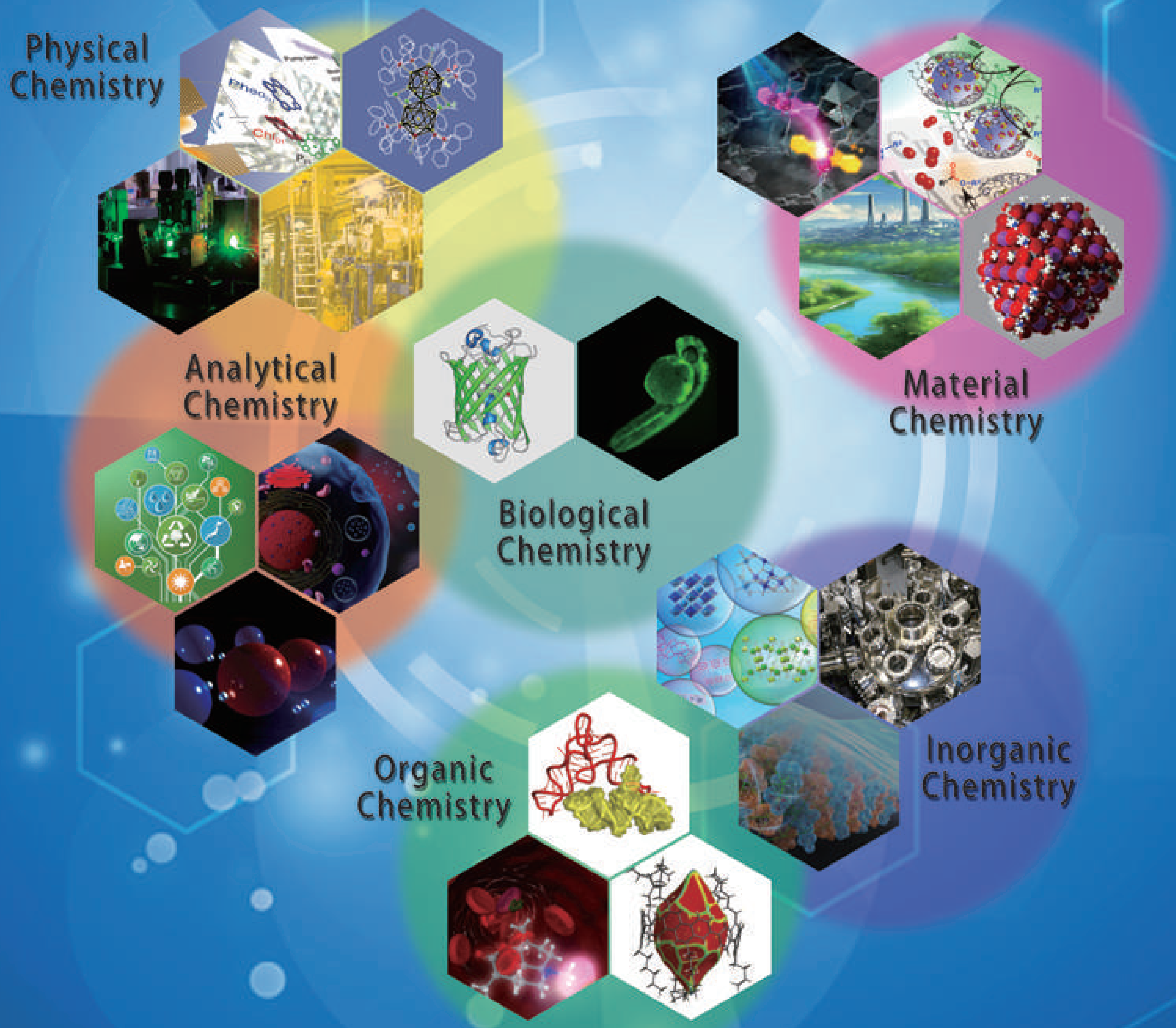
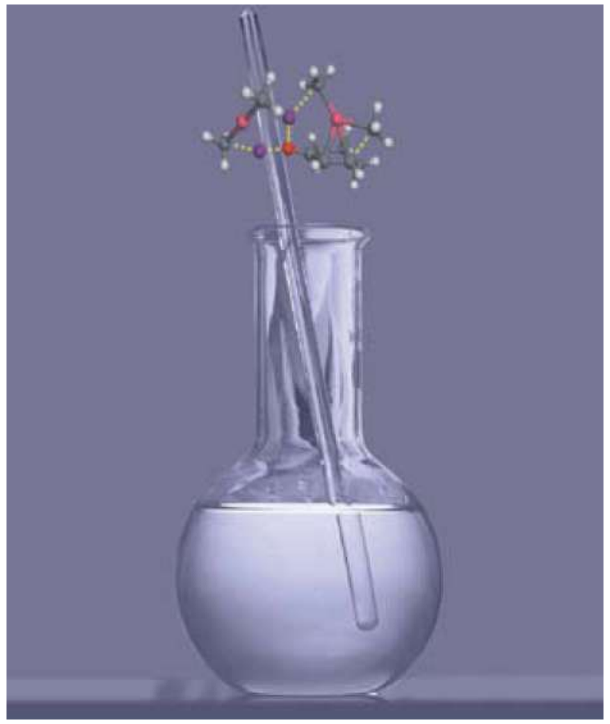
CHEMISTRY

Department of Chemistry,
School of Science,
The University of Tokyo



Laboratories in Department of Chemistry

Department of Chemistry, School of Science, The University of Tokyo



The Chemistry Buildings (Main Bldg., East Bldg., West Bldg.) of the Graduate School of Science are located in the center of the University of Tokyo's Hongo Campus. For the past 150 years, the University of Tokyo has made history in research and education. As a place that drives advances in modern science, the Department of Chemistry has nurtured a great many chemists that see chemistry as the central science and prepared them for central roles in the academic, industrial and educational sectors. The Department plays a key role in providing higher chemistry education at the University of Tokyo's School and Graduate School of Science. It is also a place of discovery, where investigators of the frontiers of chemistry gather, providing a base for advances in basic chemistry research. Outlined below are research activities currently under way at laboratories within the Department of Chemistry.

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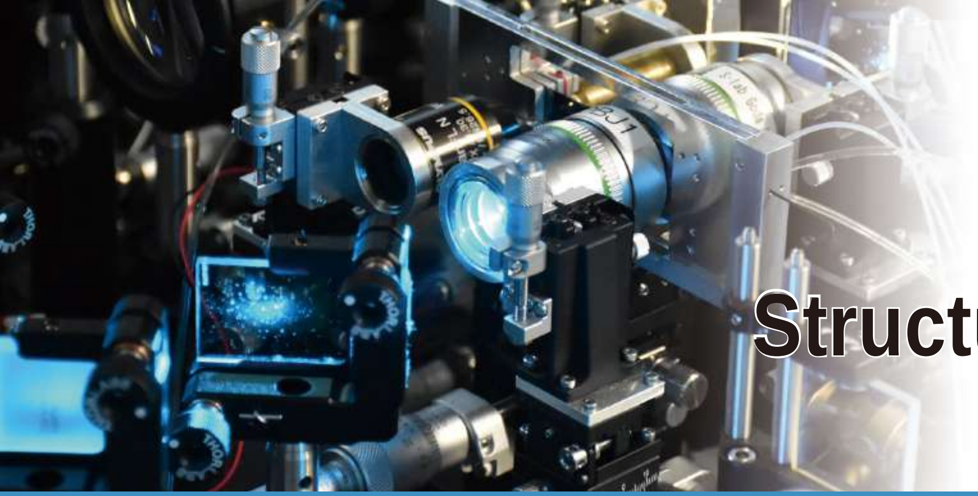
Physical Chemistry

Organic Chemistry

Inorganic & Anailtical Chemistry



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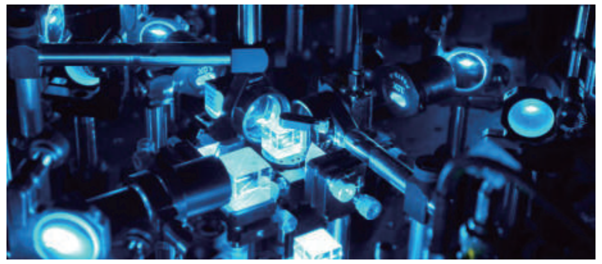
Developing serendipity-enabling technologies through the integration of photonics, nanotechnology, microfluidics, and data science

At Goda Lab, our primary mission is to develop "serendipity-enabling technologies" that align with Louis Pasteur's famous quote, "Chance (serendipity) favors the prepared mind." Our focus is on developing innovative tools for molecular imaging and spectroscopy by integrating photonics, nanotechnology, microfluidics, and data science. By utilizing these tools, we aim to discover unknown phenomena, elucidate mechanisms, and explore new applications in science, industry, and medicine. We employ theoretical, experimental, and computational techniques to tackle critical problems. Additionally, we are committed to cultivating the next generation of global leaders who will shape the world in the 21st century. We foster an international and interdisciplinary research environment that values flat human relationships, and we actively seek out talented individuals from any university or company, regardless of their field of study.

Image-activated cell sorting

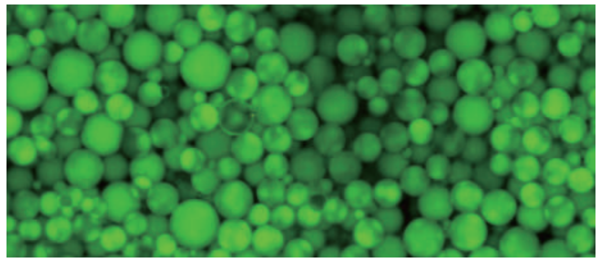
Image-Activated Cell Sorting (IACS) is a revolutionary technology that performs real-time, image-based sorting of single cells at a high rate of over 1000 events per second. Developed by a collaborative group led by Professor Keisuke Goda,[1] IACS extends beyond the capabilities of traditional fluorescence-activated cell sorting (FACS) by analyzing multidimensional images of cells, enabling high-content sorting of cells or cell clusters with unique spatial, chemical, and morphological traits.[2,3] This includes intracellular protein localization and cell-cell interactions, making IACS an essential part of holistic single-cell analysis by facilitating direct links between population-level analysis (flow cytometry), cell-level analysis (microscopy), and gene-level analysis (sequencing).



Ultrafast fluorescence microscope

Intelligent platelet morphometry

Platelets are an important type of anucleate cell found in blood, whose main role is to prevent bleeding by initiating hemostatic reactions that result in clot formation. The study of platelets and their complex physiological and pathological functions requires advanced image-based analysis techniques, such as platelet morphometry. Such techniques also aid in the development of more effective clinical strategies. To this end, we have collaborated with clinicians from the University of Tokyo Hospital to develop an innovative tool that utilizes high-throughput optical imaging and deep learning to advance platelet morphometry beyond traditional methods.[4,5]



Droplets for single-cell analysis

Exosome-based liquid biopsy

Exosome-based liquid biopsy is a rapidly evolving field in medical diagnostics, offering a non-invasive alternative to traditional tissue biopsies. Exosomes are tiny vesicles, typically ranging from 30 to 150 nanometers in diameter, that are released by almost all types of cells into the bodily fluids. These vesicles carry a variety of molecular constituents of their cell of origin, including proteins, lipids, DNA, and various forms of RNA. Our current research is focused on pioneering a groundbreaking approach in liquid biopsy technology, centering on the highly selective detection of exosomes. This innovative method aims to significantly enhance the accuracy and efficiency of liquid biopsies, offering a more refined and targeted diagnostic tool.

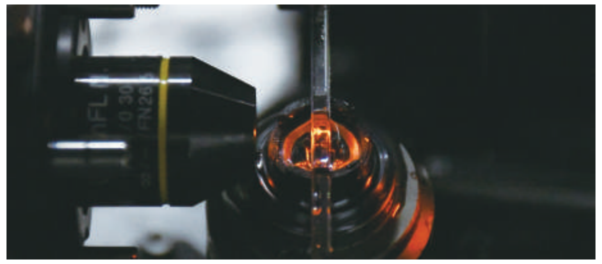
Wearable spectroscopy

Wearable surface-enhanced Raman spectroscopy (SERS) is gaining considerable traction in healthcare, and its integration into wearable devices represents a significant leap in this area. In our ongoing quest to pioneer advancements in the field of wearable SERS, our focus is on the development of innovative, flexible substrates. Over the past few years, we have successfully developed and optimized gold and silver nanomesh structures.[6] These structures have demonstrated remarkable flexibility and efficiency, serving as the cornerstone for our current SERS substrates. Building upon this foundation, we are now channeling our efforts into exploring and harnessing the vast potential of wearable SERS in various biomedical applications.[7]

Clean room for nanofabrication

Drosophila-based drug discovery

Development of new drugs is hindered by the tremendous expense, time, and effort required. Conventional drug development methods that use cultured cells, mice, and patient samples make it challenging to achieve an efficient drug discovery process. As an alternative, we propose the use of *Drosophila* (fruit flies), which are easy, fast, and inexpensive to raise and breed, pose no ethical issues, and have high disease gene homology and similar drug responses to mammals. Our goal is to establish a platform for *Drosophila*-based drug screening to identify therapeutic seeds for various diseases, such as cancer, heart disease, stroke, rheumatism, and diabetes.



Large-volume imaging platform for *Drosophila*

Quantum bioengineering

Biology has been successful in applying classical physical models to explain many biological systems. However, there are still many biological phenomena that remain unexplained by classical physics. Quantum biology is a field of research that aims to answer these phenomena from a quantum mechanical perspective. We aim to take the insights gained from quantum biology one step further and develop a new field of research called "quantum bioengineering," which will create innovative quantum technologies inspired by the findings of quantum biology.[8]

Lasers for high-resolution microscopy

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Solid State Physical Chemistry


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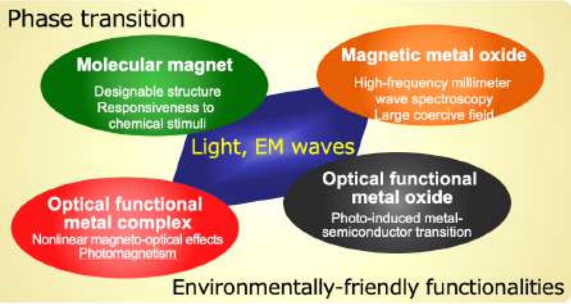
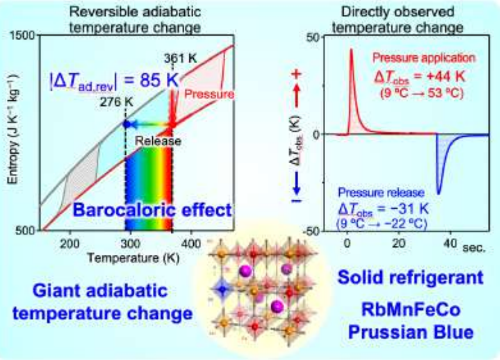
Development of novel functional materials responding to light and electromagnetic waves for solving environmental and energy issues

We are working on the development of novel functional materials responding to light and electromagnetic waves and materials for solving environmental and energy issues. Various materials from metal complexes, such as Prussian blue, to metal oxides and metal alloys have been investigated by chemical synthetic approach. Regarding correlation phenomena of magnetism and light/electromagnetic wave, we have been promoting research on magneto-optical and nonlinear optical magnetism. By utilizing nano-scale chemical synthesis, novel functional materials were synthesized from abundant elements such as iron or titanium; epsilon-iron oxide, ε-Fe_2O_3, showing huge coercive field and high-frequency millimeter wave absorption, and lambda-titanium oxide, λ-Ti_3O_5, exhibiting photo-induced metal-semiconductor transition at room temperature as well as heat storage properties that proposes a novel concept of preserving heat energy for a prolonged period. We are working on environmentally friendly research with a view to technology applications contributing to big data, IoT, and renewable energy.



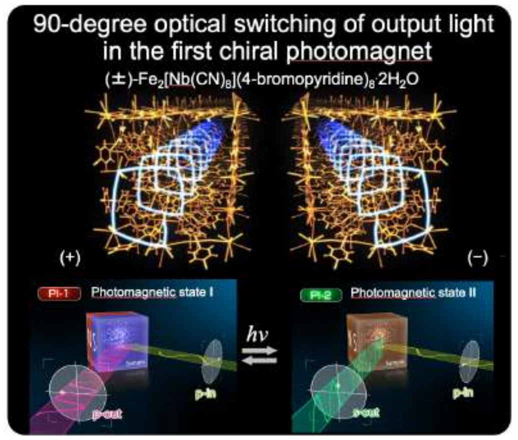
Synthesis of magnetic materials with novel magnetic functionalities based on molecular design

We are studying metal complexes to realize novel magnetic functionalities based on molecular design. Metal complexes are excellent in terms of optimization of the crystal structure by changing organic ligands and designing of metal ions based on magnetic chemistry, which is a big advantage in molecular design. We have synthesized high-spin clusters, and one-, two-, and three-dimensional network metal assemblies. Furthermore, the design of functional magnetic material is possible utilizing the flexibility of the metal complex and the variety of coordination geometries around the metal ion, e.g., magnetic materials responding to physical stimuli such as light, heat, pressure, and to chemical stimuli such as gas adsorption, molecular adsorption, and humidity. We have pioneeringly reported various novel functionalities, for example, a magnet exhibiting two compensation temperatures, a humidity-sensitive magnet, a porous magnet that responds to solvent vapor, and so on. Recently, we have reported a metal complex that exhibits both ferroelectricity and ferromagnetism. Furthermore, we have synthesized a cyanide-bridged metal complex that shows the effect of increasing and decreasing temperature, upon applying and releasing pressure. We have reported that it shows the world's largest reversible adiabatic temperature change among the calorific effects of solid-solid transition refrigerants. The realization of highly efficient solid refrigerants is expected.



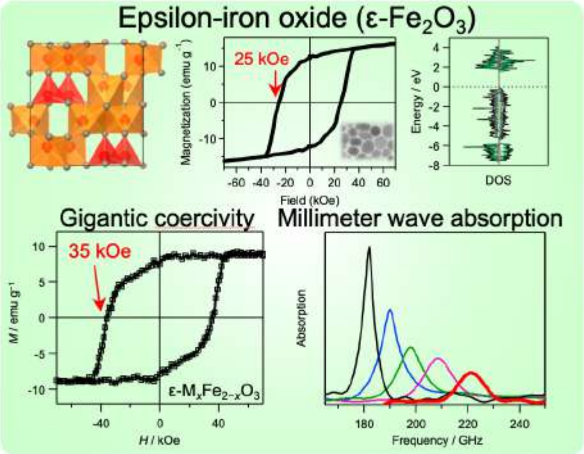
Observation of new magnetic phenomena and functionalities associated with magneto-optical correlation

One of the important features of ferromagnetic metal complexes is in their broad range of color due to visible light absorption, suggesting a possibility of controlling the electronic states and magnetic characteristics by means of visible light. From this point of view, we have synthesized various photomagnetic materials using metal complexes and observed novel phenomena including photoinduced magnetic pole inversion and photoinduced magnetization, in which paramagnetism and ferromagnetism are reversibly photoswitched. Recently, we have observed light-induced spin-crossover ferromagnetism and 90-degree optical switching of the polarization plane of second harmonic light. Furthermore, we could control light using the magnetic materials that we develop. We focus on nonlinear magneto-optical effects and have reported the second example of magnetization-induced second harmonic generation (MSHG) in a bulk ferromagnet, the first example of MSHG in a chiral ferromagnet, and the first observation of magnetization-induced third harmonic generation (MTHG) in a ferromagnet. Furthermore, from recent the studies on phonon observations by terahertz light, we observed low-frequency oscillations of Cs^+ ions in a Prussian blue framework and also a new developed Cs-detection method using terahertz light.



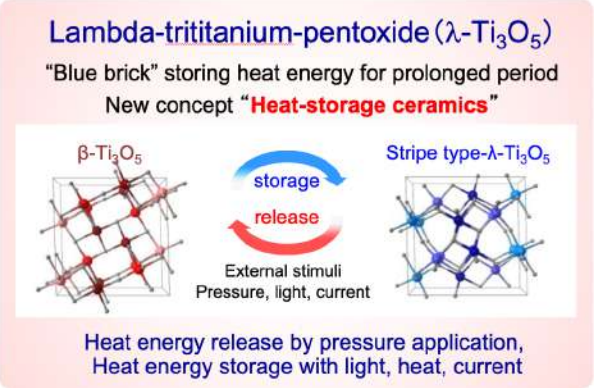
Study of novel magnetic oxides with electromagnetic environmentally protective function

Magnetic metal oxides, represented by iron oxides, have been used in our lives for their chemical stability and insulation property. We have been studying the synthesis of novel magnetic oxides by chemical approaches and have succeeded to isolate a single phase of ε-Fe_2O_3 for the first time. ε-Fe_2O_3 shows a large coercive field (H_c) over 20 kilo-oersted (kOe) at room temperature, which is the largest H_c value among magnetic oxides. Recently, we succeeded to enlarge the H_c value and achieved a gigantic H_c value of 35 kOe in a metal substituted ε-Fe_2O_3. This H_c value is comparable to those of rare-earth magnets. Due to such a large magnetic anisotropy, ε-Fe_2O_3 can be reduced to a single nano-size of less than 10 nm while maintaining its magnetic order, and we discovered that it is the world's smallest hard ferrite magnet at 7.5 nm. Furthermore, we discovered that metal-substituted ε-Fe_2O_3 can effectively and frequency-selectively absorb millimeter waves, which have the highest frequency of all magnetic materials. We are also promoting research into applications of these properties, such as magnetic recording media and millimeter wave absorption materials, and some of these are being developed in the market as the thinnest and lightest high-performance millimeter wave absorbers.



Synthesis of a metal oxide with room-temperature photoreversible phase transition and proposal of a novel concept “heat storage ceramics”

Titanium oxides containing Ti^{3+} are colored black and have electron spins. We have investigated black titanium oxide by nano-scale chemical synthesis, and discovered a new type of metal oxide, lambda type trititanium pentoxide (λ-Ti_3O_5). This material shows photoinduced phase transition from black colored lambda phase (metallic conductor) to brown colored beta phase (β-Ti_3O_5) (semiconductor). Moreover, the reverse phase transition was also observed by photoirradiation. This is the first example of a metal oxide which shows photorewritable phenomenon at room temperature. Since λ-Ti_3O_5 is very economical and environmentally friendly material and is obtained as nanoparticles, λ-Ti_3O_5 is expected as a next generation high-density optical storage material. Additionally, λ-Ti_3O_5 is capable of preserving heat energy for a prolonged period, proposing a novel concept of “heat storage ceramics.” This material absorbs and releases a large heat energy of 230 kJ L^{-1}, and the preserved heat energy could be released by applying a weak pressure of 60 MPa. Furthermore, the present system could store the heat energy by electric current or light and release the heat energy by various external stimuli repetitively. The present heat storage ceramic is expected as a new material for solar thermal power generation systems or for realizing efficient uses of industrial waste heat generated from furnaces.



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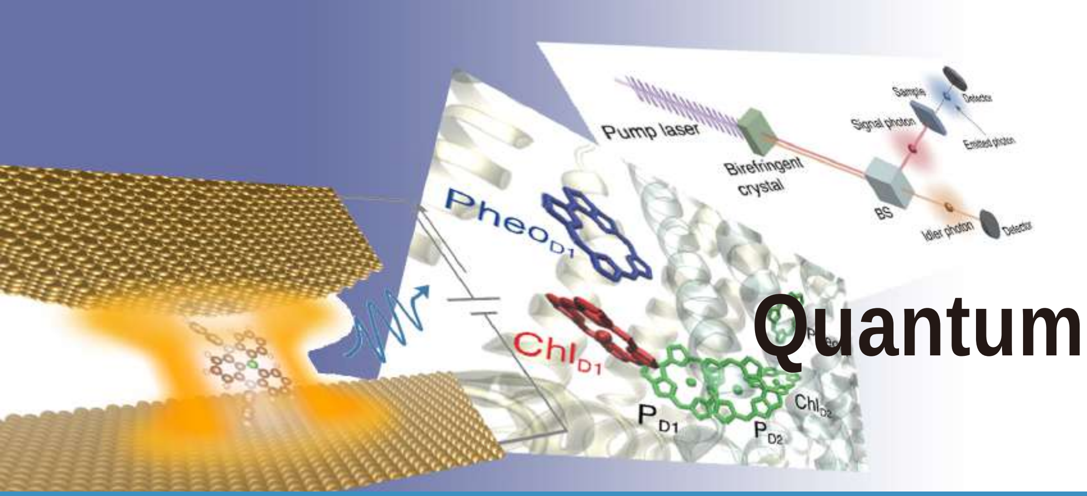

Quantum Chemistry

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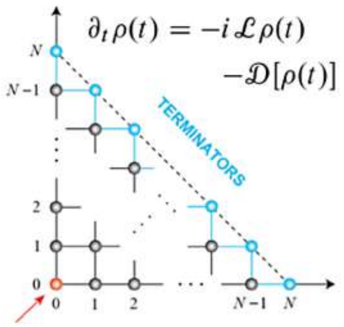
Quantum Science and Technology Meets Physical Chemistry

In the Iwanami Rikagaku-Jiten, physical chemistry is defined as "a branch of chemistry that uses physical theories and physical measurement methods to construct a theoretical system for the structure, properties, and reactions of substances." The Ishizaki group, through its commitment to integrating cutting-edge physical methodologies into the realm of physical chemistry research, aims to address the foundational question of how the properties of individual molecules are interconnected with the manifestation of functions in molecular systems characterized by higher-order structures, including phenomena pertinent to life. This pursuit is undertaken in an interdisciplinary fashion, leveraging the synergy between diverse scientific disciplines to elucidate the intricate relationships between

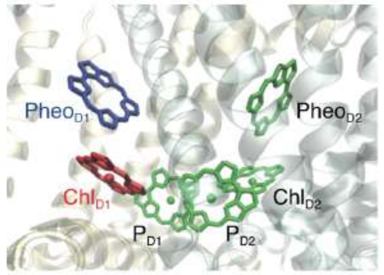
Development of a fundamental theory of quantum dynamics in condensed-phase molecular systems and its application to nonlinear optical response theory

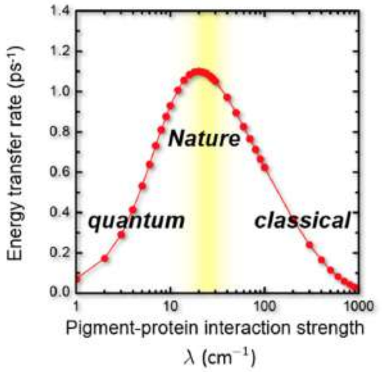
Quantum mechanics plays a pivotal role in numerous physico-chemical processes; nevertheless, its quantum mechanical calculation of the dynamics of electrons and atomic nuclei is constrained to small systems. One rational approach involves the treatment of a super-many-degree-of-freedom system, such as a solvent or protein, as an "environment," and the construction of a theoretical model by considering the degree of freedom that is to be focused on as an open system. However, it should be noted that such a dynamic process involving the "collapse of quantumness" cannot be described by unitary time evolution using the Schrödinger equation. Therefore, a dynamics theory based on the density operator is required. To this end, we have been developing a fundamental theory to describe the dynamic processes of quantum systems, with applications in the fields of chemistry and biophysics [J. Phys. Soc. Jpn. 74, 3131 (2005), J. Chem. Phys. 142, 212403 (2015), J. Phys. Soc. Jpn. 89, 015001 (2020), and Phys. Rev. Lett. 132, 170402 (2024)]. The significance of our findings lies in their recognition as a practical method that can accurately calculate the quantum dynamics of physical chemistry systems and calculate time-resolved optical responses from the same theoretical basis.



