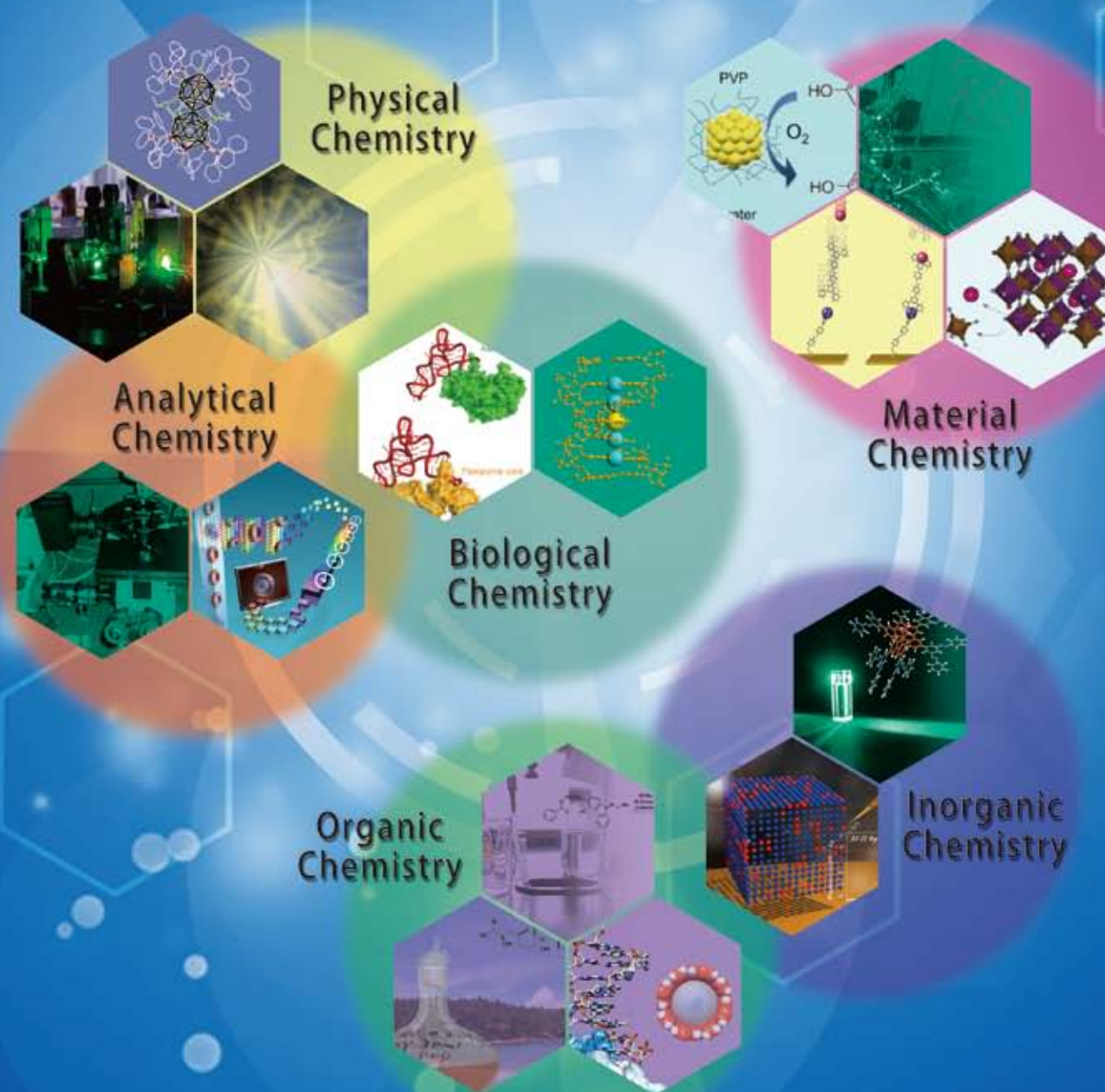


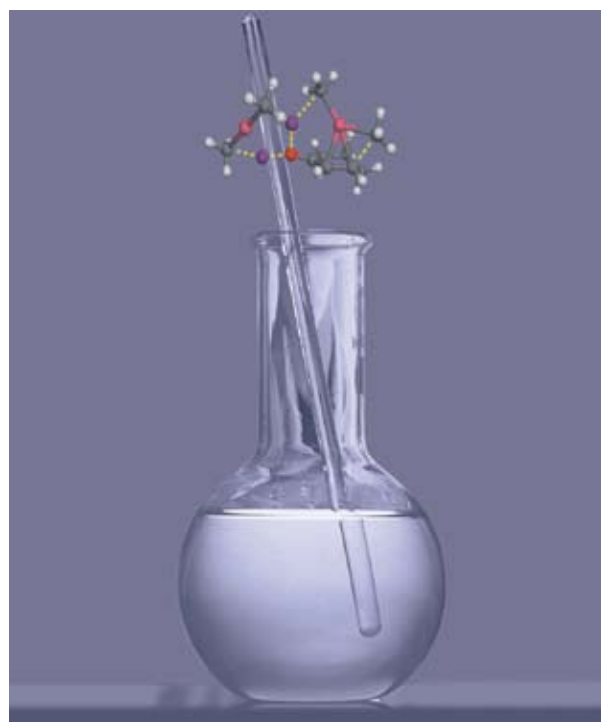
CHEMISTRY

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



Laboratories in Department of Chemistry

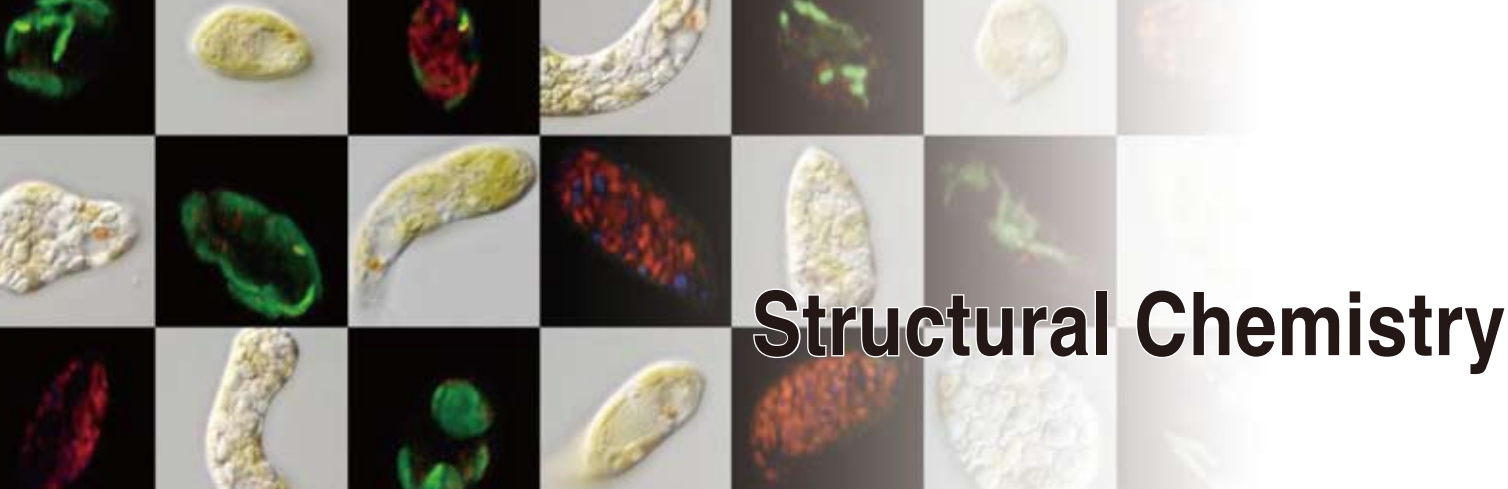
Department of Chemistry, School of Science, The University of Tokyo



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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Structural Chemistry

Molecular Imaging & Spectroscopy for Data-Driven Science



Figure 1: Members and collaborators of Goda Lab

Goda Lab is aimed at developing innovative laser-based molecular imaging and spectroscopy technologies together with multi-dimensional analytics that will revolutionize life sciences and medicine. Specifically, the technologies are designed for discovering new biological phenomena, elucidating unknown mechanisms, and exploiting new applications. The technologies are based on an integration of theoretical, experimental, and computational techniques in physics and chemistry combined with molecular cell biology, electrical engineering, computer science, artificial intelligence, biomedical engineering, applied mathematics, mechanical engineering, and nanotechnology. Directed by Prof. Keisuke Goda, Goda Lab fosters an international and interdisciplinary research environment. Goda Lab constantly seeks for ambitious individuals from any university in any field who have the will to play a leading role in scientific exploration and have a major impact on the world. Furthermore, Goda Lab encourages students to start their own startups based on their research achievements. To date, two startups have been launched based on technologies developed in Goda Lab.

Coherent Raman spectroscopy with optical frequency combs

Frequency combs have attracted much attention from physicists and chemists since the Nobel Prize in Physics was given to the development of frequency combs. A frequency comb is an optical spectrum that consists of a series of equally spaced frequency modes with narrow linewidths and can therefore be used as an optical ruler. Goda Lab aims at developing fast continuous methods based on frequency combs for coherent Raman spectroscopy and exploiting their unique applications.



Figure 2: Ultrafast fluorescence microscope

Label-free biochemical imaging for medical applications

Fluorescence detection based on fluorescent dyes has become one of the most widely used methods in scientific research and clinical practice such as identification of cellular signaling, protein folding, and cancer tumor. Despite its high sensitivity, it has limitations such as toxicity, long decay times, and interference with normal biological processes. To circumvent these limitations, Goda Lab currently develops new types of high-speed label-free spectroscopy-based biochemical sensing technology.



