicular to the wafer. A large (or small) positive frequency-shift is depicted using a bright (or dark) color.

References

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2) Z. Lu, R. Yanagisawa, S. Moriguchi, T. Ueda, K. Nakamoto, T. Minato and H. Onishi, *Jpn. J. Appl. Phys*. **64**, 05SP05 (2025).

Engineering of PET Hydrolase for Plastic Recycling and Environmental Remediation, and Engineering of Plastic Binding Domains for Detection and Quantification of Particles

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Keywords Solid–Liquid Interfacial Reaction, Protein-Engineering, Single-Molecule Observation

Plastic is an indispensable material in our daily lives. It is used in a wide variety of products because it is low-cost, mass-producible, and easy to mold and process. However, due to its convenience, the amounts of plastic used and disposed are increasing every year, raising concerns about its environmental impact and sustainability. Therefore, there is a need to develop efficient and environmentally friendly recycling methods, as well as simple and rapid methods to detect plastics that have leaked into the environment.

We are attempting to obtain more active mutants by exhaustively mutating amino acid residues on the enzyme surface and screening their activity using a dispensing robot. We are also attempting to create plastic adsorption domains by modifying the amino acids constituting the adsorption surface of the carbohydrate binding domain and using a phage display method.

These studies will promote the recycling of used plastics by enzymatic degradation and promote more sustainable use of plastics. In addition, by creating a protein that detects and stains plastics, we will contribute to the protection of the natural environment by monitoring the small plastics runoff into the environment (Figure 1).

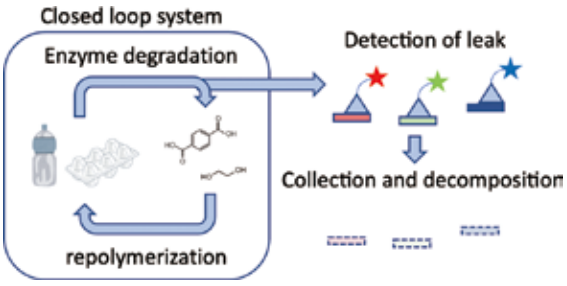

Figure 1. Scheme of plastic recycling and detection system.

Selected Publications

- T. Matsuzaki, T. Saeki, F. Yamazaki, N. Koyama, T. Okubo, D. Hombe, Y. Ogura, Y. Hashino, R. Tatsumi-Koga, N. Koga, R. Iino and A. Nakamura, "Development and Production of Moderate-Thermophilic PET Hydrolase for PET Bottle and Fiber Recycling," *ACS Sustainable Chem. Eng.* **13**, 10404–10417 (2025).
- Y. Ogura, Y. Hashino and A. Nakamura, "Direct Screening of PET Hydrolase Activity in Culture Medium Based on Turbidity Reduction," *ACS Omega* **9**, 34151–34160 (2024).
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- A. Nakamura, K. Okazaki, T. Furuta, M. Sakurai and R. Iino, "Processive Chitinase Is Brownian Monorail Operated by Fast Catalysis after Peeling Rail from Crystalline Chitin," *Nat. Commun.* **9**, 3814 (2018).

1. Development and Production of Moderate-Thermophilic PET Hydrolase for PET Bottle and Fiber Recycling

We developed a highly efficient PET hydrolase variant, PET2-21M, that functions under moderate temperature conditions and enables practical enzymatic recycling of PET bottles and blended fibers.[1)] PET recycling is an urgent challenge, since mechanical methods usually yield downgraded materials and chemical recycling requires harsh reagents and conditions. Enzymatic approaches offer a sustainable alternative, but natural PET hydrolases typically show low activity at moderate temperatures, limiting their industrial applicability. We aimed to engineer a robust enzyme with high catalytic efficiency, thermostability, and broad substrate scope.

We started from our previously optimized variant, PET2-7M, and introduced additional beneficial mutations using random mutagenesis, rational design, and structural insights. We identified seven novel mutations that enhanced activity, and we further modified surface charges to improve PET binding. Inspired by structural features of HotPETase, we redesigned the substrate-binding cleft. By combining these improvements, we created PET2-14M-6Hot, and then advanced it to PET2-21M with 21 total mutations. These changes substantially increased enzyme activity and maintained stability around 60 °C, in contrast to many existing hydrolases that require higher temperatures.