Energy Transfer and Charge Separation Processes in the Initial Stages of Photosynthesis

The development of the aforementioned results is currently underway, with the objective of analyzing energy transfer and primary charge separation in photosynthetic systems. Classic theories such as the Redfield theory and the Förster theory, which are low-order perturbation theories, have been widely used as standard theories for describing energy transfer. However, the energy transfer dynamics in natural photosynthesis occur in a parameter region where the validity of these classical theories is unclear. Consequently, the description and understanding of this process had remained a significant challenge in the fields of physical chemistry and biophysics research on the initial processes of photosynthesis. While numerous studies had been directed towards the development of higher-order perturbation theory, our research focused on the "time scale of dynamic fluctuations" of the electronic states of pigment molecules induced by the protein environment. Our findings indicate that the timescale of these fluctuations is comparable to that of energy transfer, thereby highlighting a critical deficiency in existing theoretical frameworks. Specifically, we identified an absence of comprehensive description of the "time scale of dynamic fluctuations" [J. Chem. Phys. 130, 234110 (2009)]. In light of this finding, we have developed a theoretical framework that elucidates the dynamics of energy transfer in regions of parameters that are not adequately addressed by prevailing theories [J. Chem. Phys. 130, 234111 (2009), Proc. Nat. Acad. Sci. 106, 17255 (2009).] Notably, the observation that the rate of energy transfer is maximized in the parameter region corresponding to natural conditions represented a significant breakthrough in the fields of physical chemistry and biophysics research on the initial stages of photosynthesis.

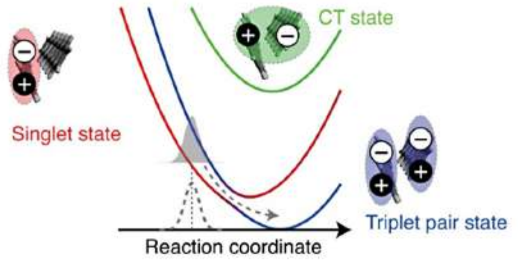




Moreover, the concept of "dynamic fluctuations that control quantum phenomena" has had a significant impact on related fields such as quantum physics and has contributed to the revitalization of quantum biophysics in Europe and the United States. [Annu. Rev. Condens. Matter Phys. 3, 333 (2012), Nature 543, 647 (2017). J. Phys. Chem. B 125, 3286 (2021)].

In addition, we are currently engaged in an effort to elucidate the initial charge separation process that instigates energy conversion in photosynthesis in green plants. This endeavor involves the synthesis of theory and electronic state calculations. It has been previously established that the nature of the initial charge separation reaction in the photosystem II reaction center of green plants differs significantly from that of red bacteria. This discrepancy has been a subject of ongoing research, and the situation remains unclear and in flux. Our theoretical research has achieved a unification of multiple experimental data sets from the past two decades, including the substantial disturbance in the electronic state that is inevitable due to the charge and the "robustness against inevitable errors" resulting from temperature fluctuations with a time constant of several hundred femtoseconds [J. Phys. Chem. Lett. 9, 4921 (2018)]. We are currently pursuing a comprehensive understanding of the energy conversion process in plant photosynthesis.

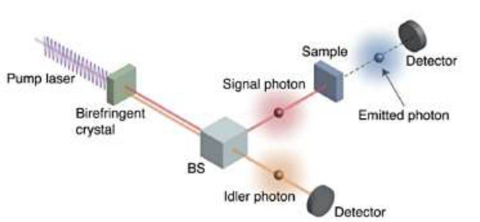
Dynamic Functional Properties in Molecular Materials

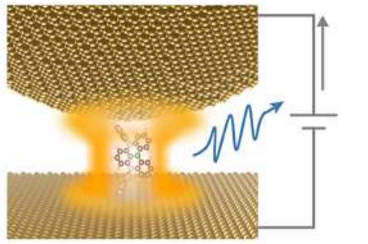


In light of the insights and theoretical/computational advances derived from the research on the photosynthetic light-harvesting system previously outlined, our research is currently expanding to encompass the dynamic functional properties of molecular materials [J. Phys. Chem. Lett. 7, 363 (2016), Phys. Rev. Lett. 121, 026001 (2018)]. In organic solar cells, the energy required for electron-hole pairs to undergo charge separation from a bound state is much greater than the thermal energy at room temperature. This prompts the investigation of unanswered questions concerning the physical mechanisms that enable "ultrafast, long-distance charge separation without the recombination of separated charges," as suggested by ultrafast spectroscopic experimental data. To address this knowledge gap, we have conducted a theoretical analysis of the charge transport dynamics, focusing on the competition between the small polaron formation process and the quantum delocalized state of the mobile charge and its destructive process in organic materials. Our findings revealed that the small polaron formation process leads to the destruction of the "quantum delocalized state of the charge that enables ultrafast, long-distance charge transfer" over a finite period of time, resulting in the transition of charge transfer to an "incoherent, slow classical hopping process." This transition has been termed the "quantum-classical ratchet mechanism," which has the capacity to delay charge recombination [Phys. Rev. Lett. 121, 026001 (2018)]. In a multitude of biomolecular systems, it has been observed that useful functions are frequently manifested through unidirectional dynamic processes, despite the presence of numerous electronic states within a relatively constrained energy range, often comparable to thermal energy. The findings of this study are expected to offer significant insights into the understanding of the "directionality" exhibited by biomolecular and molecular material systems, and the research is ongoing.

Towards a new development in physical chemistry based on light and quantum science and technology

In 2010, we conducted research that can be seen as the beginning of a recent domestic trend of discussing life-related phenomena using quantum science and technology, such as considering and visually presenting the robustness and fragility of quantum superposition states of the electronically excited states of pigment molecules encapsulated in proteins, using theories proposed in the field of quantum informatics, which has seen remarkable progress in recent years research, which can be said to be the beginning of a recent domestic trend, was conducted in 2010 [New J. Phys. 12, 055004 (2010), Nat. Phys. 6, 462 (2010)]. In recent years, we have also been working to establish the theoretical basis for a new quantum spectroscopy measurement technique that utilizes non-classical correlations of light, such as light confined in micro-optical resonators and entangled photons, with the aim of time-resolved measurement of the dynamic processes of complex molecular systems [J. Phys. Chem. Lett. 9, 1243 (2018), J. Chem. Phys. 153, 051102 (2020), Nano Letters 23, 3231 (2023), J. Chem. Phys. 160, 104201 (2024)].





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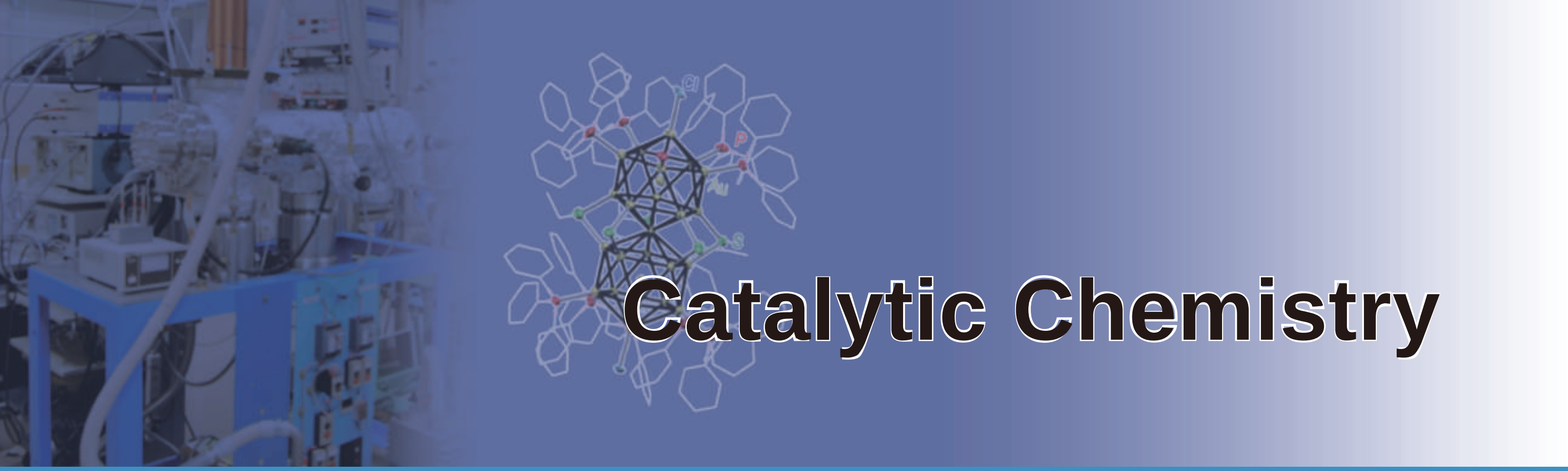

Catalytic Chemistry

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Development of novel catalysts based on metal clusters

Metal clusters with diameters smaller than 2 nm exhibit novel properties not found in the corresponding bulk metal due to their discrete electronic and unique geometrical structures. In addition, the stability and properties of metal clusters change drastically depending on the number of the constituent atoms (cluster size). Because of these unique features, metal clusters are promising candidates for functional units of novel materials such as catalysts and electro-optical devices. Our research activities are aimed at understanding the origin of the size-specific physicochemical properties of metal clusters and at developing cluster-based materials (Figure 1).

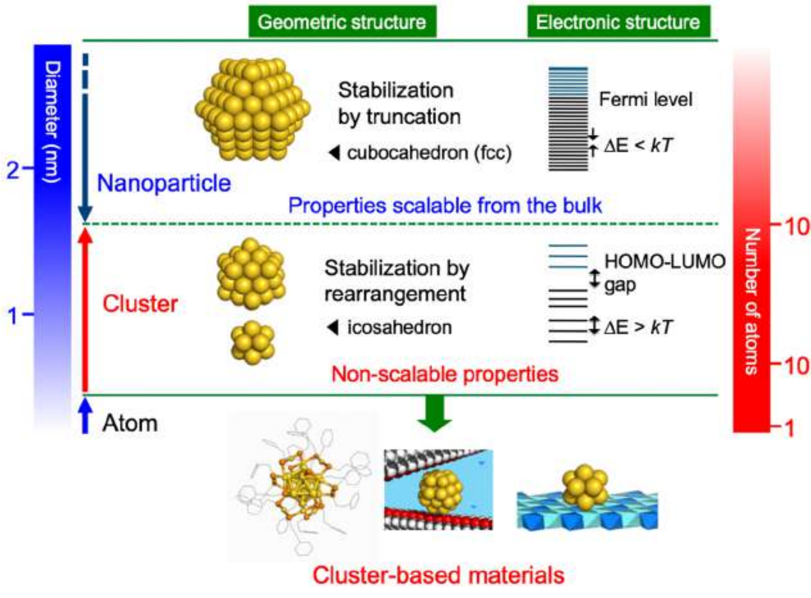

Figure 1. Development of cluster-based materials.

Atomically precise synthesis and structural characterization of superatoms

Gold clusters can be systematically treated as "superatoms" because they have an electronic structure similar to that of atoms. We are developing atomically precise methods for the synthesis of "chemically modified superatoms" in which the superatoms are protected by various organic ligands. In addition, we are determining the geometric structure using single-crystal X-ray structure analysis, and evaluating the electronic structure of the superatoms using various spectroscopic methods, including our original gas-phase photoelectron spectroscopy, as well as theoretical calculations. Ultimately, we aim to elucidate the relationship between the characteristic structural factors and the electronic states of the chemically modified superatoms (Figure 2).

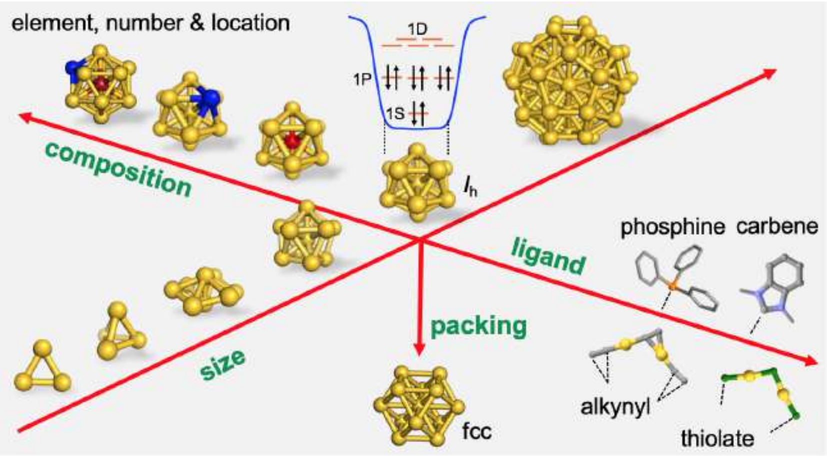

Figure 2. Diverse structural factors of chemically modified gold superatoms.

Exploration of hierarchical materials using superatoms as building units

By bonding and assembling superatoms as the basic unit, we can expect to see new physical properties based on synergistic and cooperative effects. Therefore, we are developing methods to synthesize and analyze the structures of quasi-molecules (superatomic molecules) in which superatoms are partially fused, and we are also working to develop a chemical bonding theory for superatoms (top of Figure 3). In addition, we are developing methods for constructing assemblies in which superatoms are arranged in a regular pattern, with precise control over the number, spacing, direction, and type of bonding (bottom of Figure 3).

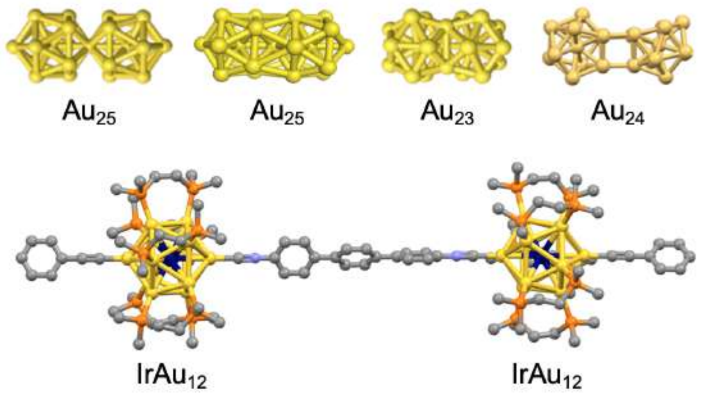

Figure 3. Examples of superatomic molecules (top) and assembled structures (bottom) of superatoms.

Exploration of novel properties and functionalization of superatoms

Superatoms are expected to exhibit unique optical and chemical properties due to their discrete electronic structure. For example, unlike bulk gold, gold superatoms exhibit photoluminescence. Using the icosahedral Au_{13} superatom as a platform, we systematically investigated the relationship between emission wavelength, quantum yield, and structural factors, and established guidelines for controlling the luminescence properties. On the other hand, in contrast to bulk gold, nanoscale gold exhibits oxidation catalysis. To elucidate the origin of the size-specific catalytic activity of gold, we have developed a method to protect gold superatoms with a partially exposed surface and to support them on a solid surface, while defining their size and chemical composition with atomic precision. Using these as model catalysts, we have elucidated the reaction mechanism by exploring the relationship between catalytic performance and structural factors such as size and doping, and proposed a design guideline for catalytic performance.

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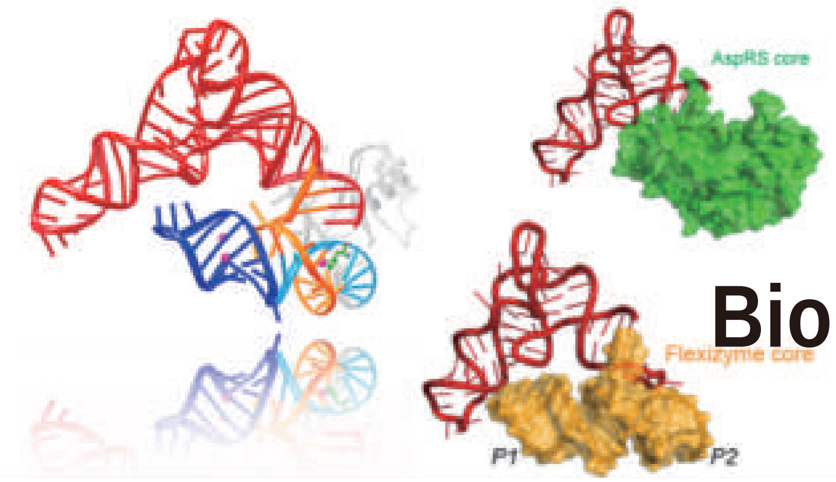

Bioorganic Chemistry

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Dissecting Life with Organic Chemistry and Devising Methods to Control at Will

In the Suga lab, our aim is to utilize organic chemistry techniques in combination with biology to tackle yet unresolved questions. In our inclusive research, we procure scientific knowledge leading to new concepts and develop novel technologies with broad applicability, which can extend to drug discovery. We provide a diligent and cooperative research environment with a goal of nurturing individuals so they are brimming with innovation and global-mindedness. The following research projects are currently in progress.

Development and application of artificial ribozymes

The "RNA world" hypothesis is based on the concept that life on Earth originated as RNA molecules without the participation of the DNA and/or protein components that are integral to modern life. As early as the 1960s, Crick and Orgel had already proposed the basic concept of the RNA world hypothesis, but this early hypothesis could not be widely accepted due to a lack of experimental evidence. The discovery of RNA molecules with enzymatic activities called ribozymes in the 1980s drastically changed this situation. However, in the modern world, very few natural ribozymes exist and they are limited to the catalysis of RNA modifying reactions such as cleavage and ligation of RNA. These limited functions are apparently insufficient to support life, that is, ribozymes would need to have been responsible for more varied enzymatic functions if the RNA world really existed. It is possible that over the course of 4 billion years of evolution the catalytic activity of proteins was favored and thus ribozymes with more diverse functions have been lost, so that just a trace of the real RNA world can be seen in nature today. Therefore, one of the themes of our lab is to artificially create ribozymes with novel catalytic activity in order to validate the concept of the RNA world. In other words, development of artificial life consisting entirely of ribozymes is one of our ultimate goals.

"Flexizyme" is one of the most successful ribozymes developed in our laboratory. Flexizyme is a short RNA molecule consisting of 46 nucleotides and it catalyzes the aminoacylation of tRNA with a wide range of natural and unnatural amino acids. Flexizyme exhibits broad substrate tolerance; it accepts arbitrary tRNA body sequences and various amino acids regardless of their side-chain structures. Therefore, flexizyme is a powerful tool for genetic code reprogramming and translation of nonstandard peptides as discussed below.

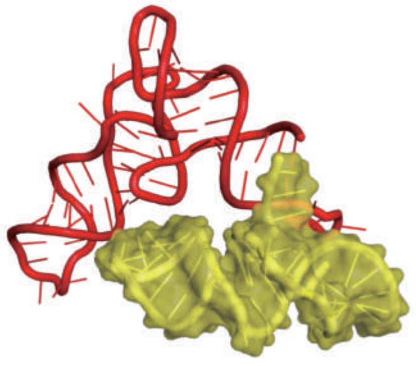

Fig. 1 Three-dimensional structure of flexizyme (yellow) and tRNA (red) The flexizyme core is docked onto tRNA^{Gln} by superimposing the minihelix on the tRNA acceptor stem. (*Nature* 2008, 454, 358-361)

Genetic code reprogramming

Genetic code reprogramming is the concept of using the translation machinery to synthesize polypeptides with the freedom to incorporate various non-proteinogenic amino acids. (Fig. 2). For this purpose, we have developed a flexible *in vitro* translation system referred to as the FIT system by integrating flexizymes with a reconstituted *E. colii* translation system. Flexizymes allow us to prepare diverse nonproteinogenic aminoacyl-tRNAs quickly and effortlessly, and the reconstituted *E. coli* translation technology provides a translation system depleted of specific nonproteinogenic amino acids. Thus, the FIT system has made it possible to reassign existing codons to desired nonproteinogenic amino acids such as *N*-methyl and D-amino acids, which have previously been challenging to incorporate. Currently, we are actively pursuing the development of further improved “next generation” genetic code reprogramming technologies.

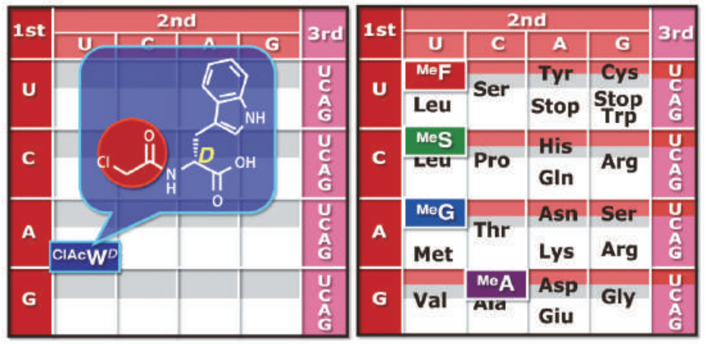

Fig. 2 Example of genetic code reprogramming
Left: Suppression of the initiation AUG codon with chloroacetyl-D-tryptophan,
Right: Introduction of four *N*-methyl amino acids (^{Me}F, ^{Me}S, ^{Me}G and ^{Me}A) into elongation codons

Ribosomal synthesis of nonstandard peptides

Peptides found as natural products often contain nonstandard structures such as *N*-methyl amino acids, D-amino acids and macrocyclic structures. Generally, these nonstandard peptides have rigid and biologically stable structures as well as high bioactivity compared to standard peptides. Moreover, many nonstandard peptides are membrane permeable, some of which have been already marketed as oral drugs. However, the discovery of such nonstandard peptide drugs has thus far been haphazard and a systematic method of discovery has not been established due to the limited availabilities of nonstandard peptides. On the other hand, the FIT system enables us to freely design and create such nonstandard peptides. We have already developed various methodologies for the macrocyclization of translated peptides and the synthesis of natural product-like nonstandard peptides using the FIT system. Now, we are trying to develop new systems for producing more complicated and pharmaceutically useful peptides.

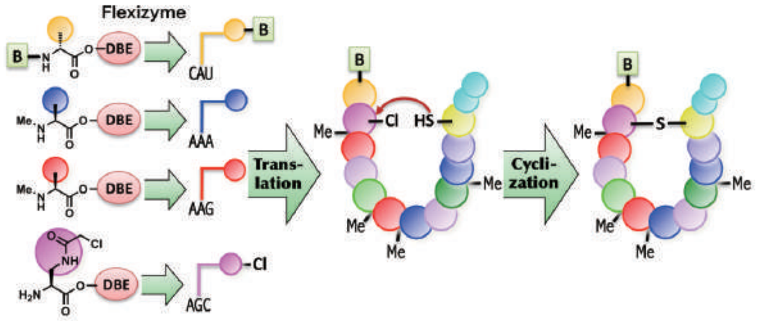

Fig.3 Ribosomal synthesis of cyclic *N*-methyl peptides
Synthesis of biologically stable macrocyclic peptides was accomplished using the FIT system.

Drug discovery using the nonstandard peptide library

For high throughput screening of bioactive nonstandard peptides, we have integrated the FIT system with an *in vitro* display method called mRNA display, with the combined system referred to as the RaPID system (Random Peptide Integrated Discovery system). Currently, we are applying the RaPID system to drug development projects with the intention of isolating nonstandard peptides inhibitors of various pharmaceutical targets. In the near future, by establishing this system as a fundamental technology of next generation drug discovery and being the first nonstandard peptide drug discovery institution to originate from Japan, we aim to deliver many achievements for the benefit of society.

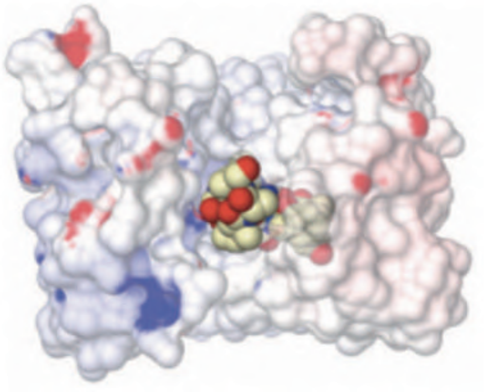

Fig. 4 Cover page of Nature Chemical Biology (2009) showing o
research project "Keys to translation"
^{HO}G (glycolic acid) was introduced at CUC codon by genetic co
reprogramming and used for macrocyclization of peptides.