Figure 3: Clean room for nanofabrication



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Extreme imaging

Conventional high-speed imaging methods are unable to capture fast dynamics in living cells due to their mechanical and electronic operation or limited sensitivity. Goda Lab aims to develop unconventional types of imaging for high-speed bright-field microscopy and confocal fluorescence microscopy and also to exploit new applications based on the imaging methods. Prominent examples of Goda Lab's previous efforts for high-speed imaging include STEAM and STAMP.

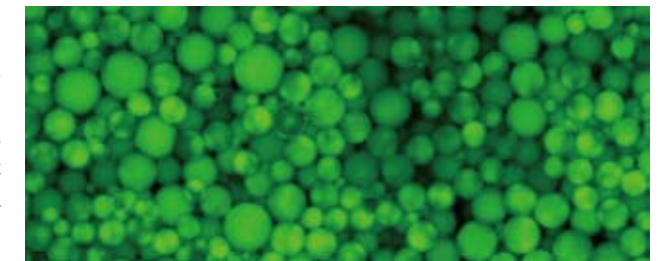


Figure 4: Droplets for single-cell analysis

Intelligent image-activated cell sorting

Fluorescence-activated cell sorting is a powerful method for analyzing and sorting cells based on their phenotypes. However, it is limited in identifying how spatial architectures of intracellular molecules are linked to their physiological functions. To answer this basic biological question, Goda Lab and colleagues have recently developed an intelligent image-activated cell sorter. Goda Lab currently aims at making new scientific discoveries and exploiting new applications based on the technology.

Molecular image cytometry for cancer detection

Cancer spread or metastasis is the primary cause of cancer death. In fact, 90% of cancer deaths are due to cancer metastasis, not the original tumor. Cancer metastasis is caused by the migration of cancer cells to more distant parts of the body via either the lymphatic system or bloodstream. Goda Lab currently develops high-throughput screening methods based on an integration of photonics and microfluidics for real-time screening of rare metastatic cancer cells in blood.

Graphene photonics for biochemical sensing

Graphene is a two-dimensional atomic-scale hexagonal lattice made of carbon atoms and has many extraordinary properties such as high stiffness and conductivity. Unique optical properties of graphene give us opportunities to develop graphene-based integrated circuits for sensitive biochemical sensing and spectroscopy applications. By combining graphene with the state-of-the-art silicon photonics technology, Goda Lab aims to develop on-chip devices for such biochemical applications.



Figure 5: Frequency comb generator

Start your own great innovations

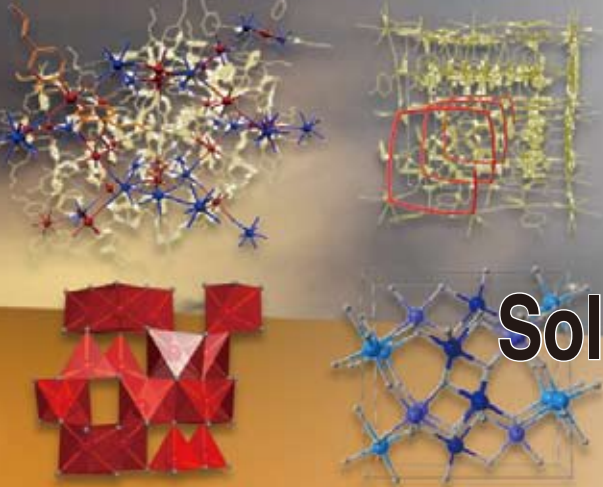
History tells us that the greatest discoveries come totally unexpected out of nowhere. While luck seems to play a role, required attributes for preparing "unexpected" events and making "planned" discoveries are curiosity, persistence, flexibility, optimism, and risk taking. Goda Lab encourages students to come up with their own ideas through brainstorming and discussion with colleagues by providing financial support to student-initiated research projects that might lead to great innovations.



Figure 6: Lasers for high-precision spectroscopy

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Solid State Physical Chemistry

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, $\epsilon\text{-Fe}_2\text{O}_3$, showing huge coercive field and high-frequency millimeter wave absorption, and lambda-titanium oxide, $\lambda\text{-Ti}_2\text{O}_3$, 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.

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.