We demonstrated significant performance gains with PET2-21M. Compared to the original PET2, our variant produced about 30 times more soluble degradation products. At 60 °C, in the presence of 20 g/L PET powder, PET2-21M depolymerized 95% of the substrate within 24 hours, surpassing LCC-ICCG, which required 72 °C to reach a comparable result. Even with reduced enzyme loading, PET2-21M remained highly efficient: at 2.5 mg/L, it maintained nearly half of its maximum activity, about twice that of LCC-ICCG under the same conditions. At 40 g/L PET, we achieved almost 80% conversion with 10 mg/L enzyme, and 44% with 5 mg/L, both outperforming the benchmark.

We also validated our variants on PET fibers and blended textiles. PET2-14M-6Hot produced 75.7 mM degradation products from pure PET fibers at 60 °C, exceeding the 70 °C performance of LCC-ICCG. For PET/cotton blends, we measured 62.8 mM compared to 46.7 mM for the comparator. For PET/PU blends at 50 °C, our enzyme generated 19.2 mM, more than double the 8.2 mM obtained with LCC-ICCG. These findings show that our engineered enzymes are effective not only for bottles but also for complex textile waste streams.

To ensure industrial scalability, we expressed our variants in the yeast *Komagataella phaffii*. We obtained high yields, with PET2-14M-6Hot reaching nearly 700 mg/L secretion. We also observed limited glycosylation, simplifying purification and downstream processing. These results confirm that our engineered enzymes can be produced in large amounts in microbial hosts suitable for industrial application.

In summary, we achieved a major advance in enzymatic PET recycling by creating PET hydrolases that combine high activity at moderate conditions with effectiveness on bottles and blended fibers. Our enzymes reduce energy demands, increase efficiency, and can be manufactured at scale. We believe this work provides a strong foundation for future development of cost-effective, environmentally friendly plastic recycling systems that align with circular economy goals.

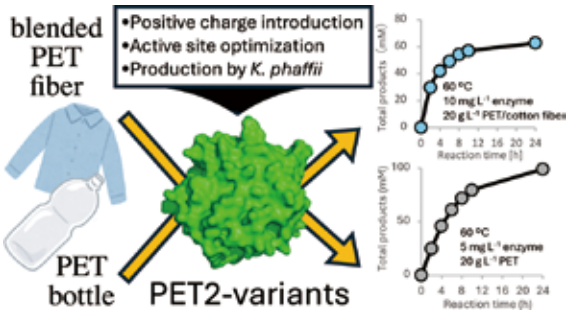

Figure 2. Scheme of PET fiber degrading enzyme development.

2. Artificial Evolution of Carbohydrate Binding Domain to PET Binding Domain

To develop a method for detection of plastics using plastic binding proteins, we developed PET binding protein using saturation mutagenesis and M13 phage display. We have already developed 2 generations of mutants which reduced the binding affinity to chitin and cellulose. Thus, we also checked the binding properties of the mutants against PET powder.

The binding affinities of six 2nd generation mutants (LWL to WVF) and one 1st generation mutant (4M) were compared with that of the template protein from *Pyrococcus furiosus* (WT). LWL showed 2.5 times higher binding amount (0.10 nmol) and similar dissociation constant (3.1 mg/mL) than WT (0.041 nmol and 3.2 mg/mL). We started to determine the binding and dissociation rate constants of LWL mutant and WT by single molecule observation for revealing the improved parameter of LWL mutant.

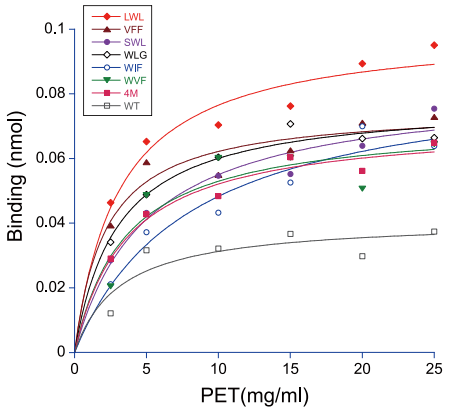

Figure 3. Binding measurement of 2nd generation of mutants against PET powder.