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Synthetic Organic Chemistry


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Creation of Novel Science Based on Organic Synthesis

Synthetic organic chemistry is the science of “making” chemical products. Our laboratory is not only continuing and expanding upon the traditional role of synthetic organic chemistry, but is also aiming to open new doors of new sciences based on the products of our synthetic endeavors. We are interested in fostering the harmonious co-existence of human activity and the environment, and strive to develop methods to make chemical products without damaging our natural environment. Our goals are: (1) to develop high yielding and highly selective organic transformations; and (2) to reduce chemical wastes by efficiently utilizing the resource of the Earth. We are also interested in developing highly efficient catalytic asymmetric reactions for the purpose of supplying fine chemi- cals, like drugs, and to solve recent energy problems from the viewpoint of synthetic organic chemistry.

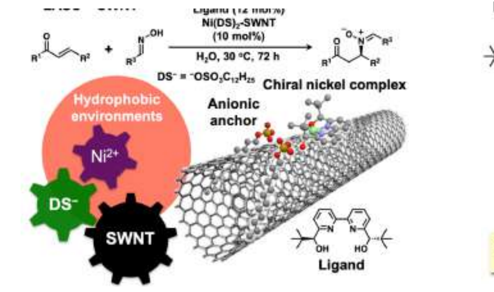
The goals of the natural sciences are to seek universal of truths of phenomena, and to elucidate the fundamental rules and basic theories in Nature. However, in chemistry, basic science and applied science are closely related. We are contributing to society by not only expanding our knowledge of the basic sciences, but also applying our discoveries for practical use. With our research activities, we strive to deliver innovative concepts in synthetic organic chemistry.

Development of organic reactions using water as a solvent

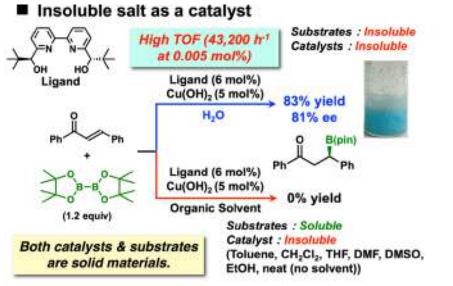
Modern organic chemistry has traditionally been structured around chemical reactions run in solution, predominantly utilizing organic solvents. In contrast, our laboratory focuses upon organic reactions in aqueous media, revealing numerous examples where reactivity and selectivity diverge significantly from those observed in organic solvents. The development of organic reactions in water not only contributes to the Sustainable Development Goals (SDGs) by providing alternatives to harmful organic solvents for humans and the environment but also promises unique synthetic strategies achievable only in water, heralding a new era in organic synthesis.

Recently, we have developed a new method for synthesizing optically active nitrones using a conceptually new surfactant-based catalyst doped with single-walled carbon nanotubes. This approach has achieved high selectivity across a broad range of substrates, surpassing the capabilities of traditional methods in organic solvents. One of our primary research topics is the development of catalytic asymmetric synthesis in water, enabling efficient production of optically active compounds. To date, we have developed asymmetric hydroxymethylation reactions, asymmetric Michael-type addition reactions, asymmetric protonation reactions, and asymmetric C−H bond functionalization of indoles.

Furthermore, we have discovered that zero-valent metals, metal oxides, and metal hydroxides, which have scarcely been used as catalysts in organic solvents, exhibit excellent catalytic activity in water. This has led to the development of highly selective bond-forming reactions, such as the allylation of aldehydes and ketones, asymmetric C−B and C−Si bond-forming reactions with α,β-unsaturated carbonyl compounds, and the 1,4-addition reactions of active methylene compounds. These reactions are exclusive to water, where they exhibit unique reactivity and selectivity.



Chiral Lewis acid integrated with SWNTs: In addition to the enhanced reactivity, stereoselective performance and long-term stability were demonstrated in asymmetric conjugate addition reactions of aldoximes to furnish chiral nitrones in high yields with excellent selectivities.



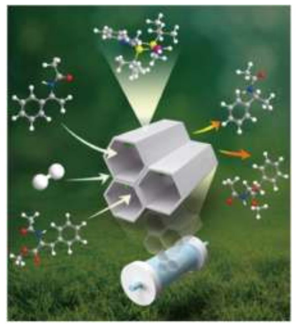
Asymmetric boron conjugate addition reaction in water using $Cu(OH)_2$ as a catalyst. Despite the fact that all involved species are practically insoluble in water, the reaction failed to give the desired adduct completely under neat (solvent-free) conditions

Development of high-performance heterogeneous catalysts

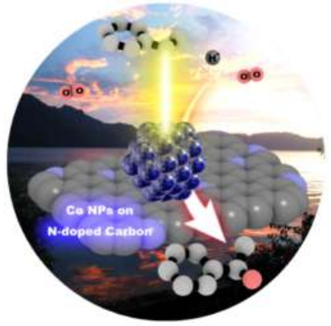
Heterogeneous catalysts can be easily separated from the product, and recovered and reused after reactions. Our laboratory has been investigating novel heterogeneous catalysts. Especially, we have developed metal nanoparticle catalysts by fine modification of supports and chiral metal catalysts by novel immobilization of chiral metal complexes in recent years.

We have developed polysilane-modified Pt, Rh, and Pd nanoparticle catalysts, which demonstrate higher activity and robustness over conventional catalysts. Our catalysts particularly showed high performance for reactions with gaseous molecules and achieved hydrogenation of various functional groups and arenes. More recently, we have developed a unique cooperative catalyst system by the combination of nanoparticle catalysts and Lewis acid catalysts. On the other hand, we have developed N-doped carbon incarcerated (NCI) earth-abundant metal catalysts such as Cu and Co. These metal catalysts had been considered less active than precious metal catalysts, however, we have developed highly active heterogeneous catalysts by the precise design of support.

We also have developed a novel immobilization method of chiral metal complexes utilizing noncovalent interactions without chemical modification of chiral ligands. We have found that various kinds of immobilized transition metal catalysts have comparable activity and selectivity as original homogeneous catalysts for flow enantioselective reactions.



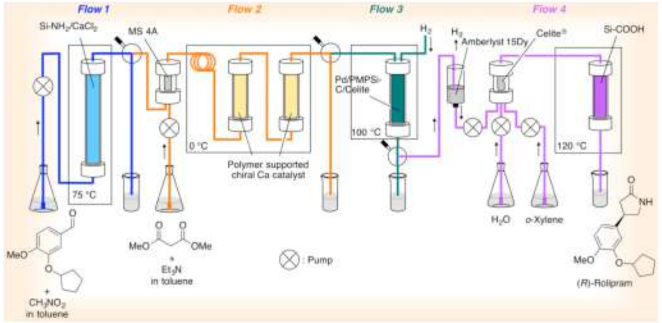
Catalytic enantioselective hydrogenation of enamides under continuous-flow condition using a chiral heterogeneous rhodium catalyst was developed.



Catalytic hydration of alkenes was achieved using N-doped carbon incarcerated (NCI) cobalt nanoparticle catalyst.

Organic synthesis in the next generation with continuous-flow reactions

Flow reactions can synthesize molecules continuously by pumping substrate solutions into a reactor. Organic synthesis utilizing flow reactions has many advantages compared with conventional batch synthesis in terms of efficiency, safety, and environmental compatibility. Among them, flow reactions with heterogeneous catalysts enable multistep synthesis without the isolation of reaction intermediates. Our laboratory has achieved continuous-flow multistep synthesis of fine chemicals utilizing catalytic transformations with heterogeneous catalysts. Particularly, we have focused on reactions with high atom-economy such as addition reactions and reduction with hydrogen gas. We have reported the continuous-flow synthesis of various kinds of fine chemicals including APIs and their intermediates such as Rolipram, Donepezil, Venlafaxine, Tamsulosin, Memantine and agrochemicals.

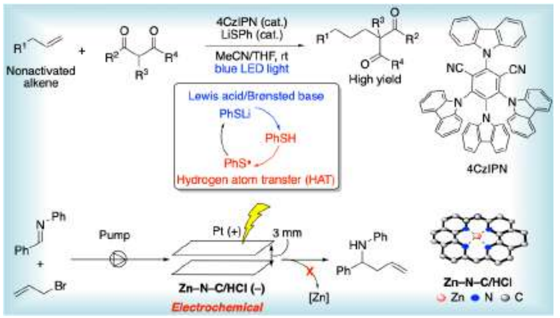


Total synthesis of optically active drug, Rolipram, using multi-steps continuous flow reaction system was achieved.

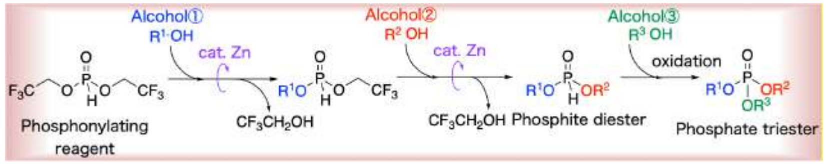
Development of new synthetic methods directing higher efficiency

Our group has a long-standing interest in developing more efficient catalytic reactions and catalytic asymmetric reactions that provides only the desired enantiomer with high selectivity. We have reported many highly functionalized metal catalysts for various asymmetric carbon–carbon bond forming reactions. While we have been investigating proton transfer catalysis for realizing high atom-economy and developing catalytic addition reactions of less reactive materials using alkaline metal strong Brønsted bases, we have also been focusing on development of photochemical reactions and electrochemical reactions, and realized efficient catalytic carbon–carbon bond forming reactions.

Our group has also achieved environmentally compatible phosphite diester synthesis using Lewis acid catalysts such as zinc and hafnium complexes. Currently, 19 compounds with repeating phosphate ester structures have been approved as oligonucleotide therapeutics. By combining our developed synthetic method with oxidation reactions, we synthesized phosphate esters without isolating intermediates, achieving the catalytic synthesis of dinucleotide dimers, which are the minimum structural units of oligonucleotides. Those synthetic method and insights are expected to be applicable for high-efficiency catalytic liquid-phase synthesis of oligonucleotide therapeutics.



(Top) Catalytic addition reactions of active methylene compounds with nonactivated alkenes using photocatalyst-lithium thiophenoxide catalyst hybrid system. (Bottom) Continuous-flow electrochemical allylation of imine using single-atom zinc on nitrogen-doped carbon as electrodes.



The environmentally friendly synthesis of phosphite diesters was achieved for efficient production of nucleic acid medicines.

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Natural Products Chemistry

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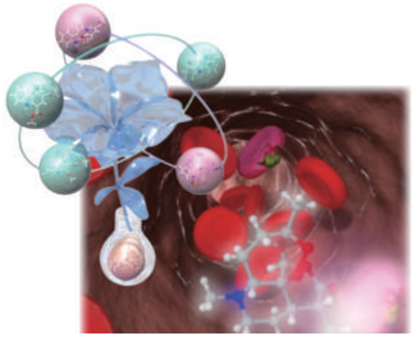
Natural product-inspired molecular design, assembly-line synthesis, and creation of functions

In the Oguri laboratory, we are developing concise and flexible synthetic approaches to generate functional molecules based on the structure, biosynthesis, and biological roles of natural products as the evolutionary consequences of life. With integration of the biosynthetic logics and modern strategies of organic synthesis, biomimetic modular assembly lines were devised to gain divergent access to skeletally diverse molecules. The densely functionalized natural products and their variants have been utilized as covalent ligands to investigate chemical genetic and medicinal research relevant to infectious diseases and tumors. We are also exploring the interface of natural products and supramolecular chemistry by harnessing the largely untapped potential of natural products bearing specific molecular recognition capabilities. Our research and educational activities are aimed at nurturing the next generation leaders who create new values and explore the frontier of chemical research and industries.



Modular assembly line synthesis of skeletally diverse molecules (Ref. 1–5)

Organic synthesis that diversifies the three-dimensional structures through generation of diverse molecular scaffolds is becoming more important as an innovative technology toward the creation of functional substances based on the regulation at atomic/molecular levels. We are exploring synthetic approaches that not only mimic biosynthetic processes generating a wide variety of secondary metabolites but also redesign the modular divergent assembly lines. Our synthetic campaigns aim to develop a concise and versatile synthetic process allowing systematic generation of “scaffold variations” through programmable manipulations of a common multipotent intermediate (Fig. 1). These investigations are formulating advanced synthetic strategies to gain expeditious and cost-effective access to the natural product-relevant chemical space with diversification of skeletal, stereochemical, and functional group properties.

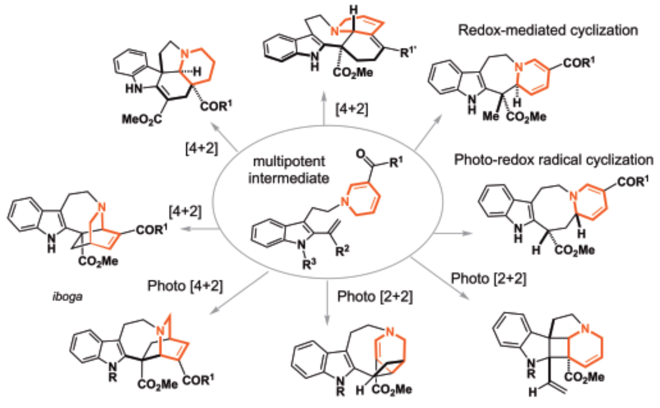


Fig. 1. Biogenetically inspired synthesis of skeletally diverse indole alkaloids.

Redesigning Biosynthetic Process: Chemo-enzymatic Hybrid Synthesis (Ref. 6–7)

Plants and microorganisms have evolved the enzymatic machinery to efficiently biosynthesize natural products under physiological conditions. Our approach focuses on the merger of the *in vitro* engineered biosynthesis and the precise organic synthesis to facilitate the generation of natural product-based complex molecules towards drug discovery and chemical genetic investigations. By streamlining enzymatic reactions and chemical manipulations, we developed a chemoenzymatic hybrid process that allowed very rapid and operationally simple access to the densely functionalized pentacyclic alkaloidal skeleton *within a single day* from two simple synthetic substrates (Fig. 2). The judicious choice of the designer substrates for the enzyme SfmC allowed divergent total syntheses of saframycins and jorunnamycins in just 4–5 pot, which could be a versatile platform for the collective synthesis of natural products and their variants.

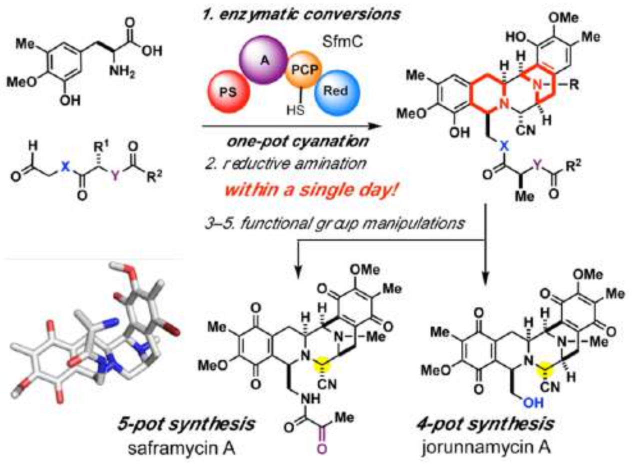


Fig. 2. Chemo-enzymatic hybrid synthetic process.

Chemical biology utilizing covalent ligands (Ref. 8–9)

Artemisinin and its derivatives, the active ingredients of traditional Chinese medicine, have revolutionized the malaria chemotherapy. Reductive cleavage of the peroxide bridge by intracellular heme iron generates carbon radical species responsible for the formation of a covalent linkage with biomolecules and the enhancement of oxidative stress. The 6-aza-artemisinins were designed by replacing a stereogenic carbon center at C6 with a nitrogen, which allowed both structural modification of the hitherto unexplored C-ring and concise *de novo* synthesis (Fig. 3). By exploiting the natural products variants, we will streamline concise synthesis, screening, and identification of the covalent complexes composed of the synthetic ligands and biomacromolecules. These efforts are expected to facilitate the development of lead candidates for the treatment of infectious diseases and cancers.

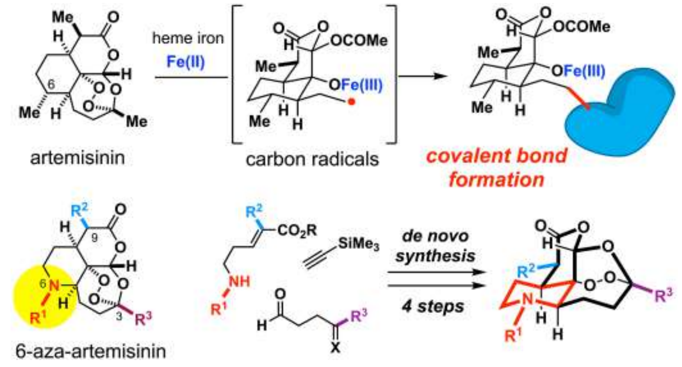


Fig. 3. Mode of action of artemisinin and modular *de novo* synthesis of 6-aza-artemisinins.

Generation of CPL emitting macrocycles utilizing natural product-based scaffolds (Ref. 10)

Our laboratory focuses on the development of self-assembling nanostructures by exploiting the precise molecular recognition capabilities of natural products. We have developed a modular synthetic approach to generate chiral D_2-symmetric figure-eight-shaped macrocyclic molecules based on a chiral C_2-symmetric alkaloidal scaffold (Fig. 4). This platform enables precise tuning of the angle, distance, and length between intersecting chromophores, providing unprecedented control over their spatial arrangement. These macrocycles exhibit bright circularly polarized luminescence (CPL), making them highly promising for applications in chiroptical materials. By integrating natural product chemistry with materials chemistry, our approach bridges these two fields and represents a significant step forward in the design of advanced molecular systems.

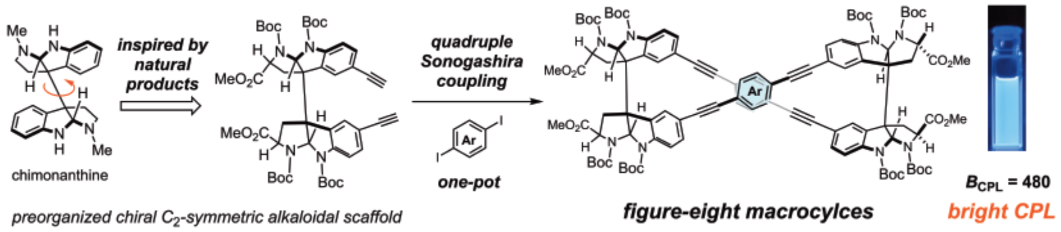


Fig. 4. Generation of high-intensity CPL emitting macrocycles utilizing alkaloidal scaffolds.

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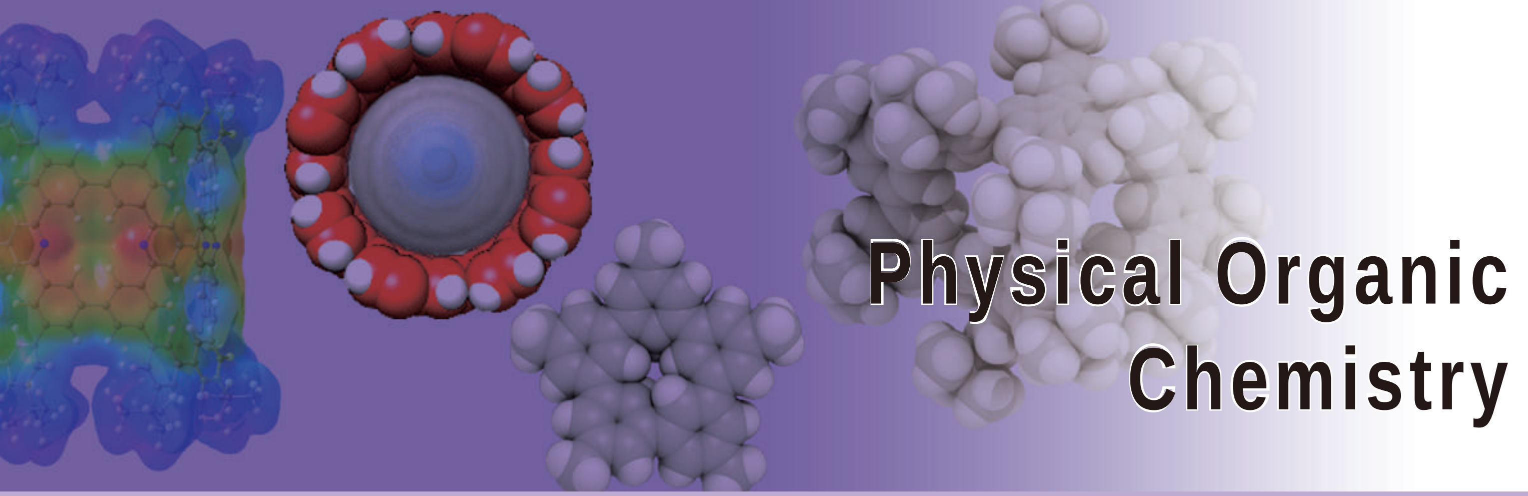

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PHYSICAL ORGANIC CHEMISTRY: Seeking for new molecular architectures, new materials and new principles

Aromatic molecules have played a pivotal role in organic chemistry since the discovery of benzene by Faraday and the proposal of the structure by Kekulé. Their importance continues to grow in the modern world. For example, they serve as one of the important building blocks of "molecular machines" and "optoelectronic materials" that could lead the progress and growth of our society. Here in this group, we are exploring aromatic molecules having novel structures and functions, giving birth to "molecular bearings with inertial rotation", "aromatic hydrocarbon materials for the optoelectronic application", "phenine nanocarbons" and "diamond twin". By creating novel molecules with the aid of organic synthesis, we are seeking for the discovery of ground-breaking principles and functions in the molecular world.

Finite carbon nanotube molecules and their nanoscience

Carbon nanotubes are unique materials of nanometer size with characteristic curved π-electron systems. Although there are growing expectations for nanotechnology utilizing carbon nanotubes, it has yet to go beyond the realm of nanoscience. This is because carbon nanotubes are a mixture of various kinds of structures, and such heterogeneous mixtures cannot possibly be handled as "molecular entities" that should bring in-depth understanding in languages of molecular science. We have created finite carbon nanotube "molecules" with rigid cylindrical structures via the bottom-up synthesis and revealed their anomalous chiroptical properties. With these molecules, we further exploited host-guest chemistry to find that various guest molecules can be encapsulated and that these guest behave as "rotors" to emerge as "molecular bearings" that achieve ultrafast GHz-THz rotations in the inertial regime in solid state (Figure 1, Reference 1).

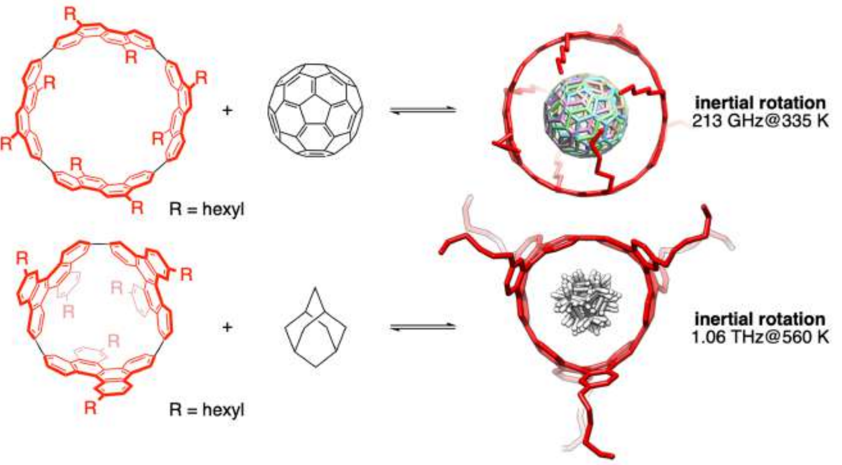

Figure 1. Molecular bearings composed of finite carbon nanotube molecules and their inertial rotation

Aromatic hydrocarbon materials for the optoelectronic application

Development of modern materials chemistry is accelerated by the design and synthesis of new organic molecules, especially, π-conjugated molecules. Among various kinds of design principles being explored, our simple molecular design adopting two basic elements, i.e., hydrogen and carbon atoms, has enabled the development of cutting-edge organic materials. Thus, we have found that the hydrocarbon materials can possess carrier transporting abilities both for holes (+) and electrons (–) and facilitate recombination of these carriers in organic light-emitting devices (OLEDs), and such multipotency has realized highly efficient OLEDs in novel single-layer architectures. The findings renovate both the molecular design and device architectures of OLEDs for highly efficient emissions, and classic design relying on multiple-element molecules and multi-layer architectures are now being overwritten by simple designs (Figure 2, Reference 2).

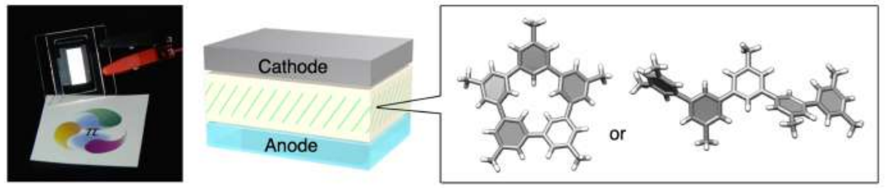

Figure 2. Highly efficient, single-layer organic light emitting devices

Gigantic nanocarbon molecules, "phenine nanocarbons"

Development of modern materials chemistry is accelerated by the design and synthesis of new organic molecules, especially, π-conjugated molecules. Among various kinds of design principles being explored, our simple molecular design adopting two basic elements, i.e., hydrogen and carbon atoms, has enabled the development of cutting-edge organic materials. Thus, we have found that the hydrocarbon materials can possess carrier transporting abilities both for holes (+) and electrons (–) and facilitate recombination of these carriers in organic light-emitting devices (OLEDs), and such multipotency has realized highly efficient OLEDs in novel single-layer architectures. The findings renovate both the molecular design and device architectures of OLEDs for highly efficient emissions, and classic design relying on multiple-element molecules and multi-layer architectures are now being overwritten by simple designs (Figure 2, Reference 2).