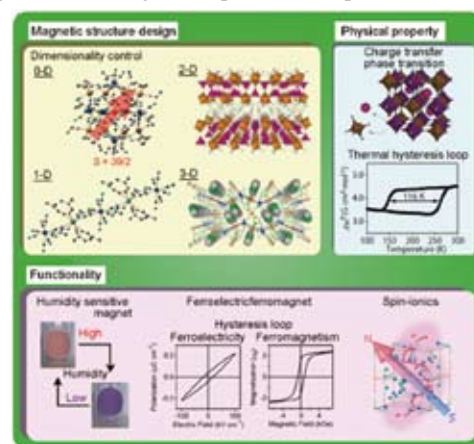


Figure 2. Structural design and generation of functionalities based on molecular design

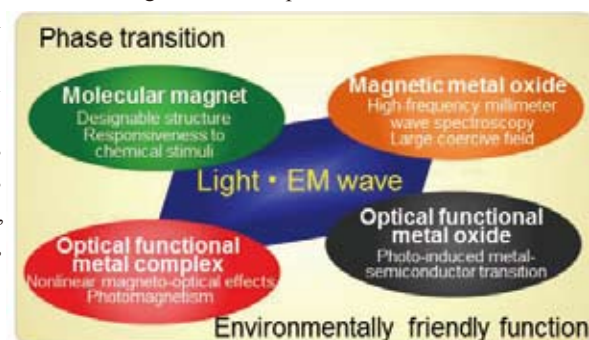


Figure 1. Conceptual diagram of material development

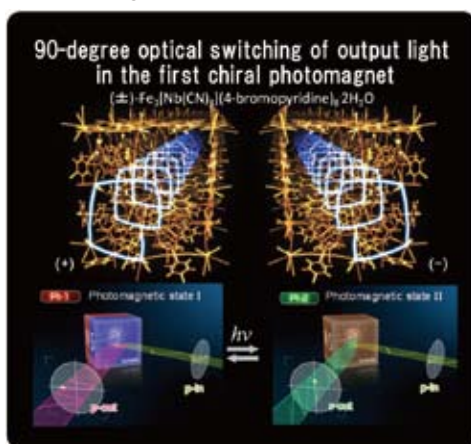


Figure 3. Novel magnetic phenomena and functionalities associated with magneto-optical correlation



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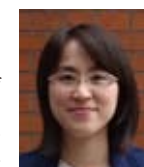
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Study of novel magnetic oxides with electromagnetic environmentally protective function

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 $\epsilon\text{-Fe}_2\text{O}_3$ for the first time. $\epsilon\text{-Fe}_2\text{O}_3$ 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 $\epsilon\text{-Fe}_2\text{O}_3$. This H_c value is comparable to those of rare-earth magnets. We have also observed that $\epsilon\text{-Fe}_2\text{O}_3$ and metal substituted $\epsilon\text{-Fe}_2\text{O}_3$ show the highest frequency electromagnetic wave absorption in the millimeter wave region, and thus, promoted applied research for high-density magnetic recording applications and for practical use as millimeter wave absorbers with electromagnetic environmentally protective function. Recently, we observed high-frequency millimeter wave absorption and a rotation of the polarization plane of the propagated millimeter wave above 200 GHz.

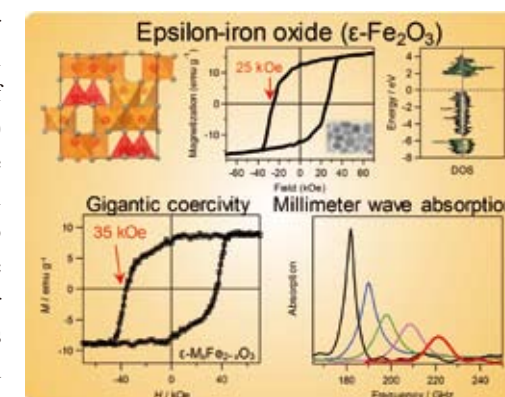


Figure 4. High performance metal oxide magnet, epsilon iron oxide nanoparticles

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 ($\lambda\text{-Ti}_2\text{O}_3$). This material shows photoinduced phase transition from black colored lambda phase (metallic conductor) to brown colored beta phase ($\beta\text{-Ti}_2\text{O}_3$) (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 $\lambda\text{-Ti}_2\text{O}_3$ is very economical and environmentally friendly material and is obtained as nanoparticles, $\lambda\text{-Ti}_2\text{O}_3$ is expected as a next generation high-density optical storage material. Additionally, $\lambda\text{-Ti}_2\text{O}_3$ 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.

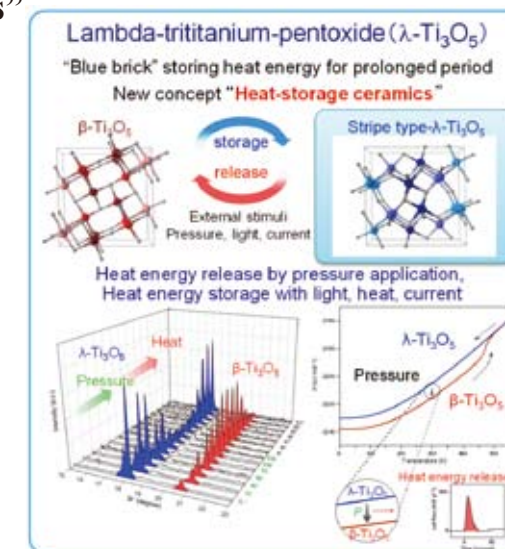


Figure 5. “Heat storage ceramics” preserving heat energy for prolonged period

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Quantum Chemistry

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/cm², 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 such as the wavelength, pulse duration, intensity, and carrier-envelope phase (CEP). From the investigation of atoms and molecules interacting with an intense laser field, we can learn fundamental aspects of the light-matter interactions.