Reference

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Molecular Science of Bio-Metal Dynamics: Understanding and Regulation of Metals in the Cells

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Keywords Cellular Iron Dynamics via Protein Interactions, Live Cell Imaging for Trace Metals by Soft X-Ray

Metals play important roles in sustaining life. Cells are mainly composed of water, proteins, and lipids, but they also contain small amounts of metals that help maintain health by being acquired from food. Those metals have been known for many years to be used as active centers of enzymes that carry out functions essential to sustaining life, *e.g.* transport and storage of oxygen, energy production, gene synthesis. However, the series of molecular mechanisms underlying metal dynamics in the body (absorption, sensing, transport, storage, and excretion of metals) and selectivity for individual metals to maintain the metal homeostasis remain unknown (Figure 1). We focus on "iron," which is the most important metal among the essential metals for sustaining life of living things, and various proteins that play a role in the selective absorption, sensing, and intracellular transport of iron in food. We are not only elucidating the structure of related proteins but also exploring their relationship with their functions in human cells.

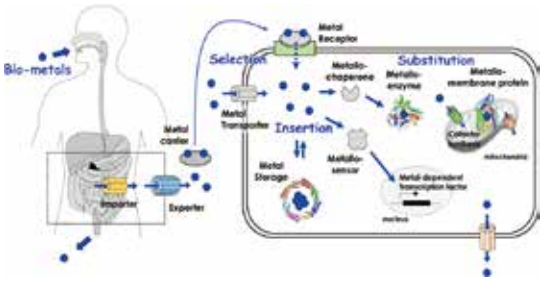

Figure 1. Our aim is to understand the uptake, trafficking, and regulation of "bio-metals" through the relay of protein–protein interactions.

Selected Publications

- M. Ganasen, H. Togashi, H. Takeda, H. Asakura, T. Tosha, K. Yamashita, K. Hirata, Y. Nariai, T. Urano, X. Yuan, I. Hamza, A. G. Mauk, Y. Shiro, H. Sugimoto and H. Sawai, "Structural Basis for Promotion of Duodenal Iron Absorption by Enteric Ferric Reductase with Ascorbate," *Commun. Biol.* **1**, 120 (2018). DOI: 10.1038/s42003-018-0121-8
- G. S. A. Wright, A. Saeki, T. Hikima, Y. Nishizono, T. Hisano, M. Kamaya, K. Nukina, H. Nishitani, H. Nakamura, M. Yamamoto, S. V. Antonyuk, S. Samar Hasnain, Y. Shiro and H. Sawai, "Architecture of the Complete Oxygen-Sensing FixL-FixJ Two-Component Signal Transduction System," *Sci. Signaling* **11**, eaaq0825 (2018). DOI: 10.1126/scisignal.aaq0825
- 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 the Hemolytic Bacterial Survival," *Commun. Biol.* **4**, 467 (2021). DOI: 10.1038/s42003-021-01987-5
- H. Sawai, "Molecular Science of Biological Iron: Dynamics and Regulation of Iron Ions and Heme Iron," *Artif. Blood* **33**, 55–63 (2025).