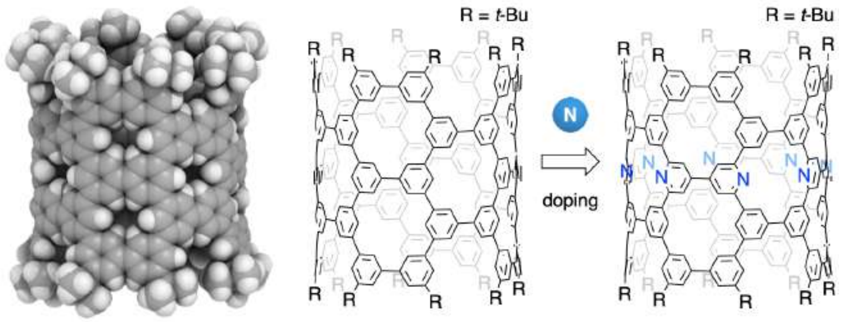

Figure 3. Phenine nanotubes (hydrocarbon and nitrogen-doped variants)

Diamond twin

As the key features of the beauty of diamonds, mathematicians disclosed the presence of "maximal symmetry" and "strong isotropy" in the network of sp3 carbon atoms, which led them to a discovery of a diamond twin. The diamond twin is a hypothetical network of sp2 carbon atoms with the identical geometrical features, although its existence has been theoretically questioned due to the strained structure composed of decagonal cages. The imaginary network (pollux) has been realized by adopting phenine as the trigonal planar vertices in a form of a minimal cage molecule, polluxene (Figure 4, Reference 4). The molecular structure in solution and crystals has been revealed to disclose the presence of a geometrically unique cage structure. Chirality has been one of the anomalous features of pollux/polluxene, which has been unveiled by the synthesis of a chiral polluxene molecule and its chiral resolution. We expect to find unique properties and applications with the cage structure with high symmetry and unique chirality.

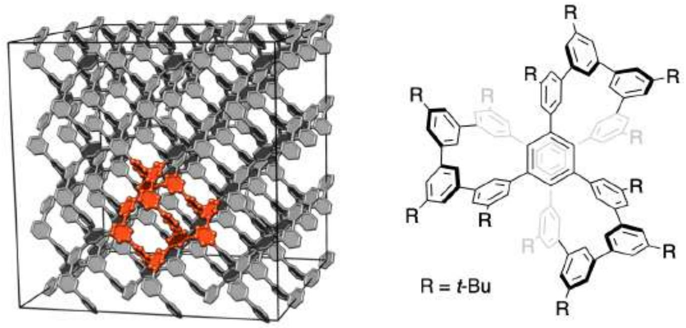

Figure 4. Phenine pollux and its minimal cage, phenine polluxene

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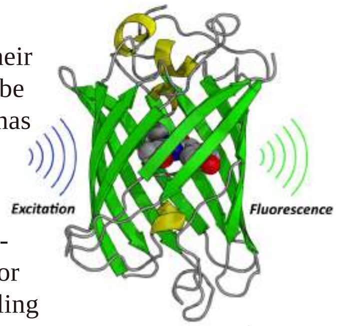
Engineering and directed evolution of protein-based tools



Fluorescent proteins (FPs) are colorful "glowing" proteins that are found in jellyfish, anemone, and coral. These proteins have the unique ability to generate a visibly-fluorescent chromophore within their structure. Amazingly, the DNA that encodes a FP can be introduced into practically any animal and be properly expressed, making the tissues of the animal fluorescent. Genetically encoded fluorescence has revolutionized many areas of cell biology because it enables researchers to use fluorescence microscopy to "see" structures and cellular processes that would normally be invisible.

Cutting edge research in the Campbell group involves converting these proteins into dynamic indicators that change their fluorescence intensity or color in response to a specific biochemical change. For example, FP-based indicators enable biologists to visualize the invisible world of intracellular signaling pathways, such as the biochemical response of cells to drug treatment, and the electrical activity of neurons in the brains of model organisms. We have a particular focus on broadening the spectrum of available colors and pushing to ever redder wavelengths. Tissue is more transparent to redder light, and so red-shifted indicators can let us see deeper into tissue.

Researchers in the Campbell group obtain interdisciplinary training in protein engineering, chemical biology, spectroscopy, molecular biology, and cell biology. All of the basic research methods are well established in our group *(1)*, but can be easily extended and applied to many new and unexplored research problems. This training is excellent preparation for a career in the biotechnology field in either academia or industry.

Past Highlights 1:Pushing the limits of FP technology using directed evolution

The Campbell research group has expanded the toolbox of coral-derived FP variants for use in a wide variety of application areas, including the construction of FP-based indicators. For example, we have developed cyan, yellow, and green-to-red photoconvertible FPs. These new FPs enabled a number of new applications including simultaneous imaging of multiple biological processes in single cells *(2)* and improved super-resolution imaging. In later work, we developed dimerization-dependent FPs (ddFPs) that increase their brightness when they form a heterodimeric complex *(3)*. This technology provided a powerful new approach for detecting protein-protein interactions in live cell. In more recent work, we developed a photocleavable protein (PhoCl) as a fundamentally new class of optogenetic tool to control protein function with light ***(4)***. PhoCl can be used light-activated transcription, gene recombination, manipulation of protein localization, and activation of enzyme activity.

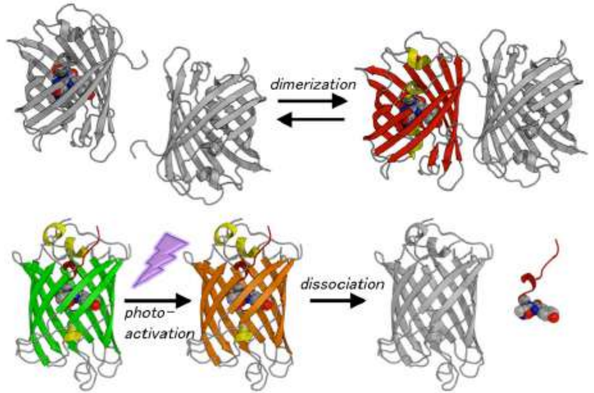


Figure 1. Novel types of optogenetic tools
We used directed evolution to produce novel fluorescent proteins as tools for imaging (upper: ddFP) and controlling (lower: PhoCl) protein function with light.

Past Highlights 2: Engineering a palette of visible fluorescence neural activity indicators

Visualization of neural activity in model organisms is a powerful approach for understanding brain function and neurodegenerative diseases. To visualize neural activity we require indicators for changes in ion concentrations, membrane voltage, or neurotransmitters. The Campbell lab launched the field of multicolor neural activity imaging with the development of a colorful palette of Ca^{2+} indicators known as the GECO series *(5)*. We initially engineered a variety of colors of Ca^{2+} indicator, including the red fluorescent R-GECO1 which has served as the basis for many other red fluorescent indicators from labs worldwide. Versions of R-GECO1 are freely used by hundreds of research groups around the world to address a diverse range of biological problems. We also reported the first near-infrared (NIR) GECI, called NIR-GECO1 ***(6)***.

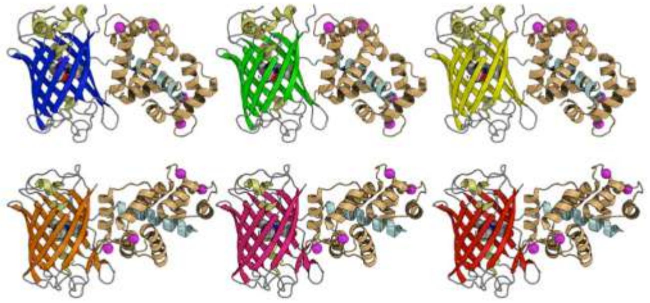


Figure 2. GECO series
The Campbell group is a world leader in the development of genetically encoded Ca^{2+} indicators. We have engineered a family of genetically encoded Ca^{2+} indicators, designated the GECO series, with a range of colors and Ca^{2+} affinities.

Current Theme 1: Indicators for intracellular metabolites

It is increasingly recognized that many diseases have causes related to changes in the way cells access or use biological energy sources. One important example is neurodegenerative diseases that are associated with changes in brain energy metabolism and, specifically, the availability of lactate. Unfortunately, we currently lack tools for multiparameter visualization of the full metabolism of a cell, and so we cannot visualize the extent to which a single cell is using each of the fundamental metabolic pathways for accessing and using biological energy. The Campbell lab is now developing high performance indicators for cell metabolic pathways and enable the full metabolism of a cell to be visualized for the first time! For example, we recently reported a series of high-performance indicators for intracellular and extracellular lactate *(7, 8, 9)*.

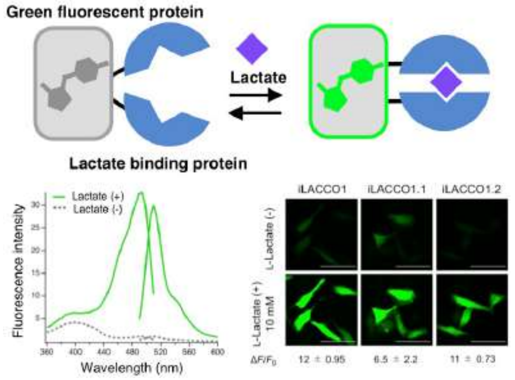


Figure 3. Genetically encoded green fluorescent lactate indicator (iLACCO)
Lactate plays a critical role in metabolism. The Campbell group developed iLACCO1 series using directed protein evolution. Upper: schematic cartoon of the biosensor mechanism. Lower: fluorescence spectra (left) and cell images (right) in response to lactate.

Current Theme 2: Indicators based on hybrid chemigenetic fluorescent proteins

An emerging approach to overcome some limitations of standard genetically encoded biosensors, in particularly in the near-infrared (NIR) region of the spectrum, are chemigenetic FPs. A chemigenetic FP is a hybrid system in which a synthetic dye is designed to covalently attach to a specific protein expressed in the cell or tissue. The Campbell lab has started converting chemigenetic FPs into a new generation of high performance indicators *(10)*. We are also working on another design of chemigenetic indicators using FPs and synthetic ligands *(11)*.

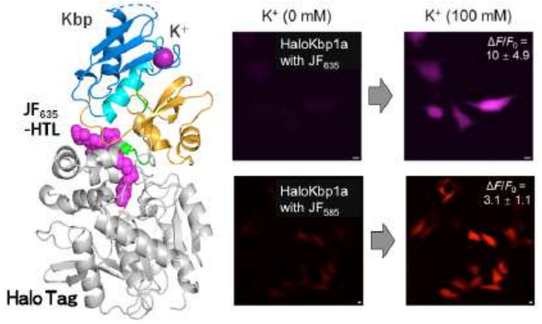


Figure 4. Chemigenetic fluorescent indicator for K^+
A chemigenetic fluorescent protein is a "hybrid" molecule that is made of a synthetic small fluorescent molecule and a protein. Shown is the 3D structure (left) and cell images (right) of our chemigenetic K^+ indicator called HaloKbp1a.

Current Theme 3: Expanding the color palette of NIR indicators

Expanding the indicator color palette into the NIR will create a variety of new opportunities for multiplexed and deep tissue imaging. The "NIR window", where tissue is most transparent, extends from ~650 up to ~1350 nm. Based on the success of NIR-GECO1 *(6)*, the Campbell lab is pioneering the development of genetically encoded indicators that absorb and fluoresce in the NIR window *(12)*. These indicators will be ideally suited to multiplexed imaging applications with existing visible wavelength indicators and optogenetic tools, as well as to perform functional in vivo optical imaging deeper inside model animals.

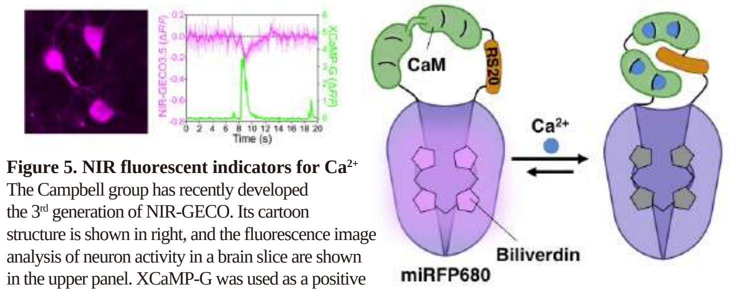


Figure 5. NIR fluorescent indicators for Ca^{2+}
The Campbell group has recently developed the 3rd generation of NIR-GECO. Its cartoon structure is shown in right, and the fluorescence image analysis of neuron activity in a brain slice are shown in the upper panel. XCaMP-G was used as a positive control sensor.

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Solid State Chemistry

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Crossroad of solid-state chemistry and electrochemistry

When atoms condense to form molecules or solids, unexpected physical properties emerge. Just as two atoms side by side can bond, forming new electronic states; aggregates of many atoms can generate countless new states, producing new materials with properties that are still unknown. In our laboratory, we focus on the syntheses of these new materials and on the discovery of their physical and chemical properties. We are also interested in the phenomena occurring at the interfaces of these materials.

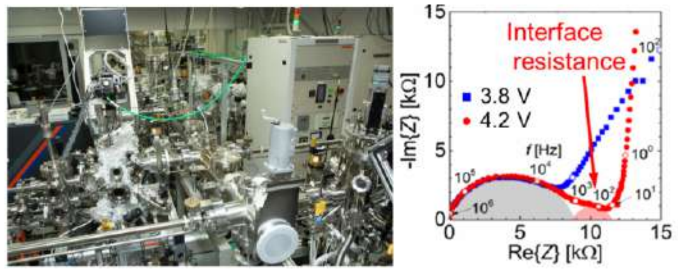
In addition to the fundamental aspects, our group also focuses on application-oriented research. At the intersection of solid-state chemistry and electrochemistry, our research targets environmental and energy materials. To this end, we create new materials, construct new devices, and evaluate their atomic and electronic structures using state-of-the-art measurement techniques. We explore solid-state chemistry from both the microscopic and the macroscopic perspectives.

Major Direction of Research

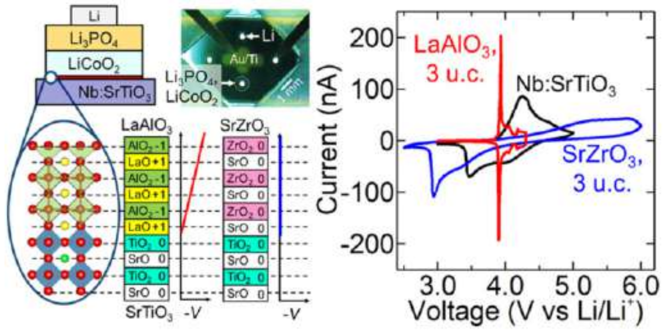
Research on All-solid-state Li battery

The development of high-voltage, high-capacity batteries is critical toward the advent of a sustainable society. Among the existing battery types, the all-solid-state Li batteries promise to realize the next-generation batteries by replacing the organic electrolytes used in conventional Li-ion batteries with solid electrolytes.

One major challenge to increasing the power of all-solid-state Li batteries is the improvement of the Li-ion conductivity across the interfaces of electrodes and electrolytes (electrode-electrolyte interface). We fabricate all-solid-state thin-film Li batteries to elucidate the Li-ion transport properties at the ideal electrode-electrolyte interfaces. Our group has already demonstrated superior Li-ion conductivity at the controlled electrode-electrolyte interface over that of liquid electrolytes. Further, we have proven that both the atomic disorder and the presence of protons in the vicinity of the interface are the origins of interfacial resistance



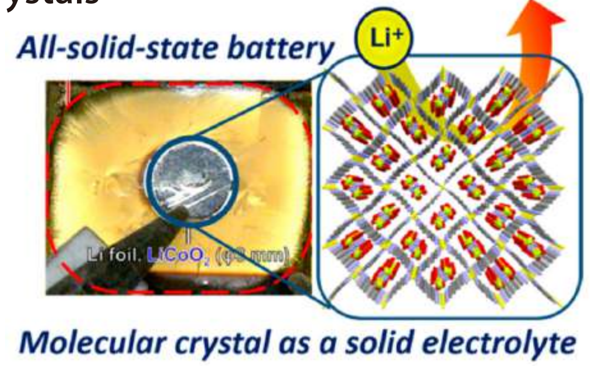
Left: Developed equipment for thin-film battery fabrications.
Right : The world's smallest interfacial resistance has been achieved.



Control of battery operating characteristics through interface control

Development of new functions in molecular crystals

Molecular crystals—periodic arrays of organic molecules—have recently gained much attention. The unique electronic, energy-conversion, and ion-transport properties combined with the mechanical flexibility of these molecular compounds are expected to produce exotic devices. We aim to develop the solid-state ionics of molecular crystals by introducing our knowledge of inorganic-materials design. Our group has already used this approach on the LiFSA(SN)$_2$ molecular crystal to demonstrate an all-solid-state Li battery with high Li-ion conductivity [5]. In addition, we are developing metal-organic-framework (MOF) thin films and investigating their electronic properties for electronics applications.



Application of molecular crystals to all-solid-state Li batteries

Accellerating chemistry research using machine learning and robots

This project aims to shift a paradigm in creating a new perspective on materials science research. Our group is currently developing an "autonomous experiment system" that introduces machine learning and robots to materials-science research, opening an enormous search space for material exploration. Using this system, future researchers will be able to utilize a large amount of data and to immerse themselves in more creative research.

Our system autonomously determines the optimum synthesis conditions that maximize the properties of films. Using Bayesian optimization, a machine learning technique, this optimization has been achieved at a rate that is 10 times faster than the average human researcher. Currently, we are tuning the machine learning algorithms for chemistry experiments; we are expanding this autonomous experiment system to investigate the syntheses of substances—both organic and inorganic, solid and liquid —to construct the new perspective on materials science.

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Analytical Chemistry

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Opto-bioanalysis Inspired by Chemistry and Biology

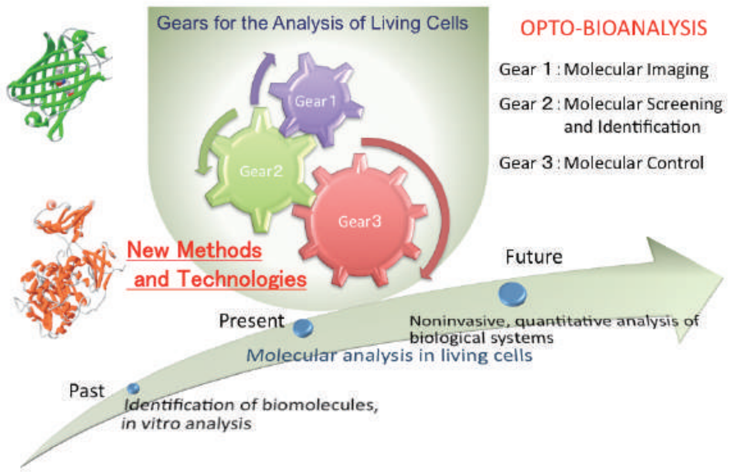

Fig. 1. Major three themes in the analytical chemistry laboratory.

We are studying to develop novel methods for the analyses of biological molecules and systems in living cells. The goals of our research activities are 1) to develop analytical methods for visualizing functions of biomolecules and their dynamics in living cells and animals, 2) to develop methods for identifying new molecules involved in intracellular signaling, and 3) to create optogenetic modules that control enzymatic and receptor activities with external light. We are also striving to develop analytical reagents and methodologies based on protein structures and functions to achieve discoveries of new biological phenomena (Figure 1). Our works will contribute not only to basic science to reveal the mechanisms of molecules on the life science field, but also to technological applications such as new drug development through providing a new chemical library screening method.

Methods of imaging biomolecules in living cells

Recent advances in analytical methods, such as capillary electrophoresis and mass spectrometry, have made great contributions to the progress in biological research. It should be noted, however, that such analyses are, for the most part, destructive or invasive because they need cell lysates before detection of a target molecule. The true physiological functions of biomolecules could be elucidated if their functions and dynamics would be analyzed noninvasively in living cells and animals. We are developing novel imaging methods for visualizing functions and dynamics of biomolecules, so as to determine when, where, and how much intracellular small molecules, RNAs, and proteins exhibit their functions. The representatives are techniques of fluorescence imaging to visualize RNAs and protein-protein interaction, methods of super-resolution imaging to visualize protein cluster formation, and methods of detecting intracellular protein phosphorylation and enzymatic activities in living cells (Figure 2). In these achievements, we have created analytical tools for molecular recognition and photo-signal conversion through protein engineering using particular proteins of which structures and functions have been well investigated. We are also developing Raman microscopic system for noninvasively investigating biomolecules without any labeling techniques.

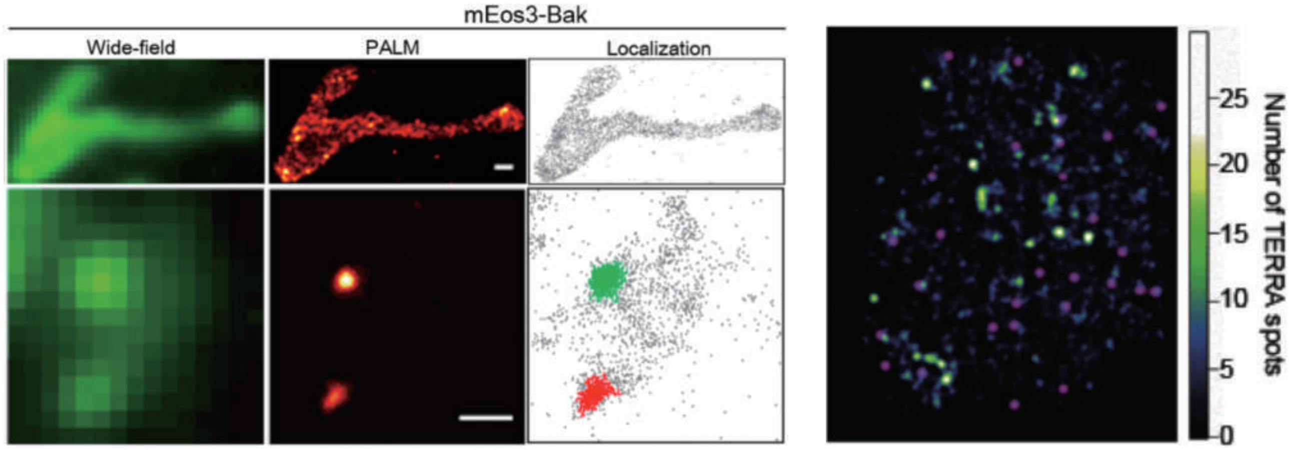

Figure 2. Left: Superresolution single molecule images (PALM) of Bak proteins on the mitochondrial membrane.
Right: Localization of Telomeric RNAs. Purple dots indicate telomere regions in the nucleus.

Identification of molecules to control biological functions.

The identification of novel biomolecules such as functional peptides and chemical compounds depends largely on the development of screening methods. Thus, novel high-performance screening method in combination with a wide variety of chemical and genetic libraries will bring discovery of novel effective compounds for target biomolecules. We are developing high-throughput screening systems for large-scale chemical libraries using fluorescent and bioluminescent proteins. We have already established different cell lines for screening the compounds that regulate G-protein coupled receptors (GPCRs) (Figure 3). We have also developed new methods to identify functional peptide sequences that transport a protein into different organelles such as mitochondria and endoplasmic reticulum. Such new screening system will lead deeper understanding of new physiological phenomena in living systems.

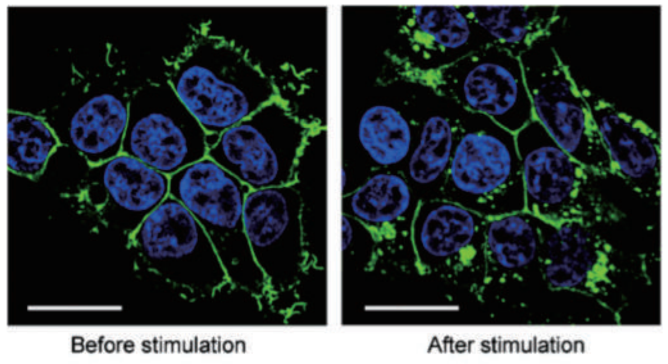

Fig. 3. Localization alteration of GPCR (somatostatin receptor) (green). Stimulation with somatostatin induces GPCR-βarrestin interaction, results in internalization of the GPCR.

Optogenetic methods for controlling biological activities using external light

Functional control of biomolecules in living cells has mainly been achieved by the use of chemical compounds such as inhibitors of enzymes. However, Optogenetics has revolutionized bioanalysis by providing means to control cell signaling directly with a spatiotemporal manner in discrete cell types. We are developing new functional protein modules to manipulate enzymatic and membrane receptor activities in living cells and animals using external light. For example, we have succeeded in controlling the activity of a kinase (Akt) to manipulate intracellular signaling quantitatively. We have also developed a method for origomerization of a plasma membrane receptor (DCC) to control the direction of neural axon elongation (Figure 4). These light-driven controlling system promises to revolutionize our understanding of intracellular signaling and cellular communications in living animals.

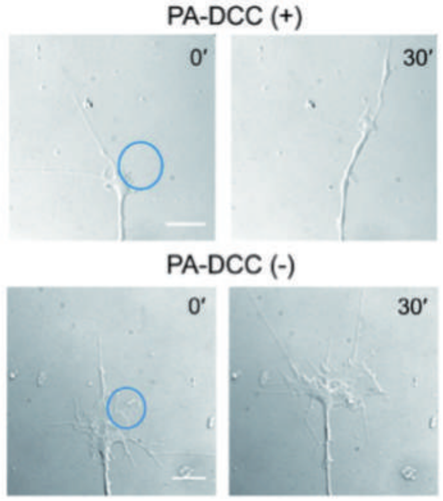

Fig. 4. Photo control of the direction of neuronal axon elongation. The axon of neurons expressing photo-activatable DCC (PA-DCC) are guided to elongate to the photo-irradiated direction (blue circles).