Figure 1 shows a variety of phenomena induced when molecules are exposed to an intense laser field. In the relatively low field intensities, the axis of molecules can be “aligned” or “oriented” along the laser polarization direction. In the higher field intensities, molecules are dressed by light, and the dynamics of molecules are governed by a newly formed potential energy surface called a light-dressed potential energy surface. When the laser field intensity becomes even higher, electrons in molecules are taken away one after another through the tunnel ionization, and multiply charged molecular ions are formed. These multiply charged molecular ions dissociate into fragment ions having large released kinetic energies by the Coulombic repulsion among the fragment ions. This decomposition process of molecules into fragment ions with the high kinetic energies is called Coulomb explosion.

In these 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) “population inversion in N_2^+ and lasing,” (7) “theory for describing atoms and molecules and their dynamics in an intense laser field,” (8) “quantum computing applied to atomic and molecular problems,” and (9) “material processing by the extreme ultraviolet femtosecond laser pulses.”

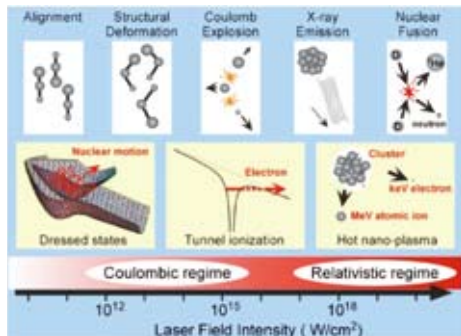


Figure 1. Dynamics of molecules in intense laser fields [1].

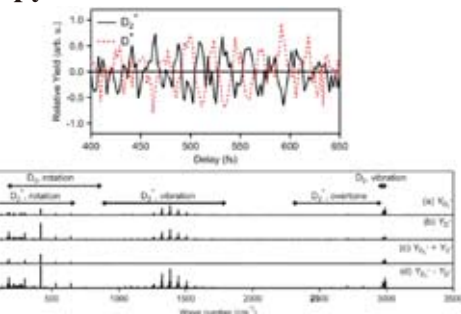


Figure 2. The results of SURF spectroscopic measurements of D^+ and D_2^+ . The ion yields as a function of the delay time between the pump and probe pulse and the Fourier transform spectra [2].

Ultrafast molecular imaging by laser-assisted electron diffraction

When electrons are scattered by atoms and molecules in a laser field, the scattered electrons can gain or lose their energy by multiples of the photon energy. This is a phenomenon called laser-assisted elastic electron scattering (LAES) [6]. By using the LAES process induced by an ultrashort laser pulse as an ultrafast shutter for the measurement of an electron diffraction pattern of molecules, ultrafast geometrical changes of molecules can be probed with extremely high temporal resolution. By this laser-assisted electron diffraction (LAED) method, we recorded an electron diffraction pattern of carbon tetrachloride, CCl_4 , at the moment of the irradiation of femtosecond laser pulses [7]. We also developed a method of terahertz-wave-assisted electron diffraction in which a monocycle terahertz-wave pulse is used as a streaking electric field for the scattered electrons and observed a terahertz-wave-assisted electron scattering process of Ar [8].

We also developed an experimental apparatus for measurements of laser-assisted electron impact ionization (LAEII) and found that the scattering cross section of electron impact ionization of Ar, in which an electron in the 3p orbital is ejected, increases in an intense laser field (Fig. 3). By this measurement, it was revealed experimentally that an electronic wave function of Ar is described as that in a state distorted by an intense laser field (a light-dressed state). By LAEII measurements, we can reveal how the wavefunctions of atoms and molecules are distorted in an intense laser field in real time [9].

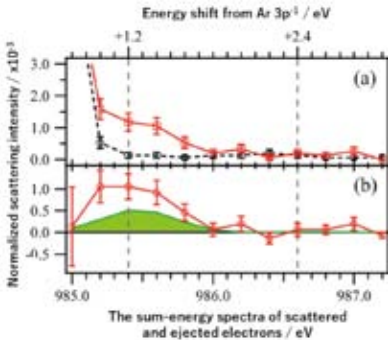


Figure 3. The sum-energy spectra of scattered and ejected electrons obtained by LAEII of Ar atoms. The scattering cross section increases at the energy corresponding to one-photon absorption processes.



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Development of theories to describe molecular dynamics in strong laser fields

By extending the first-principle quantal theory called multi-configuration time-dependent Hartree-Fock (MCTDHF) theory, 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]. We also performed first-principles molecular dynamics calculations of the ejection processes of H_3^+ from methanol dication and revealed the existence of the reaction pathways in which a neutral H_2 moiety appears within the dication first, and then, H_3^+ moiety is created within the dication and ejected from the dication [12].