1. Development of Intracellular Fe Imaging in Living Cells Using Soft X-Ray Microscopy

The eminent physician of ancient Greece, Hippocrates, is reputed to have stated that "iron acts as a medicine," thereby underscoring the maintenance of metal homeostasis within the human body, as well as the pathological consequences arising from altered metal quantities and distributions, which remain enigmatic to this day. Therefore, the regulatory mechanisms of metals in the body and the factors of diseases related to altered metal concentrations are not yet fully understood. In response to these issues, our group, together with Dr. Iwayama's group at UVSOR, has started to develop new techniques to visualize metals in living cells by chemical species using soft X-rays from this year. Dr. Iwayama has developed the "contact-type soft X-ray microscope"[1] for biological samples. This technique allows the measurement of transmitted X-ray images of biological samples at the K- or L-edge energies of metal elements. Biological samples are placed on a Ce:YAG scintillator and covered with a Si_3N_4 membrane. The transmitted X-ray image is converted into a visible-light image by the scintillator and then captured by a CMOS camera. By changing the photon energies, we can obtain photon-energy dependence of transmitted images. From the Lambert-Beer's law, we can obtain a XANES spectrum for each pixel of the image. The experiment was performed on the beamline BL4B at UVSOR.

Our group is conducting research on iron in living organisms. Iron is an essential metal for all living organisms because of its unique chemical properties that control physiological functions essential for life.[2] Conversely, iron within cells is predominantly found in the reduced form of iron ions (Fe^{2+}). However, in a cellular environment where oxygen is present, excess iron can promote reactions that generate hydroxyl radicals, the most potent reactive oxygen species. Oxidized iron ions (Fe^{3+}) have extremely low water solubility and low toxicity.[3] However, in a reducing intracellular environment, they are easily converted to Fe^{2+}, indicating that the accumulation of Fe^{3+} can also be a factor in non-alcoholic steatohepatitis, multi-organ dysfunction due to iron overload (hereditary hemochromatosis) and neurodegenerative diseases. Therefore, the technique that can distinguish between Fe^{2+} and Fe^{3+} in living cells and tissues and simultaneously observe their distribution and local concentrations would be useful, but such technology has not yet been developed. First, we tried to observe intracellular iron levels in MDCK cells. However, due to the low iron concentration, we were unable to obtain soft X-ray transmission images with sufficient intensity for analysis. Therefore, in this study, we attempted iron imaging using red blood cells, which have the highest iron content in the body, as a model cell. We succeeded in observing the localized distribution of Fe^{2+} and Fe^{3+} in red blood cells isolated from preserved bovine blood (Figure 2). Moving forward, we will develop a comprehensive library of XANES spectra of hemoglobin to visualize the distribution of iron in hemoglobin based on their states, such as oxygen-bound or met form. We will also conduct similar iron imaging studies in cells with high iron content, such as liver cells.

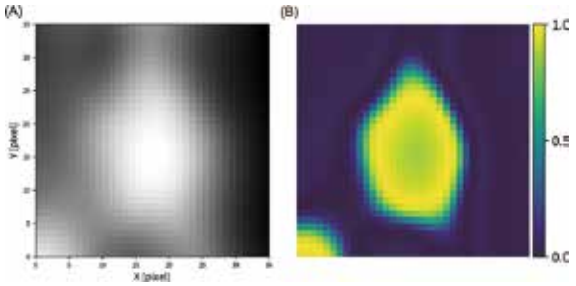

Figure 2. Fe imaging results of a single red blood cell from bovine blood. (A) XANES image of the cell detected at 700 eV. (B) Maps of spectral features calculated from the XANES spectra at each pixel position. This map shows that the Fe^{2+} species are located in the yellowish area.

In addition to developing this new technology, our group has been engaged in research for a few years on the interactions of proteins involved in the absorption, concentration sensing, transport, and storage of iron in cells. We also investigated the maturation process of iron-binding proteins using intracellular iron delivery chaperones.[4] This year, we initiated research endeavors aimed at identifying novel genes (proteins) that are influenced by fluctuations in intracellular metal levels. This objective will be achieved by CRISPR screening in cases where intracellular metal levels are high.

Our research has begun to focus on establishing a framework for the future, in which diseases stemming from disruptions in metal homeostasis can be identified at an early stage. This objective will be pursued by leveraging the application of soft X-ray spectroscopy, a technique employed in materials science, to develop novel methodologies within the realm of life sciences (Figure 3).