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Inorganic Chemistry

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At-will motion of ionic and redox species towards energy chemistry

This century is featured by the ubiquitous access for information and electric vehicles, which stand on energy science and technology. We propel “energy coordination science” by the creation of the nanospace, the size of which is comparable to molecules and ions,controlling the inter-molecular or inter-ionic interaction, and targeting the unique behavior of ions and physical properties. Functional molecules are often regarded as molecular machines or robots, and in addition to the construction, we intend to the construction of a molecular system by the functional linking of these molecules.

Energy conversion by thermo-responsive molecular science

Thermocell is a group of thermoelectric devices that uses the thermal shift of redox equilibrium to generate electric power from a temperature difference. Thermocells can be constructed from inexpensive materials such as iron, iodine and organic molecules. The cost of the electricity generated by thermocells is estimated to be reduced to one-fifth of the conventional semiconductors. Further, the Seebeck coefficient (voltage generated per unit temperature difference) of thermocells is typically one-order-of-magnitude larger than the semiconductors, which means thermocells can generate higher voltage from the same temperature difference compared to the semiconductors. We are trying to make a paradigm shift in thermocells by combination with the thermo-responsive molecular science.

We demonstrated that a thermo-responsive polymer attached with a redox-active group can generate thermal voltage from a temperature difference (Fig. 1a). This polymer has a unique thermo-responsive and redox-responsive properties. Below room temperature, this polymer is soluble in water (called the coil phase) at both its oxidized and reduced form. In contrast, when the tempearture is increased above room temperature, this polymer starts to aggregate with each other (called the globule phase) at its reduced form while its oxidized form stays in the coil phase. This phase behavior suggests that this polymer can undergo the redox-responsive coil–globule phase transition above room temperature. We found that the Seebeck coefficient increases to 2 mV K^{-1} at the temperature region at which this unique phase transition takes place (Fig. 1b).

We are studying variety of molcules and polymers showing the unique thermo- and redox-responsive phase transition. The changes of their solvation structure induced by the redox reaction is the key to enhance the Seebeck coefficient of thermocells, and one of our goal is to use thermocells for waste-heat recovery.

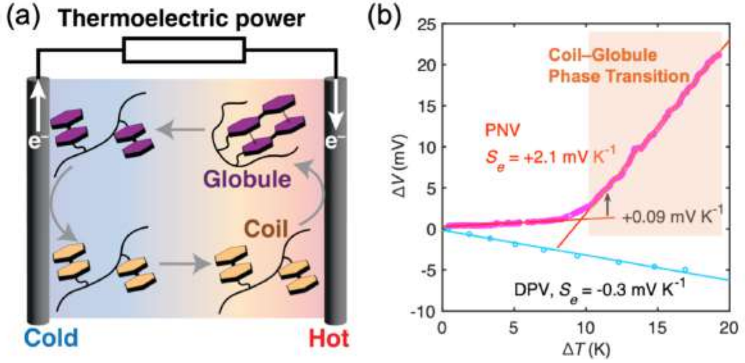


Fig. 1 (a) Thermocell generating power from the coil–globule phase transition of a thermo- and redox-responsive polymer (b) Thermoelectric voltage produced from redox equilibrium of this polymer (PNV)

Redox-responsive phase transition of soft matter

Soft matter is a class of materials showing “soft” nature, often represented by polymers, proteins, colloidal dispersions and liquid crystals for example. We study the interaction between the solvent and the polymer chains or the small molecules which constitute the soft matter. Our primary interest lies on the control of intermolecular force by redox reaction to change the phase of soft matter. Phase change of materials in general is often accompanied with release/absorption of heat or drastic changes in volume and stiffness. If we can control the phase transition by electrochemical method, the materials physical property can be accurately and precisely controlled by electric signal. We can apply this function in various application such as thermoelectric conversion, smart windows (Fig. 2), sensors and actuators.

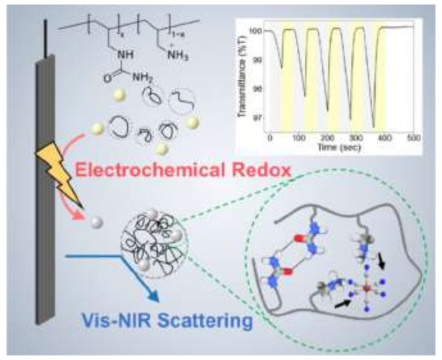


Fig. 2 Phase transition of a cationic polymer in response to the electrochemical redox reaction of an iron complex. The transmittance of visible–near infrared light through this polymer solution changes reversibly in response to the electric stimuli.

Exploring pore chemistry and functional design of metal–organic frameworks

Metal–organic frameworks (MOFs) are crystalline porous materials constructed by the coordination of metal ions and organic linkers, possessing ordered and periodic networks. The physical and chemical environments of the MOF pores can be readily tuned by taking advantage of their synthetic versatility, which enables researchers to design various MOFs with fine architectures for different applications like gas separation, catalysis, sensing, etc.
Our group studies solid-state ionics and redox chemistry in MOF pores, deeply engaged in exploring the confined pore effect on host-guest interactions, designing pathway-selective self-assembly structures, and investigating the electrochemical redox activity of MOFs. We have reported various MOFs with unique physical and chemical property. For example, our group has developed a solid acidic MOF (Zr-mel-NH_4) featuring exceptional stability in aqueous ammonium environments and strong acid sites (Fig. 3a). Benefiting from the ion-exchange sites within the uniform nanoporous structure, Zr-mel-NH_4 is the first MOF capable of selectively extracting ammonium ions from saltwater (Fig. 3b). Zr-mel-NH_4 finds potential application in the ammonia recovery from wastewater to support the nitrogen economy in the society.

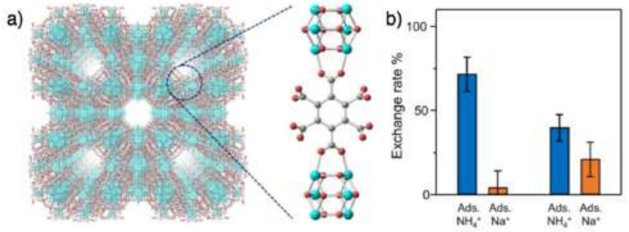
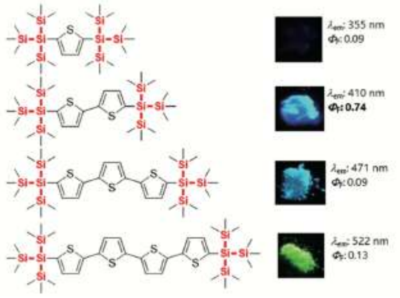


Fig. 3 (a) Crystal structure of Zr–mel–NH_4. Blue, red and gray balls show Zr, O and C atoms, respectively. (b) Selective adsorption of NH_4^+ by Zr–mel–NH_4 in saltwater.

Functional Organosilane Compounds

New molecular designs and synthetic strategies are also investigated to synthesize functional materials based on group 14 elements. Palladium-catalyzed arylation of secondary group 14 hydrides and 2,2'-diiodoarenes gave the corresponding dibenzometallole in good yields, and we succeeded in tuning the solid-state emission properties by the substituents on an aromatic ring. In addition, we reported the synthesis of aryl oligosilanes in high yield without Si-Si bond cleavage. These compounds intensely emitted in the solid-state, and they were applied to organic EL materials.



Structures of aromatic oligosilanes and their luminescence under UV irradiation. These compounds show intense emission in the solid-state.

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Functional Inorganic Chemistry

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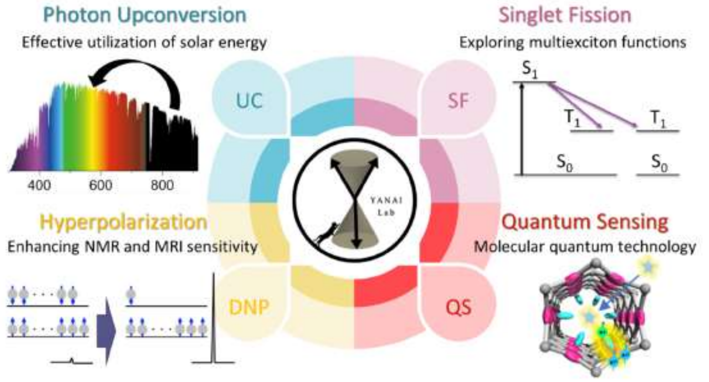
Creation of Functional Materials with Optical and Spin Properties

The Yanai Laboratory aims to achieve “new materials and new functions” that will bring about innovation in energy, environment, medicine, and quantum information science by making full use of the power of “molecules” and “light”. In terms of optical functions, we are developing materials for light energy conversion that involve multiple excitons, such as photon upconversion and singlet fission. In terms of spin functions, we are developing materials that make NMR and MRI more sensitive using hyperpolarization and enable sensing using quantum coherence. In these fields, we are conducting research with the motto “functions that only we can produce!” by investigating new interdisciplinary fields. In addition, the Yanai Laboratory is focusing on the development of researchers who can pioneer new fields by acquiring (1) basic research skills, (2) the ability to “break into” different fields, and (3) the ability to generate new ideas, as well as the development of human resources who can play an active role worldwide by being involved in and leading international joint research.



Photon Upconversion

Photon upconversion is a wavelength conversion technology that converts low-energy light with long wavelength into higher-energy light with shorter wavelength. By utilizing the long-lived photoexcited triplet state of molecules, it is possible to upconvert weak light with low intensity, such as sunlight, with high efficiency. Upconversion at such low excitation light intensity is difficult to achieve using other methods, and is a unique optical function of molecules.

Upconversion from near-infrared to visible light is strongly desired for applications in the creation of renewable energy, such as solar cells and photocatalysts, and in photobiology, such as optogenetics and photodynamic therapy. We have succeeded in upconverting near-infrared light to visible light with high efficiency using only molecules, and have also reported the first optogenetics using molecular upconversion. In addition, upconversion from visible to UV light is expected to be applied to artificial photosynthesis, antibacterial and antiviral applications. We have developed the first highly efficient upconversion chromophores that convert visible light to UV light with an efficiency of over 20%, and have succeeded in developing new molecules that function even with sunlight and indoor light. We are currently working seamlessly on everything from basic research to application development with the aim of commercializing upconversion materials.

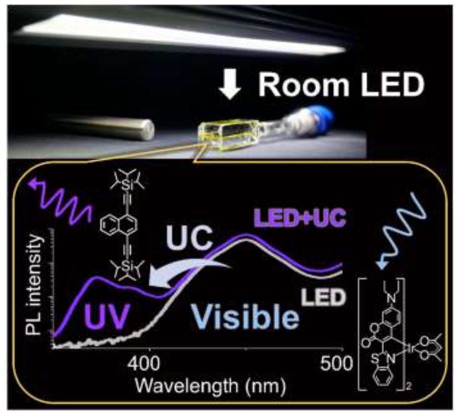


Fig. 1 Visible-to-UV photon upconversion

Hyperpolarization of Nuclear Spins

NMR and MRI are measurement techniques that are indispensable to modern chemistry, biology, and medicine, but they have the fatal flaw of being extremely insensitive. For this reason, MRI can only observe water, which is abundant in living organisms, and it is difficult to observe in cells using NMR because of their low-concentration proteins. A technique for increasing the sensitivity of MRI and NMR using electron spin is called hyperpolarization. We are aiming to increase the sensitivity of MRI and NMR at room temperature and body temperature by using photoexcited states in hyperpolarization.

A hyperpolarization method using photoexcited triplet states has mainly been studied in the field of quantum physics using single crystals, and it has been difficult to apply it to biology. Therefore, by combining materials chemistry with the quantum physics of triplet hyperpolarization, we have developed original nanomaterials that can transfer polarization to biomolecules and original polarization sources that can be directly dispersed in water and biomolecules.

With the aim of creating ultra-sensitive systems to be used with MRI and NMR around the world, we are developing new triplet polarizing agents that will make tumor MRI probes ultra-sensitive, and are also taking on the challenge of developing ultimate technologies such as hyperpolarization in vivo.

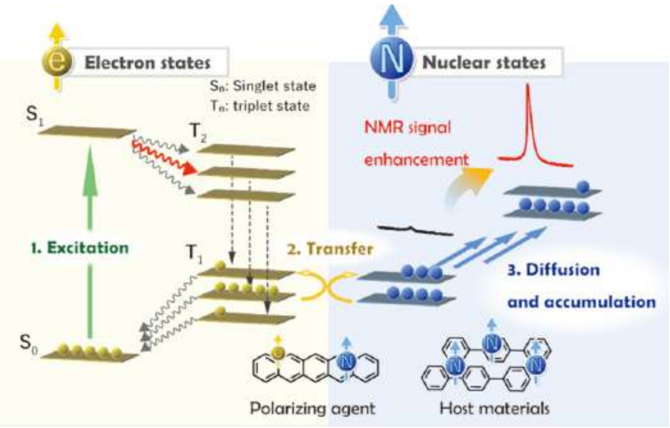


Fig. 2 Mechanism of nuclear hyperpolarization using photoexcited triplet states

Quantum Sensing

In the midst of the second quantum revolution, we are trying to find our own answer to the question “What role should chemistry play in the quantum age?” by looking at the interface between quantum and life. While many quantum phenomena function in clean, dry environments, life phenomena are complex and wet. It is hoped that by applying quantum technology to living systems, it will be possible to understand and control biological events with unprecedented precision. We believe that we can use the power of chemistry to impart the desired quantum properties to molecules, and that this can be used to elucidate and control biological phenomena. We call this new interdisciplinary field “quantum biochemistry”.

Quantum bits (qubits) made up of molecules have the advantage of being small in structure and being able to be precisely controlled. Efforts to realize quantum sensing using molecular qubits are still in their infancy. We are proposing a quantum coherence that can respond to chemical stimuli by incorporating a molecular qubit into nanoporous metal-organic frameworks (MOFs). By combining MOFs with various structures and qubits, we aim to realize a “Quantum Nose” that can sense specific chemical species with ultra-high sensitivity. We are also using singlet fission as a method for imparting quantum properties to molecules. Singlet fission is a phenomenon in which a singlet exciton splits into two triplet excitons, and we are also working on quantum sensing that uses the strongly coupled triplet pair state generated as an intermediate of singlet fission.

Fig. 3 Quantum sensing by the integration of molecular qubits and MOFs

Design and Synthesis of Supramolecular Metal Complexes

We are also taking on the challenge of designing new supramolecular metal complexes. For example, we have synthesized molecular capsules and porous crystals with intricate low-symmetry structures, using novel macrocyclic compounds with asymmetrically arranged coordination sites as ligands. In addition, we are working on the construction of highly functional bio-supramolecular systems by conjugating metal complexes with DNA molecules. This includes the development of DNA-based molecular machines and computational circuits driven by metal ions as external stimuli.

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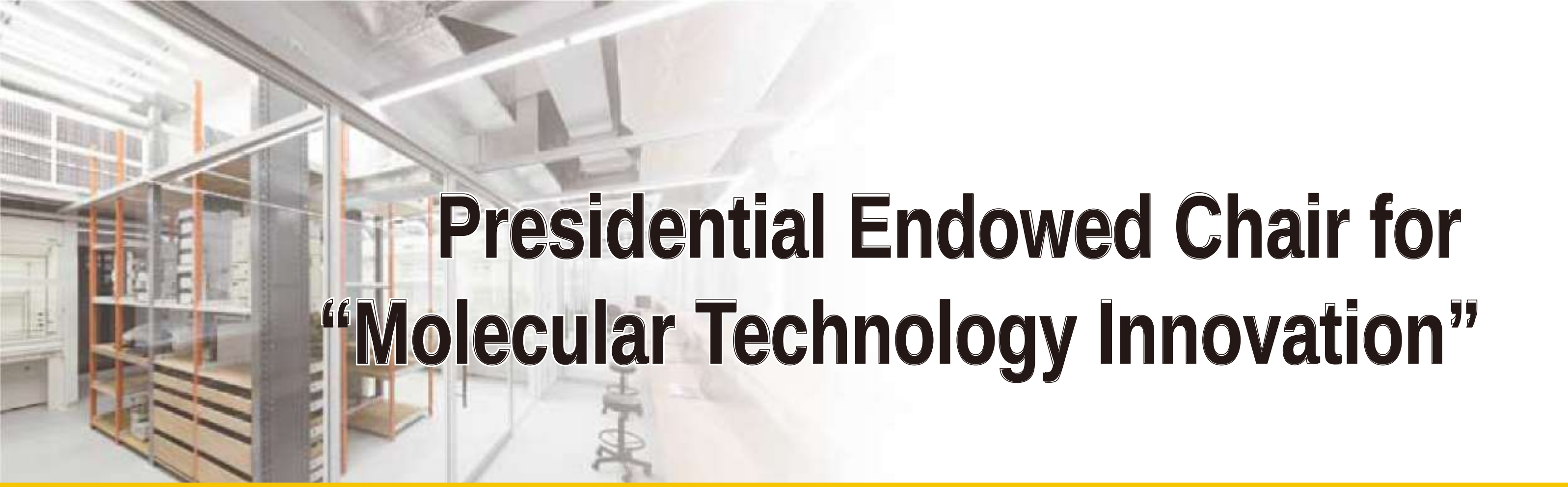

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New reactions, new materials, and new principles explored by organic chemistry

It has long been the dream of chemists to elucidate the intrinsic nature of atoms, molecules, and their assemblies, together with controlling their functions. We are exploring new concepts of structural chemistry and the creation of new functional materials using original synthetic tools developed by ourselves. We are also promoting research into the creation, property control, and biological function of molecular assemblies at angstrom or nanoscale level, and even above (nano-integration). This research is based on fundamental investigations into the structure and reactivity of organic molecules, using various tools such as high-resolution electron microscopy, scanning probe microscopy, and theoretical calculations, together with the development of powerful synthetic methods. These studies are supported by research grants from the Ministry of Education, Culture, Sports, Science and Technology, with the ultimate goal to reach for scientific dreams, to sustain healthy life, and to address environmental issue and resources depletion.

Single-molecule atomic-resolution time-resolved electron microscopy. Seeing is believing

“Watching the movements of individual small molecules with your own eyes”… this has been a dream of people for many years. In 2007, we realized this dream by observing in real time the changes in the shape of organic molecules packed in carbon nanotubes (Ref. 1) and named this method SMART-EM (see Figure 1a). Figure 1a shows one of the images of the conformational change of saturated hydrocarbon molecules with spherical boron markers installed as a head part. In addition, we elucidated the mechanism of bioactivity of the antibiotic daptomycin (Fig. 1b, Ref. 2), saw short-lived, microscopic intermediates in chemical reactions, and determined their reaction mechanisms (Ref. 3). The world's most advanced high-speed, high-resolution electron microscope installed in the hospital campus next to the chemistry building (Fig. 1c) has played a pivotal role in this research.

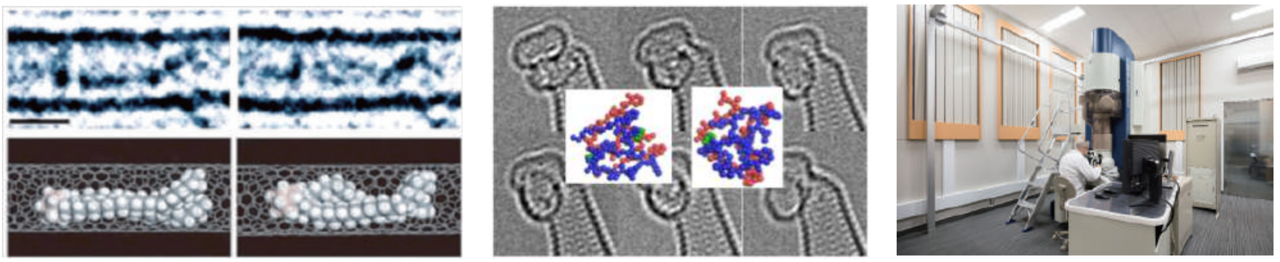

Figure 1. Electron microscope and dynamic molecular images. a. World's first video of molecular movement. b. Motions of daptomycin dimer. c. Electron microscope in the Molecular Life Innovation Building

Using the SMART-EM technique, we can see the dynamic world of atoms and molecules that people have never seen before. For example, a video recording of ion pairs of Na and Cl gathering together in several seconds to form a tiny crystal attracted the attention of people worldwide, from elementary school students to the general public (Figure 2, Ref. 4; https://youtu.be/Xo1yTnJo8Zs). A new field of "cinematic molecular science," which links cutting-edge science and science education through molecular imaging, is opening up (Ref. 5).

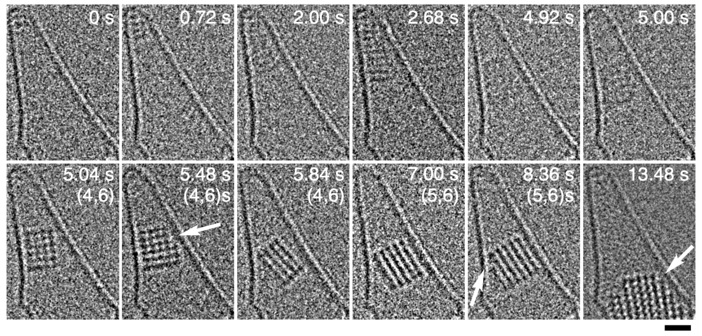

Figure 2: A nanocrystal of salt suddenly appears at the tip of a carbon nanotube in a vacuum (at 5.04 sec)

Organic Synthesis without Relying on Scarce Resources: Element Strategy

In 2004, we proposed the concept of "element strategies." Since the 1990s, we have been at the forefront of the development of organic synthesis using iron, a "ubiquitous element," as a catalyst. Iron is more difficult to control as a catalyst for organic synthesis than noble metal catalysts such as palladium because of its diverse spin and redox properties due to its degenerate 3d orbitals. We have developed a highly active catalytic system by taking advantage of the small redox potential of <0.55 V between Fe(III)/Fe(I), and developed a highly efficient and selective C–H bond activation reaction (Ref. 6). Figure 3 shows an example of a polymer synthesized by C–H activation of thiophene (Ref. 7) and an efficient and long-lived perovskite solar cell that utilize the polymer made by iron-catalysis as a hole transporting material (Ref. 8).

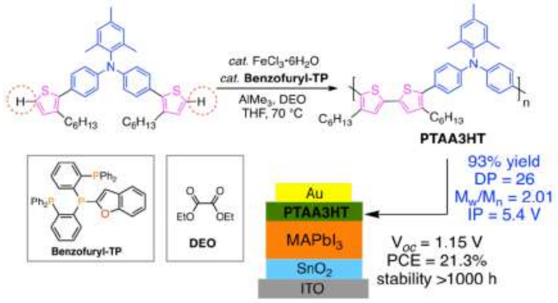

Figure 3: Iron-catalyzed polymerization by C–H bond activation as the key reaction.

Organic Electronics Materials Based on Iron-catalysis

Lightweight, flexible, and printable organic electronic devices are one of the keys to solving the energy problem. We as organic chemists have been working on basic and practical research in this field for the past 20 years. Polyacetylene, the fundamental framework of organic conductors, is too flexible and unstable. We discovered some time ago that the conjugated molecule can be stabilized by incorporating a planar 1,4-dihydropentalene skeleton, which requires complicated synthetic steps. Recently, we developed a simplified synthesis of a variety of planar conjugated molecules using highly active iron catalysts (Ref. 9). We designed a molecule having both an electron-donating thiophene moiety and an electron-withdrawing indanone moiety. The molecule showed strong absorption in the near-infrared region and can be used in fabricating efficient near-infrared detectors. Using this molecular design concept, we synthesized a cell imaging reagent with boron and nitrogen doping (Ref. 10) and a spiro molecule with good circularly polarized emission properties (Ref. 11). We very recently developed a high precision synthesis of blue light-emitting quantum dots for LED devices (Ref. 12), ultra-thin molecular films utilizing the self-assembly of organic fullerenes (Ref. 13), and the electrolytes for efficient lithium-ion batteries.

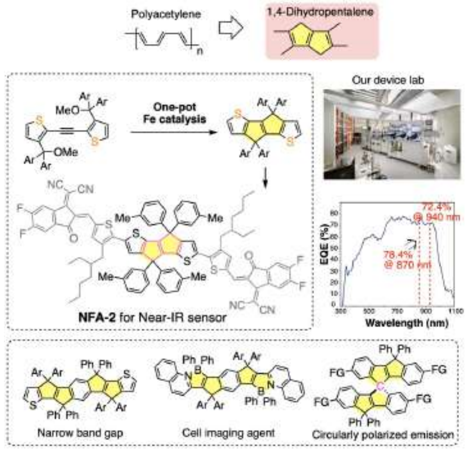

Figure 4: Iron-catalyzed synthesis of planar conjugated molecules and application to near-infrared detectors

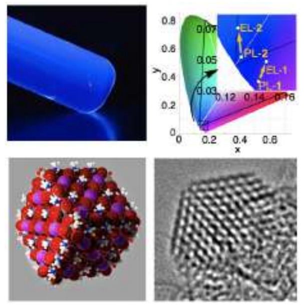

Figure 5: Quantum dots glowing in deep blue. Emission characteristics and SMART-EM image

Our Educational Philosophy: Fostering Scientists and Engineers with a Global Visibility

The important purpose of our research activities is to nurture scientists and engineers who are visible to the world through cutting-edge research. Furthermore, we hope that students will form the foundations of researchers through experiments and discussions in the laboratory and expand their curiosity, knowledge, and human network through research discussions (Fig. 6) and research experiences with our international laboratory members.

Figure 6 Tateshina group seminar (2022 Spring)

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Quantum Frontiers

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Molecular science in intense laser fields, Attosecond science, and Quantum computing

Quantum Frontiers Laboratory was established in April 2023 to take over the activities of the Quantum Chemistry Laboratory until March 2023, and to further expand the frontier of molecular science. Professor Yamanouchi, the laboratory's group leader, is promoting the research activities in "Next Generation Laser (ATTO Division)," which was started in 2017 as one of the 10-year term MEXT "Quantum leap flagship program," as the division head, to explore frontiers in attosecond science by developing attosecond light sources and advanced measurement systems in Japan.

We have been making an effort to establish "Attosecond Laser Facility," an international user facility for frontier research in attosecond science, in cooperation with the Institute for Attosecond Laser Facility, established in 2022 under the Committee for Presidential Initiative of the University of Tokyo, and the Center for Attosecond Laser Science, School of Science.