Mechanism of N_2^+ lasing

In a laser filament produced by focusing intense femtosecond laser pulses into air, emission of coherent light from N_2^+ by amplified stimulated emission is observed at a wavelength of 391 nm, which corresponds to the transition from the excited electronic $B^2\Sigma_u^+$ state to the electronic ground state $X^2\Sigma_g^+$ (Fig. 4). We have shown by theoretical simulations and experimental measurements [13, 14, 15] that the population inversion required for the amplification can be interpreted by a sudden turn-on mechanism, in which N_2^+ is suddenly exposed to an intense laser field after the ionization of neutral N_2 and that, by the interaction with the laser field, the population in the $X^2\Sigma_g^+$ state of N_2^+ is transferred to the first electronically excited $A^2\Pi_u$ state, which further increases the extent of the population inversion between the $B^2\Sigma_u^+$ and $X^2\Sigma_g^+$ states.

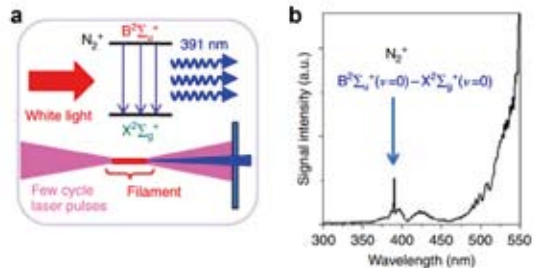


Figure 4. (a) Schematic of air lasing induced by a few-cycle laser pulse. (b) Emission spectrum of the lasing at 391 nm [13].

Application of quantum computing to molecular science

Quantum computers are promising for the calculation of energy levels of very large molecules that cannot be treated by classical computers. However, the results obtained using current quantum computers carry both systematic and statistical errors originating from different sources of noise, and therefore, it is necessary to implement error mitigation techniques. We have shown how the Hückel molecular orbital energies of π -bonded molecules such as benzene can be evaluated on the superconducting qubit type quantum computer *ibm_kawasaki* [16]. We also developed a reduced multi-state contracted variational quantum eigensolver (RMC-VQE) method and calculated the Fermi resonance vibrational-energy levels of CO_2 and the corresponding wave functions (Fig. 5) [17]. It was shown that a quantum computer is a promising tool for calculating the vibrational energy levels of polyatomic molecules in vibrational spectroscopy [18].

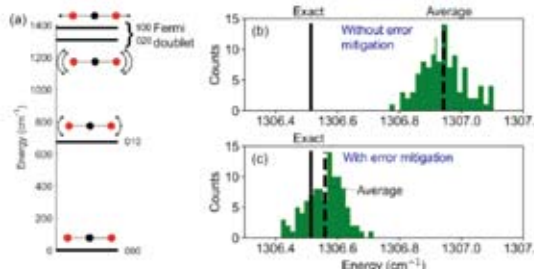


Figure 5. (a) Vibrational energy levels of the CO_2 molecule. Energy histogram of the lower level of the Fermi doublet calculated by a quantum computer (b) without error mitigation and (c) with error mitigation [17].

Extreme ultraviolet femtosecond laser processing

By focusing femtosecond laser pulses into a rare-gas medium, extreme ultraviolet (EUV) femtosecond laser pulses are generated through the high-order harmonics generation process. We focus the EUV laser pulses into a submicron spot by using a high-quality focusing mirror (Fig. 6) [19, 20]. By irradiating the metal and semi-conductor materials with focused EUV laser pulses, we achieved submicron laser processing [19, 20].

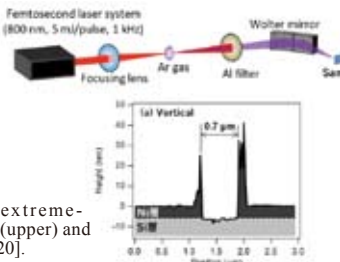


Figure 6. An experimental setup for extreme-ultraviolet femtosecond laser processing (upper) and the recorded ablation spot profile (lower) [20].

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Catalytic Chemistry

Development of novel catalysts based on metal clusters

Metal clusters with diameters smaller than 2 nm show novel properties that are absent 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 activity is directed toward understanding the origin of the size-specific chemical properties of metal clusters and toward the development of cluster-based nanocatalysts (Figure 1).

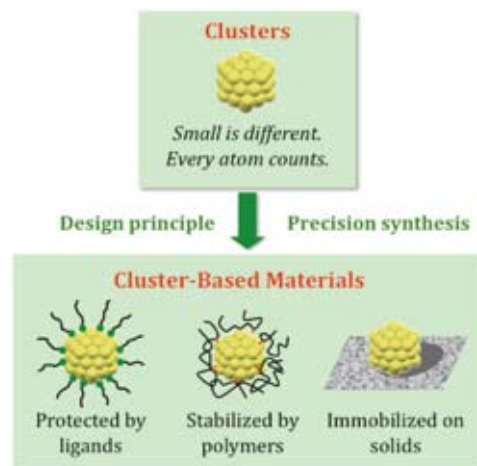


Figure 1. Development of cluster-based materials. The clusters are stabilized against aggregation by various methods depending on the application.