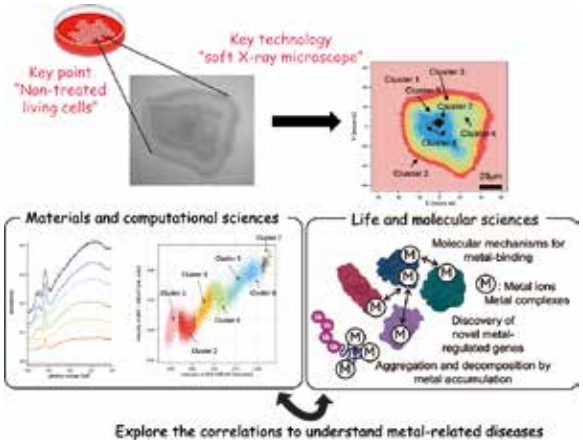

Figure 3. Concept diagram of this study.

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3) H. Sawai, *Artif. Blood* **33**, 55–63 (2025).
4) H. Sawai *et al.*, *Iron in Biology: Molecular Structures, Cellular Processes and Living Systems*, Royal Society of Chemistry, 75–88 (2025).

Integration of Quantum Chemistry and Machine Learning for a Deeper Understanding and Rational Design of Functional Materials

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2020 Associate Professor, Keio University
2024 Associate Professor (Cross Appointment), Institute for Molecular Science
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Awards
2017 11th PCCP Prize
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2021 The Chemical Society of Japan Award for Outstanding Young Women Chemists for 2021
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Keywords Materials Informatics, Lanthanide, Computational Chemistry

We develop computational methods, apply them to elucidate mechanisms, and design materials using data science techniques such as machine learning (ML). Currently, our research focuses on the following subjects:

(1) Lanthanide Photofunctional Materials

Lanthanide (Ln) luminescence, originating from 4f–4f transitions, has been applied in various optical materials. While the 4f–4f emission wavelengths of Ln complexes are almost independent of the surroundings, the emission intensities are heavily influenced, making the design of appropriate ligand crucial. To get deeper insights into Ln luminescence, we proposed the energy shift method, which has contributed to the understanding and design of various Ln materials and has also been applied to non-Ln systems. However, it could not handle 4f–5d and charge transfer excited states, which are particularly important for cerium and europium complexes. To address this limitation, we are developing an updated method. In addition, we have constructed a database of cerium complexes containing 1.7k geometries and electronic properties. We plan to make this database public and further develop it into a platform for optical function prediction *via* ML.

(2) Transition Metal Catalysts

Transition metal (TM) complexes play a crucial role in organic synthesis, catalyzing a wide variety of chemical reactions. The catalytic abilities of TM complexes can be finely tuned by manipulating ligand-induced electronic and steric effects, which are key to controlling the reactivity and selectivity of specific reactions. In recent years, however, chemical products are being produced in smaller quantities and with greater variety, reducing the time available to study the synthesis conditions for each product. To address this challenge, we are constructing a database of TM complexes with various organophosphorus ligands, ranging from monodentate to multidentate skeletons. For descriptors applicable to different skeletons, we propose using the reaction energies of elementary reactions, such as oxidative addition and transmetallation. Our goal is to accelerate catalyst design by developing an ML model where our descriptors serve as explanatory variables and experimental catalytic activity results are used as objective variables.

Selected Publications

- S. Gocho, H. Nakamura, Q. Gao, T. Kobayashi, T. Inagaki and *M. Hatanaka, "Excited State Calculations Using Variational Quantum Eigensolver with Spin-Restricted Ansätze and Automatically-Adjusted Constraints," *npj Comput. Mater.* **9**, 13 (2023).
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- *M. Hatanaka, Y. Hirai, Y. Kitagawa, T. Nakanishi, *Y. Hasegawa and *K. Morokuma, "Organic Linkers Control the Thermosensitivity of the Emission Intensities from Tb(III) and Eu(III) in a Chameleon Polymer," *Chem. Sci.* **8**, 423 (2017).