Furthermore, in addition to promoting ultrafast intense laser field science [1,2] and attosecond science [2,3], we have been conducting a research project on quantum computing, "Qudit-boson quantum-operation realization by trapped ions (2023–)," to develop quantum algorithms and construct a trapped-ion-type quantum computer in collaboration with RIKEN, Institute of Science Tokyo, Tokyo Metropolitan University, DIC Corporation, and Hamamatsu Photonics K.K. under the CREST Quantum Frontiers Program.

Ultrafast molecular dynamics in intense laser fields

Recent advances in laser technology made it possible to generate an ultrashort-pulsed intense laser field whose field intensity is as high as 10^{15}-10^{16} W/cm^2, which is comparable with or even larger than the Coulombic field within atoms and molecules. In such an intense laser field, electrons in atoms and molecules are influenced largely by the external electric field of light, and consequently, the subsequent dynamics of atoms and molecules are sensitively dependent on the characteristics of the light pulse. From the investigation of atoms and molecules interacting with an intense laser field, we can learn fundamental aspects of a light-matter interaction (Fig. 1).

In the past few decades, our group has been investigating the following research subjects; (1) "ultrafast hydrogen migration" in hydrocarbon molecular ions by the "coincidence momentum imaging" method, which records momentum vector distributions of fragment ions generated through the Coulomb explosion in an intense laser field, (2) strong-field ultra-high resolution Fourier-transform spectroscopy, (3) "laser-assisted elastic electron scattering" to investigate ultrafast electron dynamics within atoms and molecules in an intense laser field and "laser-assisted electron diffraction" to probe ultrafast variation of the geometrical structure of molecules with the femtosecond temporal resolution, (4) attosecond spectroscopy in which photoelectrons and photo-ions are detected after molecules are ionized by high-order harmonics generated using few-cycle laser pulses, (5) excitation processes of atoms and molecules in laser-induced filaments, which are formed by focusing intense laser pulses into gaseous media, (6) the mechanism of population inversion in N_2^+ and lasing, (7) theory for describing atoms and molecules and their dynamics in an intense laser field, (8) application of quantum computing to atomic and molecular problems, and (9) material processing by the extreme ultraviolet (EUV) femtosecond laser pulses.

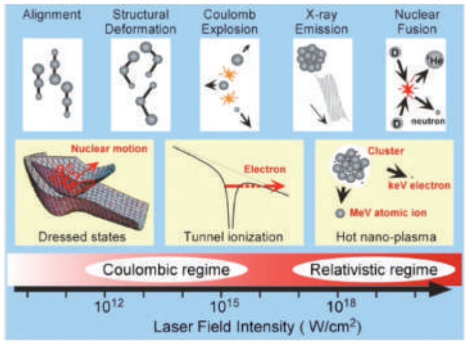

Figure 1. Dynamics of molecules in intense laser fields [1, 2].

Real-time measurements of ultrafast molecular dynamics and SURF spectroscopy

When molecules are irradiated with extreme ultraviolet (EUV) light, molecular ions are generated not only in the electronic ground state but also in the electronically highly excited states upon the ionization. To probe in real time the vibrational and dissociation processes of molecular ions in the electronically highly excited states, we have constructed a pump-probe beamline that can irradiate a sample gas with few-cycle near-IR laser pulses and EUV light pulses generated as high-order harmonics of the few-cycle laser pulses and developed a velocity map imaging spectrometer that detects fragment ions with a position-sensitive detector. Using this experimental setup, we have performed pump-probe measurements with an O_2 sample gas and measured the delay-time dependence of the kinetic energy distribution of O^+ generated via the dissociation of O_2^+ (Fig. 2). By numerical simulations, we have shown that O_2^+ oscillates in the $a^4\Pi_u$ state with a period of about 40 fs and dissociates in the $3^2\Pi_u$ state over a period of several tens of femtoseconds [4].

By pump-probe coincidence momentum imaging measurements of methanol, CH_3OH, using few-cycle intense laser pulses, we revealed that the yield of the H_3^+ periodically oscillates as a function of the delay time and that the period of the recorded oscillation (~38 fs) obtained by the Fourier transform corresponds to the period of the C-O stretching vibration of methanol cation [5]. By extending the delay time range of the Fourier-transform spectroscopy, we determined the vibrational frequency of D_2^+ to a precision of 10^{-4} cm^{-1} (Fig. 3) [6]. By the method of strong-field ultra-high-resolution Fourier-transform (SURF) spectroscopy with an extended delay time range of 500 ps, we determined the spin-orbit splitting energies of rare gas atoms to a relative precision of 10^{-7}. Furthermore, we have extended the delay time range up to 13 ns by introducing a long-arm interferometer and determined the hyperfine structure in the spin-orbit levels of $^{83}Kr^+$ with a precision of 10^{-5} cm^{-1} [8].

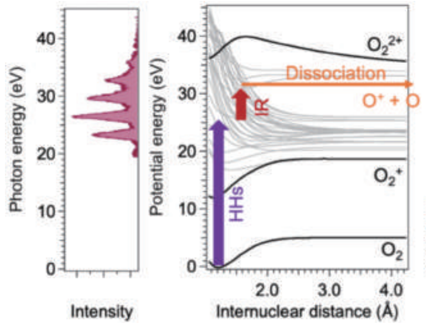

Figure 2. Pump (EUV) — probe (near IR) measurements of ultrafast dissociation dynamics of electronically highly excited states of O_2^+.

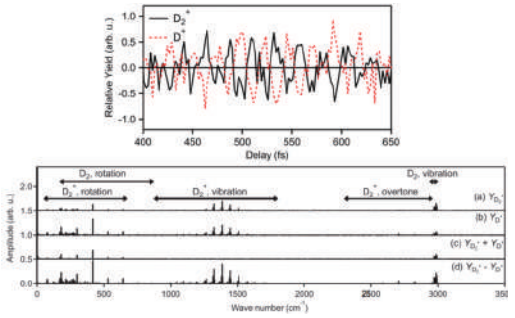

Figure 3. The results of SURF spectroscopic measurements of D^+ and D_2^+: The ion yields as a function of the delay time between the pump and probe pulse and the Fourier transform spectra [6].

EUV femtosecond laser processing

By focusing femtosecond laser pulses into a rare-gas medium, high-order harmonics of femtosecond laser pulses in the EUV wavelength region are generated. We focused the EUV laser pulses into a submicron spot on a surface of metal and semi-conductor materials using a focusing mirror with high surface accuracy and achieved submicron-size laser processing (Fig. 4) [9, 10].

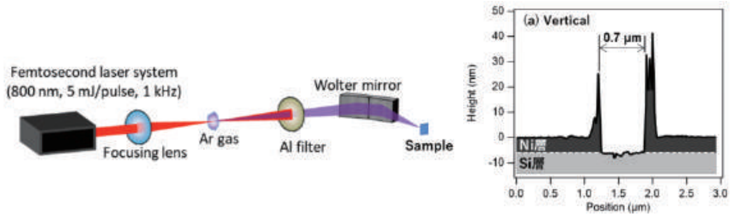

Figure 4. An experimental setup for extreme-ultraviolet femtosecond laser processing (left) and the recorded profile of the ablation spot on the Ni thin-layer-coated Si substrate (right) [10].

Development of theories to describe molecular dynamics in intense laser fields

By extending the first-principle quantal theory called multi-configuration time-dependent Hartree-Fock (MCTDHF) method, by which multi-electron dynamics in atoms and molecules interacting with an intense laser field can be calculated, we developed the extended MCTDHF method to calculate electro-protonic wave functions [10, 11]. When molecules are irradiated with an intense laser pulse, various dynamical processes such as electronic, vibrational, and rotational excitations and ionization proceed simultaneously. By the MCTDHF method, we have performed a numerical simulation of H_2^+ interacting with a 400-nm few-cycle intense laser pulse and showed that the electronic, vibrational, and rotational excitations are properly described [13].

Application of quantum computing to molecular science and development of a trapped-ion-type quantum computer

In recent years, there has been remarkable progress in the field of quantum computing both in hardware and in software and quantum algorithms. We have applied quantum computing to a variety of problems such as calculations of vibrational wave functions of CO_2 [14], Hückel molecular orbitals [15], and spin-spin interaction [16]. We have calculated the dynamics of an interacting spin chain using two currently available quantum computers, i.e., IBM's superconducting circuit type quantum computer and Quantinuum's trapped-ion type quantum computer, and revealed that both types of quantum computers can be used for simulations of model quantum systems with high fidelity (Fig. 5) [17].

We have also performed simulations of the time evolution of a three-level system interacting with an intense laser field (Fig. 6) [18] and of a spin-boson system representing electronic energy transfer in photosynthesis [19], demonstrating the importance of selecting appropriate algorithms and error mitigation methods.

On the other hand, in the recent development of trapped-ion type quantum computers, an approach using the continuous variables has attracted attention because it can facilitate highly efficient quantum error correction. Using the continuous variables, we have theoretically proposed a method to control entanglement with higher speed and accuracy than conventional methods and have undertaken an experimental demonstration [20].

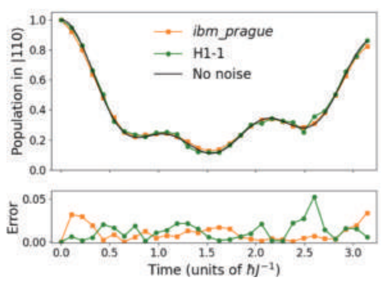

Figure 5. Upper panel: Time-dependent population in the qubit state |110〉 calculated using IBM's quantum computer *ibm_prague* (see ibm.com/quantum) and Quantinuum's quantum computer H1-1 (see quantinuum.com/). The solid black curve denotes the ideal noise-free result. Lower panel: The absolute value of the deviation of the population from the ideal noise-free case [17].

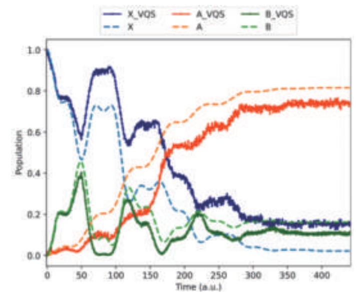

Figure 6. Results of the simulation of air-lasing using a NISQ device [18].

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Green Sustainable Chemistry Social Cooperation Laboratory

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- 2001: moved to Chemical Resources Laboratory, Tokyo Institute of Technology, and joined as Assistant Professor at Prof. M. Iwamoto’s research group.
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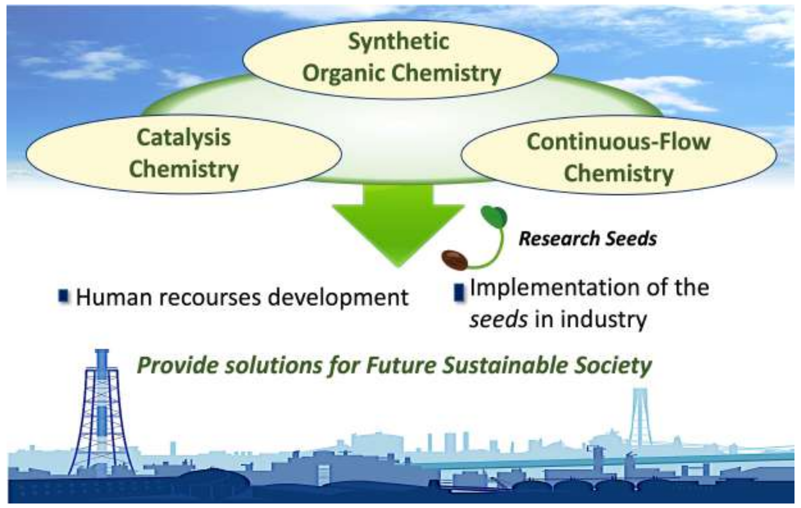
Linking cutting-edge chemistry to building a sustainable society

Green Sustainable Chemistry (GSC) Social Collaboration Laboratory was established with supporting of collaborative companies, with the aim of conducting practically oriented research and development on environmentally friendly low-load chemical processes and fostering human resources who will lead the GSC field. GSC is the ideal attitude of chemistry to build a sustainable society and is an important concept for modern society and he earth of the future. Starting from our actions, we will explore how the chemical industry can truly contribute to the future society by fusing our activities with industry-government collaboration.

Contribution for SDGs by promoting GSC research

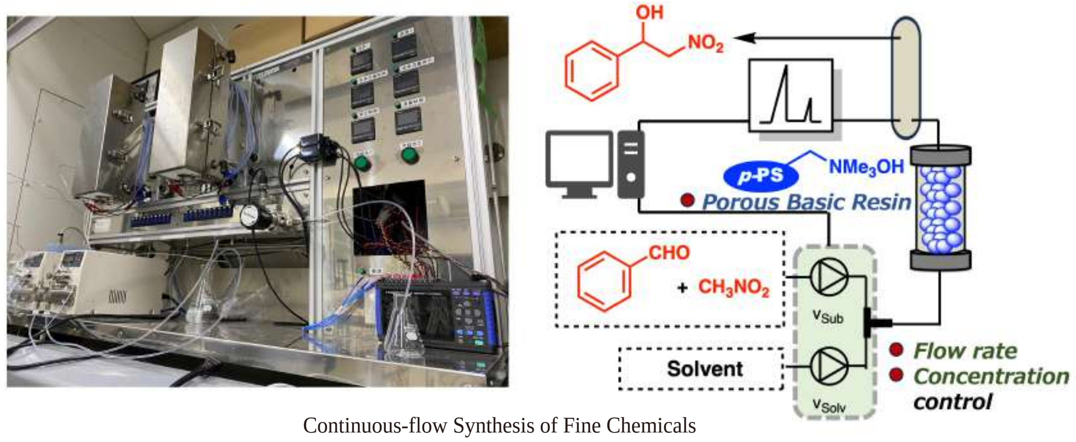
In recent years, as global environmental problems have become more and more strongly recognized, various Sustainable Development Goals and targets (SDGs) that transcend national boundaries have been formulated. Also, imagining the future beyond this goal, the challenges to be addressed by the power of science are extremely heavy. This laboratory aims to develop and put into practical use by conducting basic research with a view of achieving the goals and looking ahead. We are also focusing on developing human resources who can solve problems of the next 10 to 20 years. Our basic research aimed at developing safe chemical processes with low environmental load has the potential to contribute to social problems such as low birthrate and aging population, energy and resource issues, environmental issues, and food issues. To enhance our research, it is important to collaborate with basic university research, appropriate policies, and implementation by industry. This course promotes the above-mentioned trinity research through various collaborative research and public research programs.



Research Area of GSC Social Cooperation Laboratory

Development of continuous process for energy-saving chemical manufacturing

Although the production of functional chemicals is the key to Japan's economic growth and is considered an important issue for national economic security, the lack of facilities and manpower required for small-scale, multi-product production, and the production of many industrial waste products, including CO_2 emissions, are hindrances. To overcome this and improve the international competitiveness of Japan's chemical industry while reducing the environmental impact, it is necessary to convert the current production of functional chemicals to a continuous manufacturing process. Our research is aiming to the conversion of synthetic organic reactions that are frequently used in the synthesis of functional chemicals into continuous-flow synthesis. In particular, we are developing heterogeneous catalysts, continuous analysis methods, continuous purification methods, and continuous reaction modules, with catalytic reactions as the key. In this research, we are developing joint projects with other universities, national research institutes, and industry, and are working to build an on-demand and on-site process that can produce a wide variety of functional chemicals.

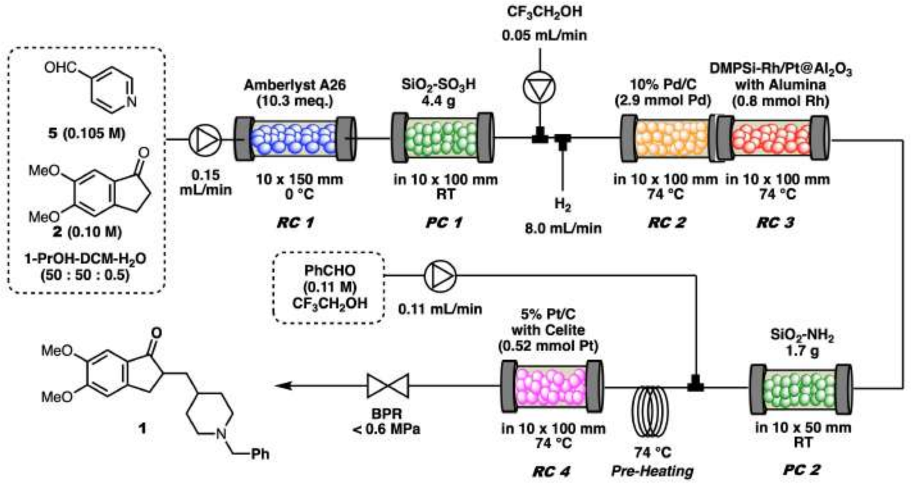


Continuous-flow Synthesis of Fine Chemicals

Sequential-flow Synthesis of Anti-Alzheimer Drug

Considering the declining birthrate and aging population, as well as the declining labor force, we need to use the power of chemistry to support health maintenance and food supply and demand, which are currently taken for granted. Pharmaceuticals are the top-ranking functional chemicals, and as mentioned above, domestic production is extremely important for this product group. We are working on the linking and continuous synthesis of pharmaceuticals by developing a catalytic continuous flow method. Recently, we have achieved the synthesis of an anti-Alzheimer drug using only hydrogen as a reactant, and the continuous synthesis of an essential drug, an antibiotic.

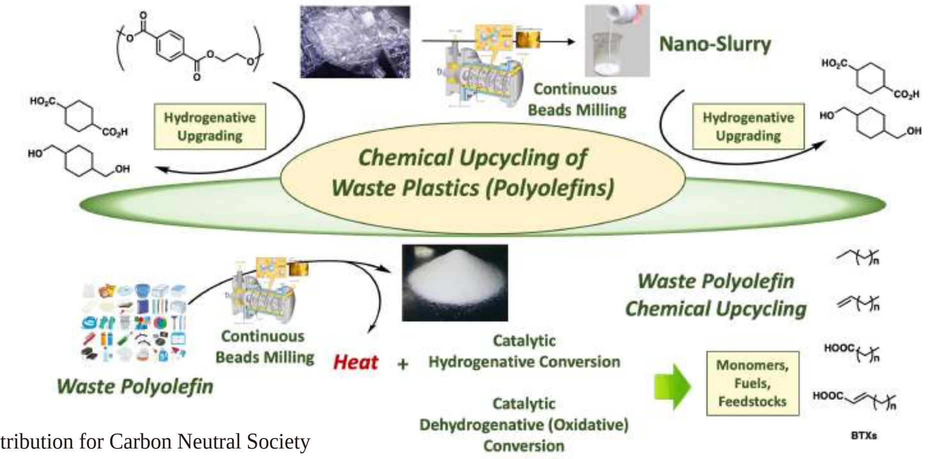
In addition, stable agricultural crop supply, protection of producers, and reduction of environmental burden are important issues for "sustainable agriculture". In this course, we are carrying out a joint project to develop ultra-high-performance pesticides and practice smart agriculture based on them. This research brings together knowledge of organic synthetic chemistry and chemical engineering, and is an important issue for the stable supply of agriculture and food in Japan.



Sequential-flow Synthesis of Anti-Alzheimer Drug

GSC research for the realization of a resource-recycling society

To achieve carbon neutrality, it is necessary to change the basis of our society from disposable fossil resources to renewable resources. What chemistry can contribute to this field is providing energy saving processes and efficiency improvement in commercializing renewable resources. We are now investigating catalytic processes that can convert non-edible biomass and biomass derivatives obtained by the reaction of non-edible biomass with carbon dioxide into basic chemicals that will be important in the future. Deploying this will lead to the production of non-edible biomass-based biodegradable plastics. We will also contribute to the realization of recycling-oriented society by developing a catalytic chemical upcycle processes of waste plastics.



GSC-Lab’s Contribution for Carbon Neutral Society

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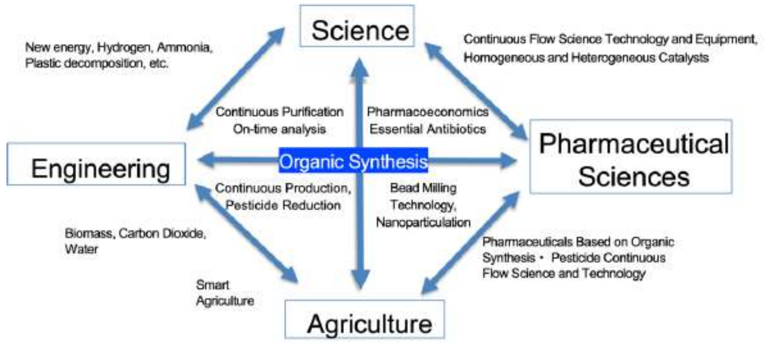
Green Material Conversion Based on Synthetic Organic Chemistry

We focus on four research topics to achieve Green Sustainable Chemistry (GSC): 1. Development of organic reactions in water, 2. Development of polymer-immobilized catalysts, 3. Development of novel reaction methods, and 4. Development of flow synthesis. The guideline "UTokyo Compass" announced that green transformation (GX) as the helicopter hand, the University of Tokyo on September 30, 2021. Therefore, from the efforts of our laboratory for GSC and GX, we created a new concept of "Green Material Conversion" as a starting point for our laboratory. Green Material Conversion is an attempt to achieve GX based on the synthetic organic chemistry. To solve issues such as environmental pollution and resource depletion, our laboratory focused on cutting-edge science and technology based on synthetic organic chemistry and attempted to solve them by all Tokyo University. Researchers in various fields, including science, engineering, pharmaceutical sciences, and agriculture, are conducting research and education on environmentally friendly chemical and material conversion processes, as well as innovative catalysts. We believe our research will contribute to achieving the SDGs and a carbon-neutral society.

Our research is contributing to the sustainable society in a wide range. The development of environmentally friendly chemical and material conversion processes and innovative catalysts will contribute to a more sustainable society, such as through the development of renewable energy sources, environmentally friendly manufacturing processes, and improved medical technology. In addition, our research is expected to have a significant impact on science and technology both domestically and internationally, and to contribute to the development of diverse and international leaders and researchers in the next generation.

Education and research across science, engineering, pharmaceutical sciences, and agriculture

Our laboratory focuses on the development of innovative and environmentally friendly chemical and material conversion processes. We develop homogeneous and heterogeneous catalysts, as well as continuous flow science technology and equipment, based on synthetic organic chemistry. From these, we attempt to innovate in fine chemical synthesis, such as pharmaceuticals, agrochemicals, semiconductor materials, and high-performance chemicals, by utilizing biomass, carbon dioxide, hydrogen, and other resources to reduce reliance on fossil fuels. We conduct education and research across science, engineering, pharmaceutical sciences, and agriculture. We will advance research and development to achieve green material conversion and realize the SDGs and a carbon-neutral society.

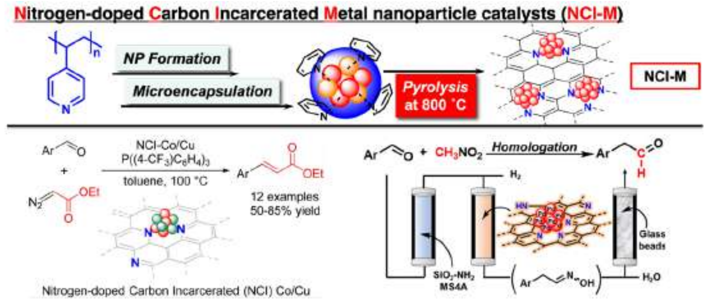


Relationship between synthetic organic chemistry and each field

Development of heterogeneous metal catalysts for application to continuous flow synthesis

Heterogeneous metal catalysts are easy to separate from the product after the reaction and can be recovered and reused. Since they are also applicable to continuous flow synthesis, the demand for the development of highly functionalized heterogeneous metal catalysts has increased in recent years. Our laboratory has been developing various heterogeneous metal catalysts and applying them to reactions recently, such as the development of N-doped carbon-supported metal nanoparticle catalysts and nitrogen-doped carbon-incarcerated metal electrodes as heterogeneous catalysts for electrochemical reactions.

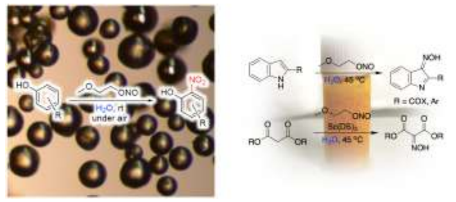
Starting from polyvinylpyridine, we developed N-doped carbon-supported metal nanoparticles. We then applied these nanoparticles to various reactions. For example, bimetallic nanoparticles prepared from cobalt and copper showed high reactivity in oxidative esterification reactions. The reactivity of this catalyst was comparable to that of gold nanoparticles. We also successfully applied a palladium catalyst to the homologation reaction of aryl aldehydes using nitromethane as the C1 source. This N-dopant significantly affected the selectivity of the reaction. It has also been successfully applied to flow reactions.



N-Doped carbon-supported metal nanoparticle catalysis

Organic synthesis in water and its application to flow reactions

Synthetic organic chemistry has been conducted using organic solvents for several decades. Based on the principles of green sustainable chemistry (GSC), we have studied switching from organic solvents to water because water is harmless to the environment and human body, as well as being safe and inexpensive. Our results have revealed that water is not merely a substitute for organic solvents, but can offer unique reactivity and selectivity. For example, we have observed enhanced reaction rates and different product ratios in water compared to organic solvents.



Reactions in water

In recent years, reactions in water have been attracting attention in flow synthesis. From these perspectives, we believe that reactions in water have potential for flow synthesis applications. We are currently developing characteristic reactions in water for flow synthesis applications, such as C–C and C–N bond-forming reactions. By utilizing the unique properties of water, we aim to develop efficient and environmentally friendly synthetic methods.