Chemistry of superatoms and superatomic molecules

Metal clusters can be treated as conventional chemical compounds when they are protected by organic ligands. We developed a size-selective and systematic synthetic method to produce gold clusters protected by ligands such as thiolates (RS), phosphines (PR₃), and alkynes. Our method yielded a series of clusters, such as Au₂₅(SR)₁₈, Au₃₈(SR)₂₄, Au₅₅(SR)₃₁, Au₇₅(SR)₄₄, Au₁₄₄(SR)₆₀, [Au₂₅(SR)₅(PR₃)₁₀Cl₂]²⁺, and Au₅₄(C≡CPh)₂₆, whose chemical compositions were defined with an atomic and molecular precision. The stabilities and structures of the ligand-protected Au clusters are understood in the framework of “superatoms” and “superatomic molecules” (Figure 2). We are currently expanding libraries of superatoms for the construction of a periodic table of artificial elements in nanoscale and superatomic molecules for the development of novel functional materials.

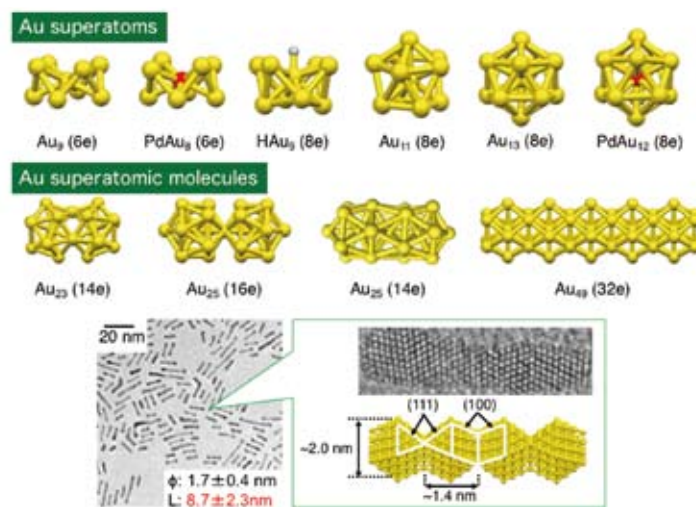


Figure 2. Gold superatoms and their dimers and oligomers. The ligand layers are omitted for simplicity.

Precision synthesis of gold cluster catalysts

We found that polyvinyl pyrrolidone (PVP)-stabilized Au clusters show catalytic activity in aerobic oxidation of alcohols when the cluster diameter is smaller than 3 nm and that the activity is enhanced with a decrease in the diameter. We also revealed by using spectroscopic methods that the small Au clusters are negatively charged by the interaction with PVP. We proposed a reaction mechanism based on the catalytic activation of an oxygen molecule via electron transfer from the gold clusters.

It is a technical challenge to precisely control the size of the clusters on solid supports. We developed a new synthetic method based on calcination of the ligand-protected Au clusters adsorbed on the supports. This approach allows us to control key structural parameters (size, composition and



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surface coverage) precisely and independently. We demonstrated remarkable effects of the structural parameters on the catalysis of supported Au-based catalysts for aerobic oxidation reactions (Figure 3).

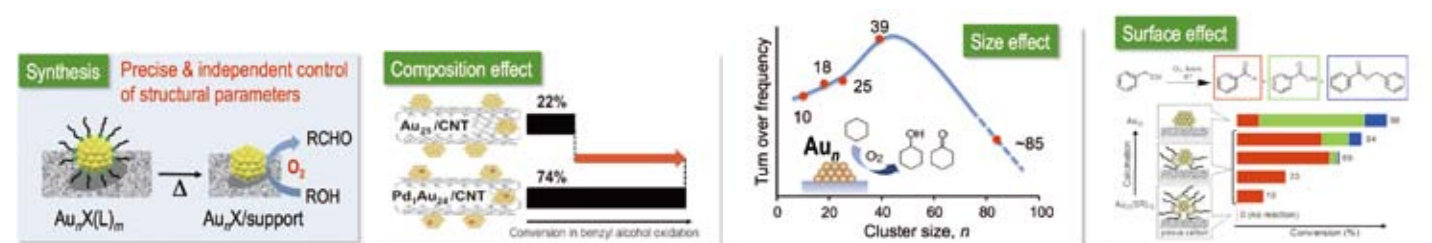


Figure 3. Controlled synthesis of supported Au-based clusters and the effects of the structural parameters on catalysis.

Elucidation of structure-reactivity correlations of free metal clusters

Guiding principles are required for the rational development of new cluster-based catalysts. Namely, it is important to understand the structural parameters (size, composition, and charge state) suitable for catalytic activation of small molecules and to explore new chemical properties of clusters. To this end, we are studying the chemical reactions of free metal clusters with well-defined structural parameters by means of home-built apparatus composed of mass spectrometer and photoelectron spectrometer, combined with theoretical calculations.