1. Ion Energy Shift (IES) Method for Exploring the Reaction Coordinate of Nonradiative Decay from Highly Excited State of Lanthanide Complexes

The exploration of minimum energy crossing points (MEXs) between potential energy surfaces (PESs) is essential for deepening our understanding of nonradiative decay mechanisms and plays a key role in the design of photofunctional materials. However, in lanthanide (Ln^{3+}) complexes, the presence of open-shell 4f electrons leads to quasi-degenerate electronic states, making MEX searches particularly challenging. To address this, the energy shift (ES) method has been used, in which the PES of a 4f–4f excited state is approximated by vertically shifting the ground-state PES by the corresponding 4f–4f excitation energy. This approach eliminates the need for explicit treatment of $4f^N$ electrons, enabling the use of large-core relativistic effective core potential (RECP) and conventional DFT methods to compute relevant states and locate key MEXs. While the ES method has greatly contributed to understanding and designing materials based on 4f–4f luminescence, it cannot be applied to 4f–5d or charge-transfer excited states (*i.e.*, $4f^{N-1}X$ states). To overcome this limitation, we proposed a new approximation, the ion energy shift (IES) method, which described the $4f^{N-1}X$ excited state using the large-core RECP for Ln^{4+} and shifted its PES to match the target excitation energy. The validity of the IES method was demonstrated by comparing its results with those of the multistate second-order perturbation theory (MSCASPT2). We applied it to elucidate the origin of the different excited-state lifetimes of hydrated Ce^{3+} complexes with and without coordination of a carboxylate ligand.

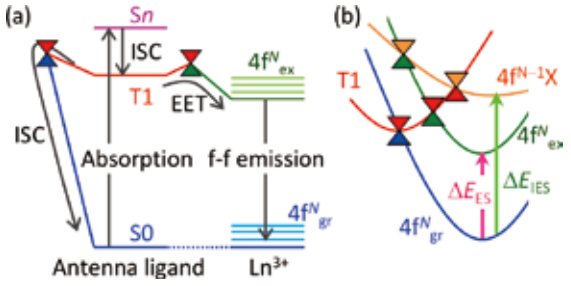

Figure 1. The Jablonski diagram of Ln^{3+} complex (a) and Schematic illustration of the ES and IES methods (b). The PES of the $4f^N$ excited states is described by shifting that of the ground state with the energy shift value of ΔE_{ES}. The PES of the $4f^{N-1}X$ excited state, in which $4f^{N-1}$ electrons were included in the large-core RECP for Ln^{4+}, is shifted to reproduce its excitation energy (ΔE_{IES}).

2. Database of Cerium Complexes for Excited State Analysis and Data-Driven Ligand Design

Since the early 2010s, the concept of data-driven materials discovery, commonly referred to as materials informatics, has gained significant traction. In response, a variety of databases compiling quantum mechanical (QM) calculations of materials have been developed. Large-scale QM datasets for molecules have also been constructed; however, due to the extreme diversity of chemical space, the field remains in a developing stage with respect to data diversity and extensibility. In particular, Ln complexes, which have broad industrial applications, pose challenges for establishing design guidelines because of their distinct structures, bonding characteristics, and physical properties. There is thus an urgent need for a database that captures the structural and electronic diversity of Ln complexes. To address this, we constructed a database of experimentally reported Ln complexes, including their optimized geometries and ground- and excited-state properties computed using DFT and TDDFT methods. In this initial study, we focus on Ce^{3+} complexes, which have recently attracted attention as photocatalysts. We collected 1635 Ce^{3+} complexes from the Cambridge Structural Database and identified key substructures that enhance excitation energy and oscillator strength by building machine learning models.