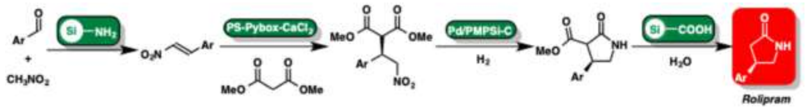
Synthesis of (*R*)-Rolipram by next-generation organic synthesis using continuous flow reaction

Fine chemicals, such as medicines, agrichemicals, and functional materials, are often synthesized in batch systems. However, those methods are not suitable from the viewpoint of GSC (Green Sustainable Chemistry) due to the production of large amounts of chemical waste. In particular, flow synthesis of chiral pharmaceuticals and fine chemicals requires asymmetric synthesis using columns with chiral catalysts. Based on these ideas, our laboratory successfully achieved the synthesis of optically active Rolipram using a continuous flow synthesis.

The active pharmaceutical ingredient (*R*)-Rolipram is a GABA (γ-amino acid) known to have important pharmacological activity in neuroscience. Therefore, we considered heterogeneous chiral calcium-catalyzed asymmetric 1,4-addition as the key reaction for the synthesis of Rolipram by continuous flow synthesis, thereby avoiding the use of homogeneous catalysts.

First, the synthesis of β-nitrostyrene from nitromethane with aldehyde was carried out using amino-modified silica gel as a catalyst and calcium chloride as a dehydrating agent. The obtained solution was mixed with malonate ester and triethylamine, and then introduced into a reaction column containing our heterogeneous chiral calcium chloride catalyst. The desired asymmetric 1,4-addition proceeded smoothly, affording the desired product in high yield with high enantioselectivity. The subsequent hydrogenation and cyclization reaction was carried out using a polysilane/carbon-supported palladium catalyst. Finally, decarboxylation was conducted at high temperature (e.g., 150 ℃) using carboxylic acid-modified silica gel, affording the desired chiral (*R*)-Rolipram in high yield with high enantioselectivity.

This synthesis represents the first example of a continuous flow synthesis using only heterogeneous catalysts to synthesize optically active compounds. Notably, this system allows for eight consecutive reaction steps to be carried out in a column for more than one week (e.g., 10 days). This innovative process allows for the continuous production of chemically and optically pure (*R*)-Rolipram. Currently, we are exploring the application of this system to the synthesis of other pharmaceuticals, chemical products, and agrochemicals.



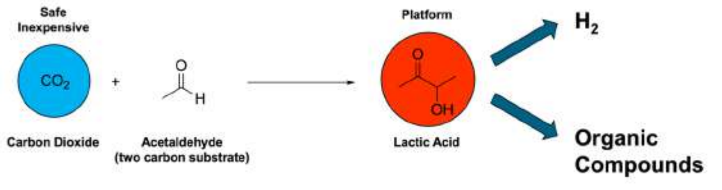
Synthesis of the (*R*)-Rolipram by continuous flow synthesis using four heterogeneous catalysts

Conversion of carbon dioxide to organic materials

The chemical utilization of carbon dioxide (CO_2) as a C1 feedstock to access value-added materials is attractive since it is a safe, inexpensive, and readily available gas. However, due to its intrinsic kinetic and thermodynamic stability, the use of carbon dioxide is limited. To overcome these barriers, we can utilize highly energetic starting materials and/or intermediates, along with a catalyst, to develop useful synthetic methodologies for incorporating CO_2 into complex organic molecules.

We have reported the incorporation of carbon dioxide into phthalides via ligand-free copper-catalyzed direct carboxylation of benzoxasiloles. We have also achieved the efficient synthesis of trifluoromethyl carboxylic acids and esters through fluorocarboxylation of gem-difluoroalkenes. Furthermore, we have developed a one-pot synthesis of α,β-unsaturated γ-lactones and lactams via sequential *trans*-hydroalumination and catalytic carboxylation of propargyl alcohols and amines with carbon dioxide.

Lactic acid (3-hydroxypropionic acid) is a versatile platform chemical that can be converted into various organic compounds, such as acetic acid and other fatty acids. Moreover, it can be used as a biofuel precursor, as hydrogen can be extracted through dehydrogenation. Leveraging our expertise in CO_2 utilization, we are currently investigating the synthesis of lactic acid from carbon dioxide and two-carbon substrates.



Transformation of carbon dioxide to lactic acid

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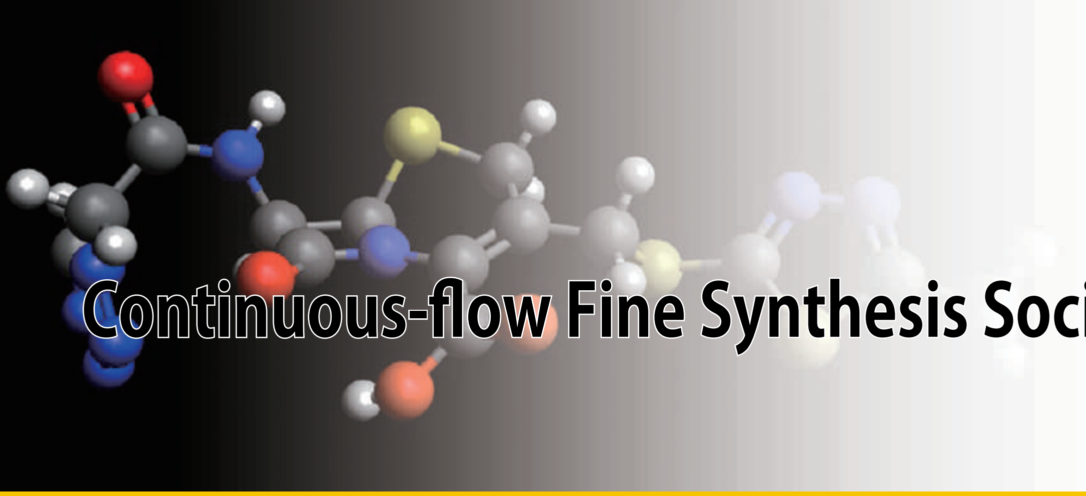

Continuous-flow Fine Synthesis Social Cooperation

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Continuous-Flow Fine Synthesis Social Cooperation Laboratory

The Continuous-Flow Fine Synthesis Social Cooperation Laboratory has been established in collaboration with SHIONOGI PHARMA CO., LTD. to conduct research and development on continuous-flow synthesis methods enabling high-efficiency continuous production of fine chemicals such as pharmaceuticals, and to develop methodologies and nurture talent to drive technological innovation in the overall supply of fine chemicals in the chemical industry.

The Continuous-Flow Fine Synthesis Social Cooperation Laboratory contributes to the realization of a sustainable society by reducing waste and achieving energy efficiency.

Research Background

In the chemical industry, the manufacturing of fine chemicals, including pharmaceuticals, has traditionally been carried out using batch methods with reaction vessels such as flasks. While this method has been a crucial manufacturing technology supporting the chemical industry for many years, it faces various challenges in terms of reaction control and safety. Particularly during industrialization, there are numerous technical challenges to be addressed, such as difficulties in scale-up and the generation of large amounts of hazardous intermediates.

Continuous-flow synthesis has been gaining attention as a new approach to resolve these issues with conventional manufacturing methods and realize more efficient and safer manufacturing processes. (Figure 1)

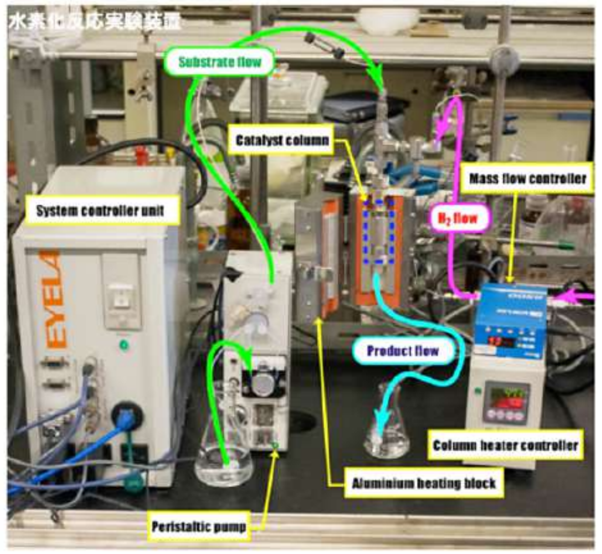

Fig.1 Image of flow synthesis equipment

This synthesis method involves continuously feeding raw materials into reaction tubes while carrying out the reaction. It enables precise control of reaction conditions such as reaction temperature and residence time, achieving high selectivity and yields that were difficult to attain with conventional batch methods, while simultaneously improving product quality and reducing manufacturing costs.

In terms of safety, continuous-flow synthesis offers significant advantages. By keeping the amount of material in the reaction system minimal, it can suppress the generation of hazardous intermediates and unstable compounds, greatly reducing risks of explosion and fire. Furthermore, reactions can be conducted in closed systems, enabling safe handling of volatile or toxic substances.

Additionally, from a manufacturing facility perspective, continuous-flow synthesis offers numerous benefits. Production volume can be easily adjusted through parallel arrangement of equipment, enabling flexible production systems that can respond to market demand fluctuations. Additionally, the compact nature of the equipment allows efficient use of manufacturing space, contributing to improved productivity.

Research Content and Achievements

Our laboratory is pursuing various research and development efforts aimed at establishing innovative manufacturing processes for important fine chemicals, particularly pharmaceuticals. As a notable achievement, we have developed a process to manufacture cefazolin sodium, an important antibiotic, using continuous-flow synthesis. Cefazolin sodium is a pharmaceutical used for surgical infection prevention, and its stable supply is extremely important in medical settings. In this research, we developed a methodology to synthesize cefazolin sodium without purifying intermediates using a two-step sequential flow reaction.

In conventional batch methods, purification of intermediates was unavoidable, resulting in labor and waste generation. However, with this method, under optimal reaction conditions, we can obtain products that can be converted to high-purity cefazolin sodium in subsequent steps without intermediate purification. We have also demonstrated that small-scale laboratory results can be almost perfectly reproduced when scaled up approximately 30-fold, proving that our developed continuous production system excels in scalability and reproducibility. (Figure 2)

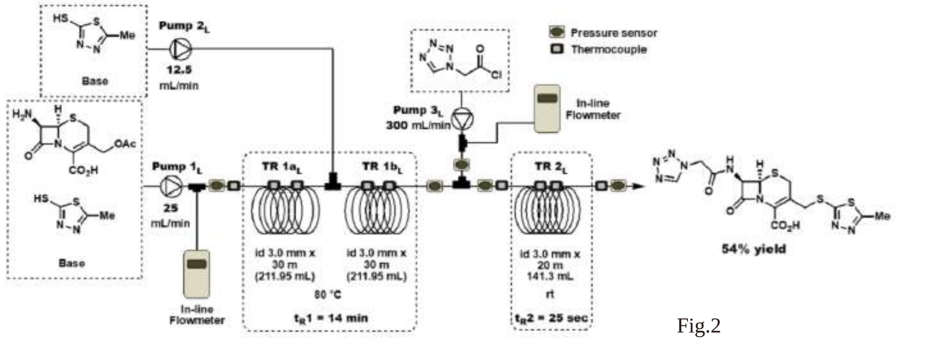

Fig.2

This successful example of continuous cefazolin synthesis stands as significant evidence of the advantages of continuous-flow synthesis. This method has achieved improved selectivity through precise temperature control, safe execution of hazardous reactions, stabilization of product quality, and overall manufacturing process efficiency.

Currently, we are expanding the application of these research achievements to a broader range of pharmaceutical syntheses. We are developing comprehensive research and development aimed at practical implementation, including the development of new synthetic

Research Content and Achievements

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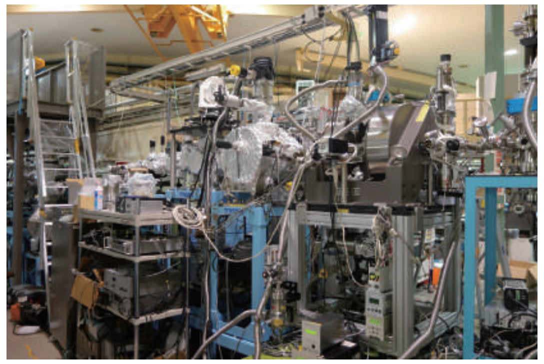
Advanced spectroscopy—Common words for modern science

The Research Center for Spectrochemistry (RCS) was founded in 1976. Current research at RCS mainly covers synchrotron radiation spectroscopy and fast Raman spectroscopy for investigating a variety of chemical and biological phenomena at molecular level. RCS undertakes development of new spectroscopic methods based on state-of-the-art laser technology as well as performing spectroscopic observation of living cells or functional materials. This research is related to chemistry as well as other scientific disciplines, including clinical diagnosis, and to the development of inter- and multidisciplinary sciences. RCS also maintains and manages various spectroscopic instruments for common use.

Electron spectroscopy using synchrotron radiation



Synchrotron radiation is produced by accelerating particles to near light speed and bending their paths with a magnetic field. This process has the advantages of brilliance and tunable photon energies from the infrared (IR) to x-ray regions. The Research Center for Spectrochemistry constructed a beamline (BL-7A) with a bending magnet to produce ultra-violet (UV) and soft x-ray radiation at the Photon Factory high-energy accelerator organization (KEK), Tsukuba. The equipment for high-resolution photoemission spectroscopy, x-ray absorption fine structure spectroscopy (XAFS or XAS), and x-ray magnetic circular dichroism (XMCD) are located at the end station, which can be utilized for the research on chemical bonding states and electronic and magnetic structures. Three kinds of gratings (150, 300, and 650 mm^{-1}) are mounted, and high brilliant x-rays from 200 to 1500 eV with high resolution are available. In particular, this beamline has become a powerful tool for studies of element-specific magnetic structures by XMCD and crystalline structures of molecules by XAFS. This beamline is open to all researchers who pursue surface science, magnetism, and photochemistry during chemical reactions.

Figure 1 shows XAS and XMCD spectra, defined as the difference in absorption spectra excited by right and left circular polarized light, of ferrimagnetic $CoFe_2O_4$ with perpendicularly magnetic anisotropy. Analysis of spectral shapes using the magneto-optical sum rules estimates spin and orbital magnetic moments separately, which becomes a powerful technique for clarifying mechanism of the functionalities of novel materials and molecules. Furthermore, we have developed x-ray magnetic linear dichroism (XMLD) technique to deduce quadrupole moment with ligand field theory calculation for clarifying novel magnetic anisotropy. Recently, we succeeded in Operando XMCD system to detect the control of orbital magnetic moments during applying external strain, which is utilized for interfacial physics and chemistry.

In order to detect the energy band dispersion around the Fermi level, we have developed high-resolution angle-resolved photoemission spectroscopy (ARPES). As an example, the band dispersions of topological insulator (TI) of Bi_2Se_3 surface are shown in Fig. 2. Dirac point which originates from relativity theory is detected by ARPES. Now we are developing the spin-resolved ARPES system and will measure interfacial electronic structures between TI and magnetic materials. These spectroscopic investigations using various energy ranges open up a novel technique of “multimodal spin-orbit measurements” to understand interfacial physics and chemistry in solids.

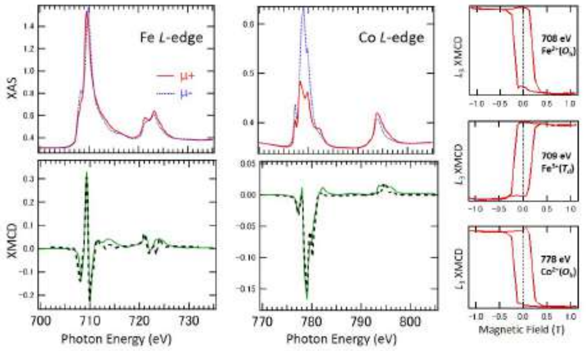


Fig. 1, XMCD of $CoFe_2O_4$ with ligand field theory calculation and element-specific hysteresis curves.

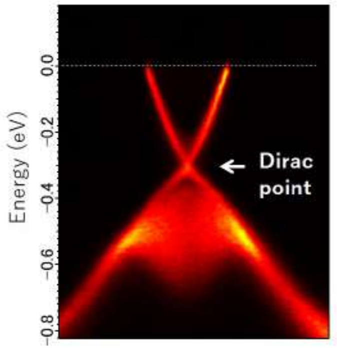


Fig. 2, ARPES image of surface states in topological insulator Bi_2Se_3.

High-throughput optical imaging and deep learning-based cell measurement

Real-time measurement of rapid and non-repetitive phenomena is essential for investigating transient events such as chemical reactions, phase transitions, protein dynamics in living cells, and disruptions in data networks. In response to this need, we have developed an innovative tool based on high-throughput optical imaging and deep learning, which we have applied to cell measurements. Specifically, we employed a technique known as frequency-division multiplexing (FDM) microscopy (Figure 3 left) [7]. This technology applies the principles of frequency-division multiplexing-widely used in optical and wireless communications—to imaging, enabling high-speed, blur-free bright-field microscopy. In our research, we focused on platelets (Figure 3 right) that are specific blood cells closely associated with thrombus formation. By advancing platelet morphology measurement to unprecedented levels, we have introduced a novel range of analytical capabilities that could not be achieved with conventional platelet morphology methods. This has shed light on previously unexplored areas of platelet analysis. We have termed this emerging field "Intelligent Platelet Morphology," which is anticipated to pave the way for a new class of diagnostic, pharmacological, and therapeutic advancements [8].

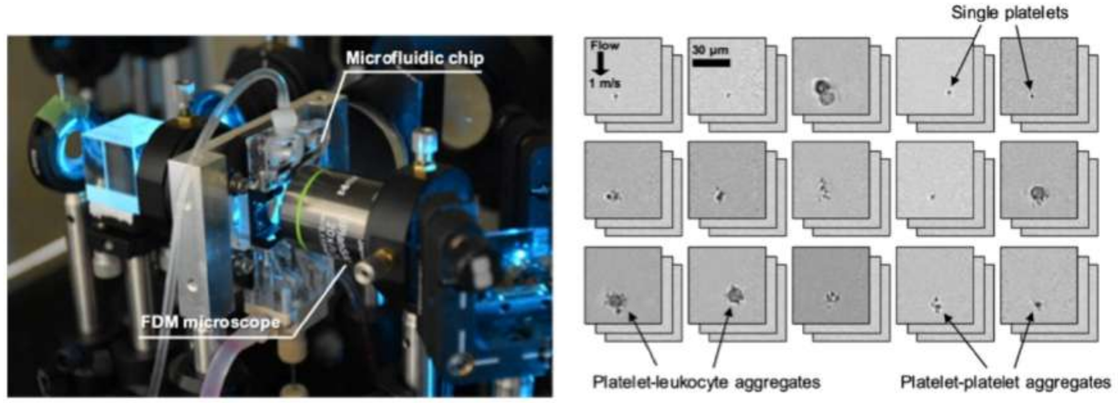


Fig. 3, Frequency-division multiplexing (FDM) microscope (left) and platelet images acquired using the FDM microscope (right)

Maintenance and management of various spectroscopic instruments for common use

RCS manages the instruments available to all researchers and students. Please contact the staff at RCS to request the use of them. Instruments for the following techniques are available for common use: powder x-ray diffraction (XRD), x-ray fluorescent (XRF) analysis, single-crystal XRD, ultraviolet–infrared (UV–IR) spectroscopy, fluorescent spectroscopy, IR spectroscopy and microscopy, nuclear magnetic resonance (NMR), gas chromatography (GC), electron spin resonance (ESR), differential thermo analysis (DTA), and thermogravimetric analysis (TG).

Fig. 4, Examplesof the instruments in RCS available for common use. ESR, NMR, FT-IR, and XRF.

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Promoting Intense Laser Science and Attosecond Laser Science,Capacity Development of Young Researchers in Photon Science

In April 2022, the Center for Ultrafast Intense Laser Science (CUILS) was reorganized to become the Center for Attosecond Laser Science (CALS), and Intense Laser Science Laboratory was established. The main objective of this transformation is to build on the foundations laid by previous research in ultrafast, high-intensity laser science and advance the development of laser and measurement techniques in the field of attosecond laser science. CALS is dedicated to pushing the boundaries of interdisciplinary research in ultrafast, high-intense laser science and to promoting the creation of educational program in photonics and optical science through partnership between academia and industry.

Advances in ultrafast intense laser science

Light has always been playing a central role in our exploration of frontiers in science. Until relatively recently, light used in science had been weak, so that the irradiation of light would not change the nature of matter. However, recent ultrashort laser technology enabled us to reach the intensity of light up to 100 million times larger than before, and it has been revealed that irradiation of light with such huge intensity can form light-dressed states in which light and matters are strongly coupled. Nowadays, intense laser science is regarded as an attractive and promising interdisciplinary research field covering physics,chemistry, and laser engineering.

Development of attosecond light sources and methodology

When atoms or molecules are irradiated with an intense femtosecond laser pulse (>10^{14}W/cm^2), high-order harmonics, whose photon energy is odd multiples of the irradiated light ($(2N+1)h\nu$), can be generated. This phenomenon is called high-order harmonics generation (HHG). Because HHG has high spatial and temporal coherence, attosecond pulse can be generated by HHG. By using attosecond laser pulses, electron dynamics induced by laser pulses can be observed. As shown in Figure 1, we generated attosecond pulses train using HHG, and constructed an experimental apparatus for attosecond time-resolved measurement.

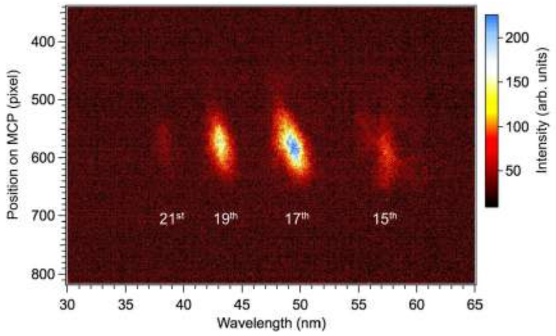

Figure 1. Spectrum of attosecond pulse train generated by focusing the output of an OPCPA (0.13 mJ/pulse, 800 nm, 7 fs) into Xe gas cell. The 15th to 21st orders of HHG were observed.

Molecular spectroscopy using intense few-cycle laser pulses

When a molecule is exposed to intense laser fields, the molecule is coherently excited through various nonlinear processes. We have developed a method to determine the energy levels of atoms and molecules precisely by observing the motion of coherently excited molecules in real time (Strong-field ultrahigh-resolution Fourier-transform spectroscopy). This technique has the following features: (i) available for low concentration molecular species, (ii) Doppler-free, and (iii) available for electric-dipole-forbidden transitions. Therefore, it is expected to enable precision spectroscopy of a wide range of molecules, from dilute samples such as H_2^+ and H_2 molecules, which were difficult to measure using conventional methods.

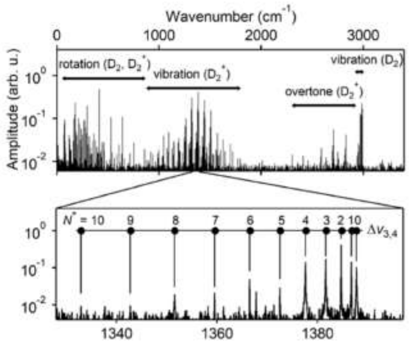

Figure 2. Rovibrational spectrum of D_2 , D_2^+ molecule by SURF measurement.

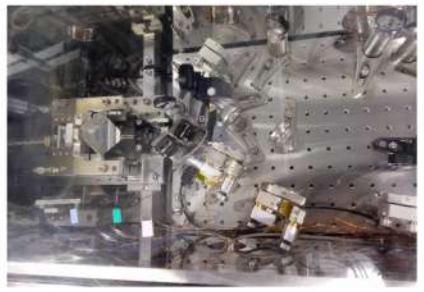

Figure 3. Long-arm interferometer for SURF spectroscopy placed in vacuum chamber. Frequency resolution: 60 MHz.

Industry-academia joint educational program in photon science

The consortium on education and research on advanced laser science (CORAL) was established in April 2007 for fostering graduate students in photon science. Since the launch of this CORAL program, its operation has been conducted by CALS as one of its main activities.

The CORAL program has been operated in cooperation with the Graduate School of Engineering at the University of Tokyo and the two other universities, the University of Electro-Communications and Keio University, having well-established teaching courses in photon science. In the CORAL program, prerequisite topics in photon science, which had been taught in undergraduate and graduate courses, were integrated systematically.

In the CORAL program, researchers and engineers from photonics-oriented companies and professors from provide graduate students in these three universities with the lecture courses, “Lectures on Advanced Optical Science I/II,” and laboratory courses, “Laboratory Course of Advanced Optical Science I/II.” Our educational activity has been supported by Advanced Laser Innovation Center (ALICe) in Quantum Leap Flagship Program (MEXT Q-LEAP) and The Forefront Physics and Mathematics Program to Drive Transformation (FoPM).

Figure 4. Laboratory courses on photon science I/II in 2023. Top-left: Nikon corp., top-right : Kyosera-SOC, bottom-left: Furukawa electric, bottom-right: Imra-UTokyo.

Optics and advanced laser science by innovative funds for students

Optics and advanced laser science by innovative funds for students (OASIS), which was started in 2008, is a scholarship program for graduate students in the second year of master courses in the University of Tokyo for supporting their research activities in photon science. This OASIS scholarship program, being operated by CUILS, has been supported by donations from companies.

Foundation URL: https://www.u-tokyo.ac.jp/ja/students/welfare/h02_10.html

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Geochemical Research Center

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Professor
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Investigating dynamics of the Earth and planets from a chemical point of view

Geochemistry can derive the direct "evidence" of the growth history of the Earth and the Solar System from a viewpoint of chemistry. Prof. Kagi's group studies physical and chemical properties of minerals and materials relevant to deep earth, including organic molecular compounds, under high pressure using various spectroscopic methods, X-ray diffraction, and neutron diffraction. Prof. Hirata's group is trying to understand the early history of the solar system and early earth including evolution of the life with developing a state-of-the-art technique for the elemental and isotope analysis. We welcome students who are interested in materials in the Earth and planets or chemistry under extreme conditions.