3. Mechanistic Study of C-Glycosylation Catalyzed by GgCGT Enzyme

C-glycosyltransferases have garnered attention owing to their ability to synthesize C-glycosides with high conversion and selectivity in one-pot reactions. Their potential in rational enzyme engineering makes them valuable for the synthesis of diverse C-glycosides. However, the detailed reaction mechanism remains unclear. To address this, we investigated the C-glycosylation of a polyphenol (phloretin) catalyzed by the glycosyltransferase GgCGT in the presence of the coenzyme UDP-glucose. Using the DFT calculations on a cluster model, we identified the most favorable pathway for C-glycosylation. The reaction proceeds *via* an initial proton transfer from phloretin to UDP-glucose, followed by the nucleophilic attack of phloretin on the glucose moiety and subsequent dissociation of UDP in an S_N2-like manner. The S_N2 step yields non-aromatic intermediate, which can be rapidly converted to C-glycoside even without an enzymatic environment. The key residue that facilitates the rate-determining S_N2 step is His-27, which stabilizes phloretin *via* hydrogen bonding. Additionally, to clarify why alternative products such as O-glycosides are not formed, we also investigated the O-glycosylation pathway. Our calculations revealed that O-glycosylation was promoted by proton transfer from UDP-glucose, like C-glycosylation, but was suppressed by structural fixation due to hydrogen bonding among phloretin, glucose, and GgCGT.

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RESEARCH ACTIVITIES
Division of Research Innovation and Collaboration

As the open innovation hub managed by IMS and companies, we conduct the research projects in collaboration with Academia, Industry and Government.

Micro Solid-State Photonics

Division of Research Innovation and Collaboration

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2019 Project Professor, Institute for Molecular Science
2023 Invited Professor, National Institute for Fusion Science
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Awards
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Keywords Solid-State Lasers, Nonlinear Optics, Micro Solid-State Photonics

"Micro Solid-State Photonics" based on the micro domain structure and boundary controlled materials, opens new horizon in the laser science. With the engineered materials of micro ceramic and single-crystal, solid-state lasers can provide excellent spatial mode quality and narrow linewidths with enough power. High-brightness nature of these lasers has allowed efficient wavelength extension by nonlinear frequency conversion: The world first laser-ignited car, high efficiency broad frequency conversions from the wavelength of 118nm VUV to 300μm–1mm THz waves, and so on. In addition, the quasi-phase matching (QPM) is an attractive technique for compensating phase velocity dispersion in frequency conversion. Lately, we propose a new architecture to realize a monolithic multi-disk laser by the surface activated bonding (SAB). This multiple thin-disk or chip gain medium for distributed face cooling (DFC) structure can manage the high-power and high-field laser with high-gain compact system. Besides, QPM-structured crystal quartz constructed by multi-plate stacking could be promising as a high-power and reliable VUV frequency conversion devices. These downsized and modularized **tiny integrated lasers** (TILA) promise the extremely high-brightness lasers to open up the new science, such as laser driven electron accelerator toward table-top XFEL, and innovation by the compact power laser (Figure 1).

Figure 1. TILA consortium toward "Laser Science and Innovation" by micro solid-state photonics.

Selected Publications

- T. Taira *et al.*, *Opt. Lett.* **16**, 1955 (1991).
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- H. Sakai *et al.*, *Opt. Express* **16**, 19891 (2008).
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- R. Bhandari *et al.*, *Opt. Express* **21**, 28849 (2013).
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- L. Zheng *et al.*, *Opt. Mater. Express* **7**, 3214 (2017).
- H. Ishizuki *et al.*, *Opt. Mater. Express* **8**, 1259 (2018).
- S. W. Jolly *et al.*, *Nat. Commun.* **10**, 1 (2019).
- Y. Sano *et al.*, *Forces in Mechanics* **7**, 100080 (2022).
- V. Yahia *et al.*, *Opt. Express* **32**, 14377 (2024).

1. Scaling Narrowband THz Generation to Large Apertures in $LiNbO_3$ and KTP[1)]

An attractive approach for generating high peak-power multicycle terahertz radiation (MC-THz) pulses is nonlinear optical down-conversion of laser pulses in periodically-poled crystals. A principal limitation to the yield, however, is the small (sub-centimeter) apertures of commercially-available crystals which restrict the amount of laser energy that can be used. Here, we explore MC-THz generation by down conversion in two types of large-aperture media for which periodic poling has been achieved in different ways: (1) extension of traditional, voltage-based poling of bulk material to larger (centimeter) scales; and (2) manual poling by assembly of large aperture sub-millimeter thick wafers in alternating orientations. We explore the dependence of efficiency on laser peak fluence and crystal length for both types of media and extend upon previous work with the wafer approach by increasing the number of wafers in the stack, implementing cryogenic cooling and testing an alternate material: Potassium titanyl phosphate (KTP). Driving with up to 0.2 J, half-picosecond laser pulses centered at 1,030 nm, we obtain conversion efficiencies of up to 0.14%, resulting in ~1% bandwidth MC-THz pulses of up to 207 μJ. (Figure 2).

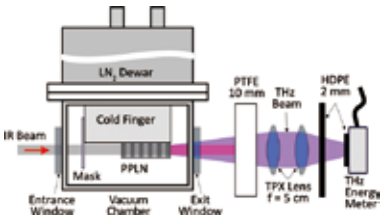

Figure 2. Optical layout showing the periodically-poled device mounted to the cold finger inside the cryostat.

2. Enhanced Thermal Conductivity of Distributed Face-Cooled Composite Laser Medium Included Thermal Resistance at the Bonding Interface[2)]

A new concept of the effective thermal conductivity (κ_{eff}) of the laser gain medium with the distributed face-cooled composite synthesized by the inter-layer surface activated bonding (il-SAB) has been proposed. The thermal resistances at the bonded interface (R) between 1at.% Nd:YAG and a *c*-cut sapphire single crystal in several composites were experimentally confirmed, and it was found that il-SAB brings negligibly small R. On the contrary, R in the bi-layer composite of 1at.% Nd:YAG and sapphire sandwiching indium foil fabricated by 6.0-kN uniaxial pressing reached 1.4×10^{-5} m^2K/W at 25 °C. In the case of the simple contact of 1at.% Nd:YAG and a sapphire single crystal, R at 25 °C was 4.3×10^{-4} m^2K/W. Consequently, effective thermal conductivities in bi-layered composites with 1at.% Nd:YAG and *c*-cut sapphire with the same thickness fabricated by il-SAB, sandwiching indium foil, and simple contacting without bonding were evaluated to be 15.3 W/mK, 13.9 W/mK, and 3.65 W/mK, respectively. Negligible R of composite gain media by il-SAB indicates that κ_{eff} of 1at.% Nd:YAG will be improved from 10 W/mK to more than 30 W/mK if sapphire parts are thicker than 12.2 times of YAG parts in composite gain media with the distributed face-cooling structure. (Figure 3).

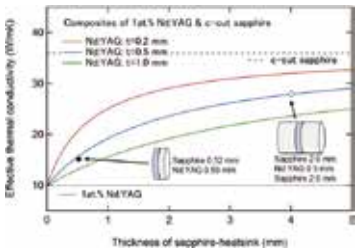

Figure 3. The dependence of κ_{eff} on the ratio of the thickness between Nd:YAG single crystal and sapphire heatsink in DFC-PowerChip.

3. Generation of High-Energy Laser Pulses at 266 nm with Sub-Nanosecond Pulse Duration and 20 Hz Repetition Rate[3)]

We developed a high-energy laser system using a microchip laser with a sub-nanosecond pulse duration and power amplifiers employing Distributed Faced Cooling, achieving pulse energies exceeding 2 J at a repetition rate of 20 Hz. This report presents the results of wavelength conversion based on this laser, achieving 266 nm in the Deep UV (DUV) range. Using KD*P crystals for wavelength conversion, we obtained a maximum pulse energy of 235 mJ at 2 Hz. However, the short pulse duration of approximately 580 ps from the microchip laser seed source causes nonlinear absorption in the crystal, challenging the conversion to 266 nm. That is why, we generated 532 nm through second harmonic generation (SHG) in LBO1, then 355 nm by SFG of the 532 nm pulse and the residual fundamental wave in LBO2, and finally 266 nm by SFG of the 355 nm and the residual fundamental wave in LBO3. We developed a high-energy UV laser system using LBO crystals, achieving 266 nm DUV pulses with a maximum pulse energy of 111 mJ and peak power of 190 MW at a 20 Hz repetition rate. (Figure 4).

Figure 4. Experimental setup of compact Deep-UV sub-nanosecond pulsed laser system with world-class output power.

References

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