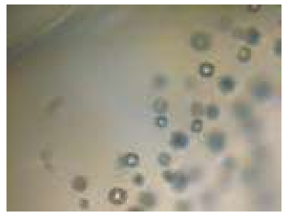
Geochemistry of the Earth's interior

The depth to the center of the Earth is approximately 6,400 km. However, humans have only been able to reach as far as 10 km. This means that we cannot directly collect deep-earth materials. Thus, in order to understand the physical and chemical environments of deep Earth and planetary interiors, we must study various materials under high-pressure conditions in laboratory-based experiments.

We focus on pressure-induced structural changes in ices, materials having hydrogen-bonding networks, hydrous minerals as a carrier of water into the deep Earth, simple organic compounds including amino acids. The main experimental techniques we use are in-situ measurements of X-ray-diffraction, neutron diffraction, and vibrational spectra under high-pressure conditions. For example, ice is a very familiar material in our daily life, but at least seventeen polymorphs have been reported, and the discovery of a new ice phase is expected in the near future. Crystal structure and properties of ice polymorphs are essential science targets in material science and planetary science. To determine the structure of an ice polymorph, we determine the atomic position of hydrogen at varied pressure and temperature conditions by neutron diffraction.

Along with high-pressure experiments, natural samples are also important to obtain information on the real Earth. We are investigating mineral inclusions contained in natural mantle-derived samples, such as diamonds which are the most typical mantle-derived minerals. In addition to deep Earth geochemistry, we are conducting surface observations with the atomic resolution on calcium carbonate, which plays an important role to the global circulation of CO_2. In future, we will estimate global circulation of volatile elements from surface environments to the deep Earth by synthesizing the obtained knowledge.

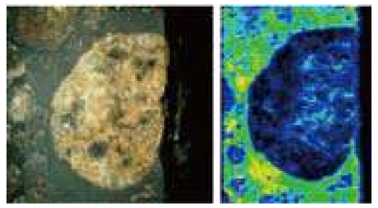
PLANET beamline at J-PARC.



Dense CO_2 fluid inclusions in olivine, a major mineral in the upper mantle.

Isotope geochemistry and cosmochemistry: measure what is measurable, and make measurable what is not so - Galileo Galilei

The geochemistry is one of the key research field to decode the growth history of the Earth and the Solar System. We are trying to understand the early sequence of the solar system, meteorites, planetesimals or the Earth's core, and also to understand the growth sequence of the continental crust and the origin and evolution of the life through the elemental and isotopic analyses of various samples including rock, mineral, fluid and biochemical tissues. To achieve this, we are developing a state-of-the-art technique for the elemental analysis using the combination of high power lasers and the mass spectrometry. Mass spectrometers utilizing atmospheric pressure Ar-ICP as an ion source (ICP-MS) have been widely used for both element and isotopic analyses for geochemical samples such as rocks, minerals, aquatic solutions, as well as gaseous samples. Since the ICP is operating under atmospheric pressure, various sample introduction techniques can be applied for analysis. Among these, the laser ablation sampling technique is likely to become a method of choice for many geochemists and biochemists because it is a highly sensitive and versatile method of elemental and isotopic analyses. Laser ablation is the process of removing materials from the surface of solid materials by the irradiation of a laser beam. Laser induced sample aerosols and vapors will be introduced to the ICP, and the ionized elements are extracted into a high-vacuum, and separated by mass. The newly developed system has blossomed to become the key technique to provide the most precise chronological data for both the rock and mineral samples. Moreover, analytical capability for *in-situ* elemental and isotopic analyses can be made in various spatial resolutions, ranging from 1 - 1,000 µm. The LA-ICPMS technique has opened up new applications for geochemistry, such as *in-situ* stable isotope studies, *in-situ* isotope-dating, and simultaneous mappings for major to trace-elements (imaging mass spectrometry). Here you can find the answer.



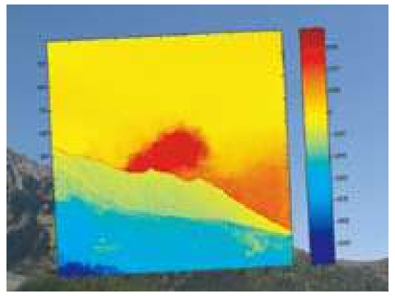
Ca-Al rich inclusions in a meteorite, the oldest rock sample.

Ion detector developed by our group.

Chemical composition and flux of volcanic gas as an indicator of dynamics of volcanic eruption

Volcanic gas is a mixture of volatiles degassed from magma and fluids from hydrothermal system. By monitoring chemical composition and flux of the volcanic gas, we can derive valuable information of magma and hydrothermal system at depth of the volcano. One of our targets is to understand the dynamics of volcanic activities through volcanic gas investigations using various optical remote sensing techniques. A remote measurement technique of volcanic gas chemistry using a FT-IR spectral radiometer and a visualization technique of sulfur dioxide in volcanic plume, both are developed at our laboratory, are powerful tools for understanding degassing activities of volcanoes. By using the visualization technique, we are able to measure sulfur dioxide flux with unprecedented high time resolution of order of seconds. We are also involved in automated measurements of sulfur dioxide flux of several Japanese volcanoes using UV spectrometer scanning systems. By integrating our observed volcanic gas data with geophysical data, we are focusing on understanding the degassing processes during long term and imminent precursory periods of volcanic eruptions. In addition to the researches above, our interest extends to diffuse degassing of volcanic carbon dioxide from volcanic edifice, which is an indicator for volcanic unrests or eruptions.

Remote measurement of volcanic gas chemistry using FT-IR spectral radiometer.



SO_2 column amount image observed at Sakurajima volcano.

Groundwater gas geochemistry of fault zones

Dissolved gases and ions in groundwater sometimes shows pre-seismic anomaly. Our goal is to understand a mechanism and develop a model to describe such anomalies based on geochemical measurements. We developed a mass spectrometer system for a continuous measurement of dissolved gases in groundwater in 2008, and we are monitoring concentration and composition changes of dissolved gases at the Atotsugawa active fault from 2010. We believe that a status of the fault can be evaluated by the gas monitoring in the near future. In addition, we developed an apparatus to measure a radon concentration by a scintillation counting technic in 2010. A radon monitor in Nakaizu observatory, which was used in our laboratory for 30 years, was replaced with the new one in 2010. This new radon monitor successfully detected an anomalous radon concentration increase before the Tohoku earthquake in 2011. We have just started to observe a state of the Miura active fault zone and the Tachikawa active faults. Not just above investigations, we will start an air geochemistry for aiming to investigate and monitor a cross-border pollution with these monitoring technics in some years.

Dissolved gas concentration in groundwater is continuously recorded by a quadrupole mass spectrometer and a radon counter.

Gas emission is monitored under uniaxial compression in a vacuum chamber.

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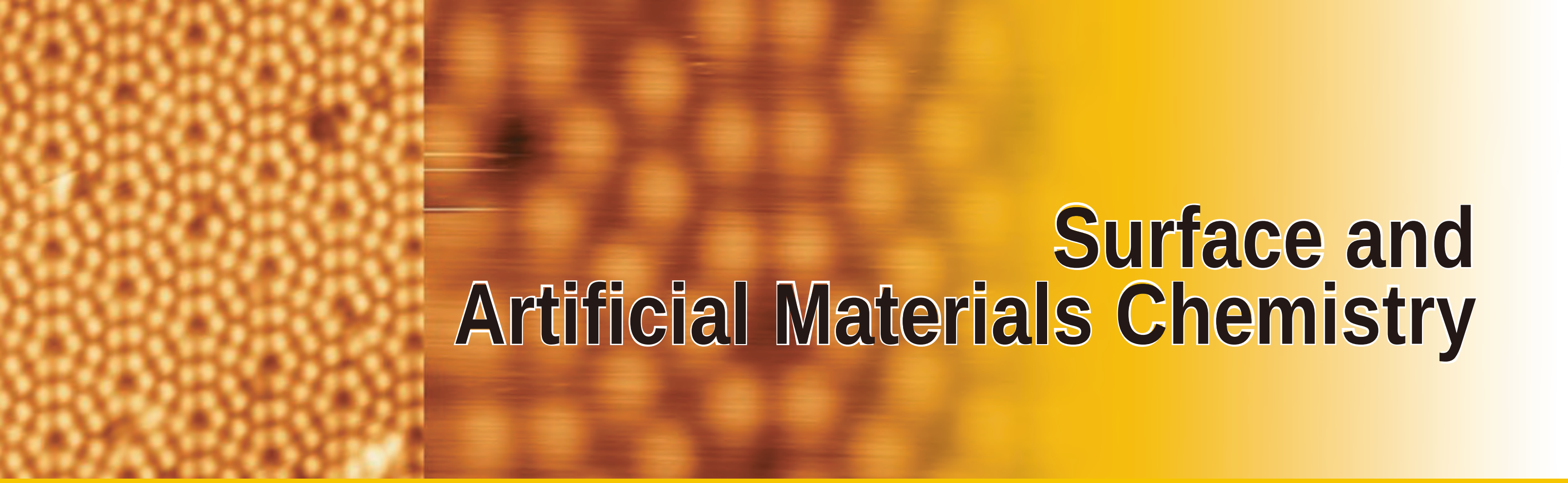

Surface and Artificial Materials Chemistry

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Exploration of novel properties at exotic heterointerfaces

All changes occurring in nature may fairly be said to start at the surfaces or interfaces. In our main target heterogeneous catalysis surface and interface phenomena play important roles in preparation processes of catalysts and actual catalytic reaction processes. Size and shape controls of nanomaterials and reaction controls are often achieved via surface and interface phenomena. Our aim is not only to understand reaction mechanisms but also to design novel catalysts for organic reactions and Green Chemistry processes based on (1) syntheses of novel nanomaterials and characterization, (2) insitu measurements for active catalysts, and (3) mechanism studies with computational chemistry.

Development of novel nanomaterials via control of interface and application to heterogeneous catalysis

Nanomaterials synthesis often takes place in solution. Figure 1 shows Co_3O_4 nanocrystals with different shpae grown in aqueous solution through oxidation of $CoCl_2$ by H_2O_2. All of them are single crystals. Use of different surfactants resulted in different shapes. Non-ionic surfactant consisted of ether bonds gave non-specific interaction, resulting in a nano sphere. Either cationic or anionic surfactant resulted in nano cube exhibiting (100) equivalent surfaces. Addition of polar organic molecules such as acetonitrile or DMF instead of surfactants gave rhombododecahedron, exhibiting (110) equivalent surfaces. Shape control was realized by different surface termination with different surfactants or polar molecules.

We have studied metal-containing ionic liquids and immobilization on solid supports. According to the scheme shown in Figure 2, imidazolium groups are immobilized on mesoporous silica SBA-15, AuCl was introduced and reduction with $NaBH_4$ was achieved to obtain Au nanoparticles, whose TEM image is shown in Figure 3 [2]. Average particle size is 2 nm and can be controllable with different reductant feed ratio and concentration. This Au catalyst can catalyze reduction of p-nitrophenol and Suzuki cross coupling reaction in water/EtOH solvent. Pd catalysts prepared in a similar way can catalyze carbonylation reactions where carbon monoxide is incorporated in product molecules [3].

Figure 4 shows the TEM image for amine functionalized graphene oxide (AP-GO) prepared by our group. It was found that AP-GO with the use of tetrabutylammonium iodide as co-catalyst can catalyze the synthesis of cyclic carbonates at atmospheric pressure and low temperature (70 ℃). This GO based catalyst exhibits superior activity owing to its large surface area with abundant hydrogen bonding donor capability and the presence of well-defined amine functional groups, resulting in a synergistic effect for the catalytic reaction. The developed AP-GO could be easily recovered and used repetitively up to seven recycle runs with unchanged catalyst activity [4].

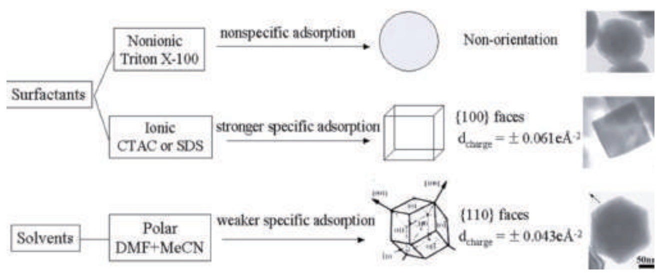

Figure 1. Shape control of Co_3O_4 nanocrystals[1]

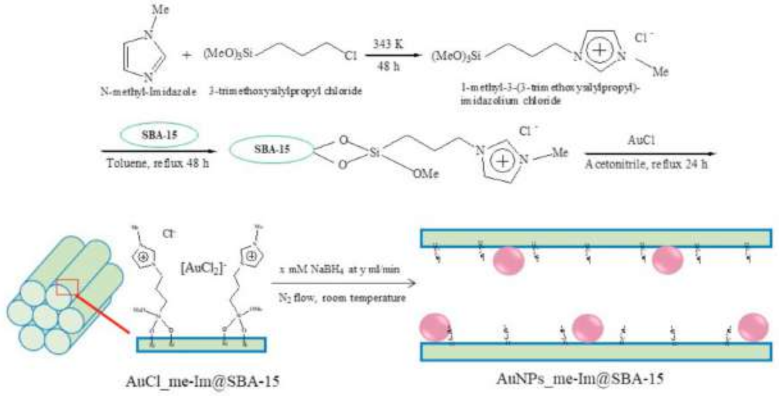

Figure 2. Preparation scheme for immobilized ionic liquid catalysts on SBA-15, introduction of AuCl and reduction to give Au nanoparticles [2]

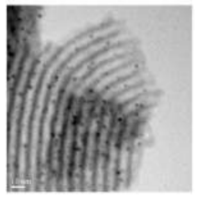

Figure 3 TEM image for Au nanoparticles supported on SBA-15 with immobilized imidazlium groups [2]

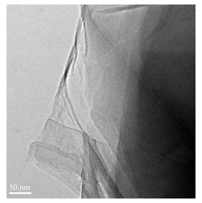

Figure 4. TEM image for the amino group functionalized graphene oxide (AP-GO) [4].

Insitu measurements for active catalysts and mechanism study with computational chemistry

Insitu measurements for active catalysts are important to study reactivity and mechanism. We are using TAP (Temporal Analysis of Products) method as shown in Figure 5, with which pulsed reactant gas with duration of 5 ms is injected to catalyst layers and mass spectrometer responses of products are recorded, for the purpose of obtaining mass balance information and kinetic parameters of the diffusion and reaction processes. In synchrotron radiation facilities we achieve insitu XAFS measurements to monitor coordination states and electronic states of active metal in catalysts in preparation and reaction processes mainly for methane partial oxidation and CO_2 hydrogenation reactions.

Computational chemistry such as Density Functional Theory calculations is important to determine active structures, transition states and energy profiles of reactions. Figure 6 shows the energy diagram for a Pt_6 cluster interacting with NH_3, NH_4^+, benzene and O_2 leading to the formation of phenol, obtained by DFT calculation. This calculation was achieved to clarify the efficient and selective synthesis of phenol from benzene and O_2 catalyzed by a Pt cluster catalyst supported in β zeolite in the presence of ammonia. An oxygen molecule dissociates on the Pt clusters to give two oxygen adatoms, and an oxygen adatom attacks a carbon atom of the benzene molecule to yield an intermediate with a Pt-O-C bond. Proton transfer from the carbon atom to the oxygen atom proceeds to give a molecule of phenol. These processes correspond to two activation barriers for the production of phenol which can be overcome by the temperature condition adopted in the experiments [5]. Recently, we are studying the mechanism of sugar alcohol conversion by hot water with Metadynamics and first-principles calculations for the utilization of biomass materials.[6]. We also measured C-K edge XAS spectra for aqueous cellobiose solution by Soft X-ray Absorption Spectroscopy and found that hydrogen bonding between cellobiose and water molecules dominate the features of XAS spectra by the first principles molecular dynamics and XAS simulation [7]. We recently reported a novel synthesis method for producing stable titanium dioxide nanoparticles (10 nm) dispersed in hydrophobic solvents using organophosphates. Our approach enables the control of nanoparticles' electric field responsiveness by altering the dispersing medium's composition, expanding their potential applications in electronics, photovoltaics, and photocatalysis [8].

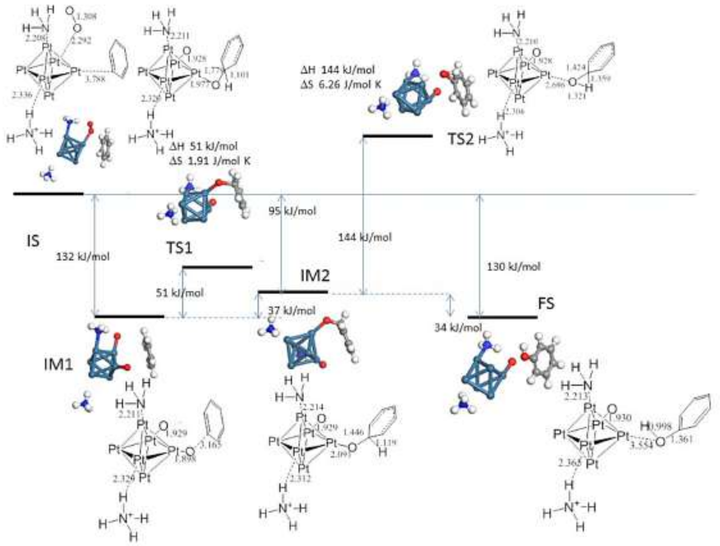

Figure 6. Energy diagram for the Pt_6 cluster interacting with NH_3, NH_4^+, benzene and O_2 leading to the formation of phenol [5].

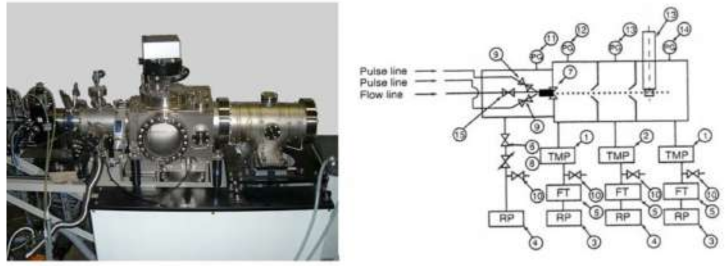

Figure 5 Photograph and diagram for TAP system.

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History

1861 The Department of Manufacturing Chemistry in the Institute for Research of Foreign Books established by the Tokugawa Shogunate. Re-established at Yosho Shirabesho,Kaisei Gakko and Tokyo Kaisei Gakko.
1877 Merged with Tokyo Igakko to form Tokyo Daigaku (Tokyo University), and the Department of Chemistry founded within the School of Science.
1880 Gakushi Kenkyuka (a school for graduate students, antecedent to the Graduate School) established.
1886 Renamed Teikoku Daigaku Rika Daigaku (Imperial University of Science), and the Graduate School established.
1888 Doctoral degrees (10 in science) bestowed for the first time.
1897 Renamed Tokyo Teikoku Daigaku Rika Daigaku (Tokyo Imperial University of Science).
1919 Renamed School of Science, Tokyo Imperial University.
1951 School of Science reorganized into five departments, including the Department of Chemistry.
1953 University of Tokyo Graduate Schools established under the new School Education Law.
1965 Graduate Schools reorganized to establish five new graduate schools, including the Graduate School of Science.
1976 Research Center for Spectral Chemistry established.
1978 Laboratory for Earthquake Chemistry established.
1991 Research Center for Spectral Chemistry reorganized.
1993 Graduate School of Science reorganized (greater emphasis placed on research and educational activities at graduate school levels).
1998 Graduate School of Frontier Sciences established
2002 The 21st Century COE Program for Frontiers in Fundamental Chemistry commenced.
2005 Center for Ultrafast Intense Laser Science established.
2007 Global COE Program for Chemistry Innovation through Cooperation of Science and Engineering commenced.
2011 Ceremony for the 150th Anniversary of the Department of Chemistry was held.
2011 Leading Graduate School Doctoral Program 'Advanced Leading Graduate Course for Photon Science (ALPS)' commenced.
2012 Leading Graduate School Doctoral Program 'Materials Education program for the future leaders in Research, Industry, and Technology (MERIT)' commenced.
2014 Global Science Course (GSC) commenced.
2018 Biomolecular Chemistry Laboratory established.
2021 "Fostering Advanced Human Resources to Lead Green Transformation (GX)" project commenced.

Facilities


Nuclear Magnetic Resonance Spectrometer

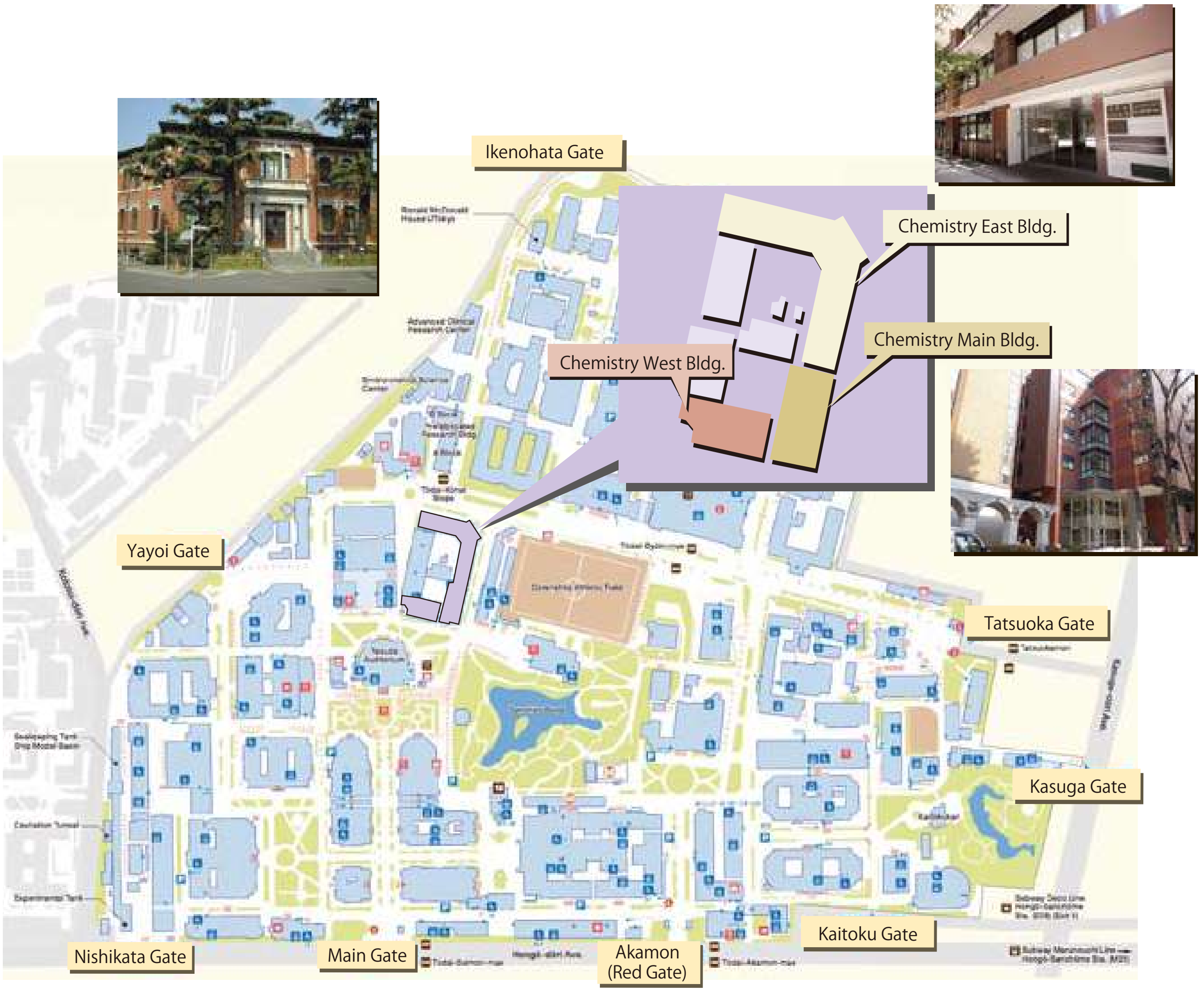

The Library of Our Department

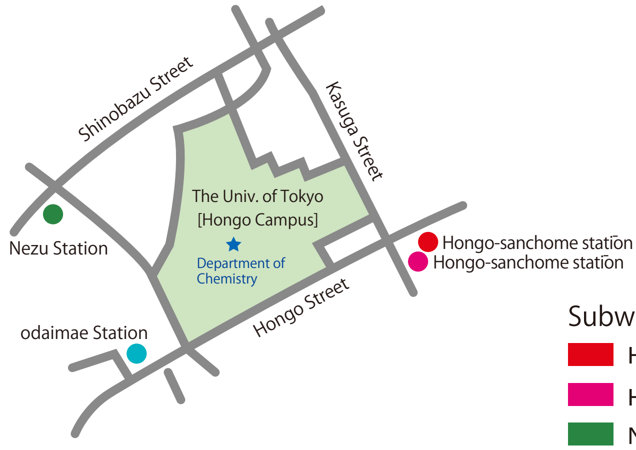

Chemistry Experiment for Undergraduate Students


Auditorium

Map of Hongo Campus (Chemistry Bldg.)

7-3-1 Hongo, Bunkyo-ku, Tokyo 113-0033, Japan
TEL: +81-3-5841-4321
E-Mail：kagaku@chem.s.u-tokyo.ac.jp
Homepage: http://www.chem.s.u-tokyo.ac.jp/





Bus

From Ueno Station: take Toei Bus 学01 for Todai-Konai and get off at Konai Bus Stop.

From Ochanomizu Station: take Toei Bus 学07 for Todai-Konai and get off at Konai Bus Stop.

Subway

- 🟥 Hongo-sanchōme Station (Tokyo Metro Line), 15 min walk
- 🟥 Hongo-sanchōme Station (Toei Subway Line), 15 min walk
- 🟩 Nezu Station (Tokyo Metro Line), 10 min walk
- 🟦 Todaimae Station (Tokyo Metro Line), 15 min walk

2025.01