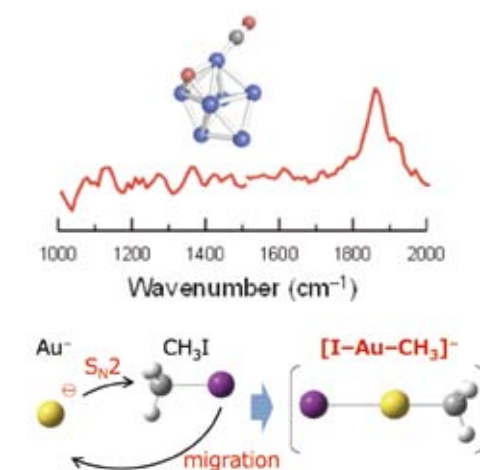


Figure 4. Activation of CO₂ by Co cluster anions and a new activation route of the C-I bond of CH₃I by Au⁻.

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Synthetic Organic Chemistry

Creation of Novel Science Based on Organic Synthesis

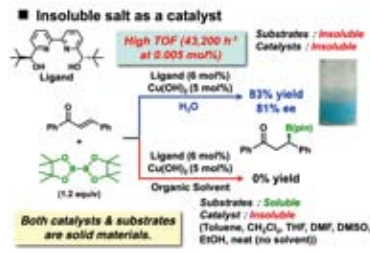
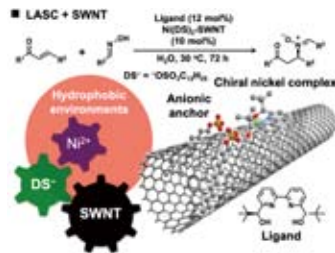
Synthetic organic chemistry is the science of “making” chemical products. Our laboratory is not only continuing and expanding upon the traditional role of synthetic organic chemistry, but is also aiming to open new doors of new sciences based on the products of our synthetic endeavors. We are interested 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 chemicals, 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

Since the advent of organic chemistry, Friedrich Wöhler’s urea synthesis in 1828, it has been systematically cultivated in organic solvents. In contrast, we have disclosed a number of examples on new reactivity and selectivity observed in chemical reactions performed in water that are not obtained in organic solvents. Now the curtain rises to exploit water positively as a solvent. Since independently-developed “organic chemistry in water” cannot be written by the traditional organic chemistry cultivated in organic solvents, “organic chemistry in water” wants systemizing. Our group has extensively engaged in the development of multifarious catalytic systems that are water-compatible. One of our fruits, Lewis Acid-Surfactant-Combined Catalyst (LASC) forms hydrophobic micelle along with water-tolerant Lewis acidity. In our recent work, a homogenized combination of nickel-based LASCs and single-walled carbon nanotubes (SWNTs) was designed to exhibit excellent activity in water. The electrochemical behavior of the central metal was modified to address the inherently low Lewis acidity of metal cations, enabling the efficient and highly selective synthesis of optically active nitrones. Like this, one of our biggest concerns is exploring catalytic asymmetric reactions in water toward efficient synthetic methodologies of optically active compounds. To date, we have developed asymmetric hydroxymethylation, Michael addition, and protonation reactions. Furthermore, we have spotlighted zero-valent metals, and metal oxides or hydroxides that have not been used so far. Their outstanding catalytic activities in aqueous environments are discovered, leading to a set of highly stereoselective bond-forming reactions such as allylation reactions of aldehydes, boron and silicon conjugate addition reactions with a considerably wide range of substrate generality. These reactions do not proceed (or are not selective) at all in the absence of water, which underscores the positive effect of water that involves in reaction mechanism rather than the role as an alternative solvent.

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.



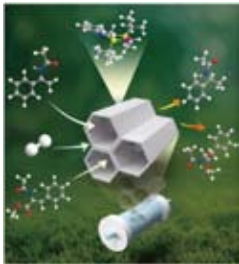
Asymmetric boron conjugate addition reaction in water using Cu(OH)₂ as a catalyst. Despite the fact that all involved species are practically insoluble in water, the reaction failed to give the desired adduct completely under neat (solvent-free) conditions.

Development of high-performance heterogeneous catalysts

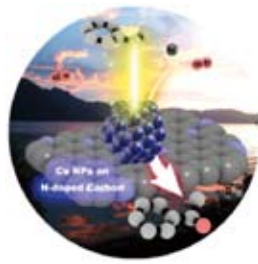
Heterogeneous catalysts can be easily separated from the product, and recovered and reused after reactions. Our laboratory has been investigating novel heterogeneous catalysts. Especially, we have developed metal nanoparticle catalysts by fine modification of supports and chiral metal catalysts by novel 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 immobilized Rh catalysts have comparable activity and selectivity as original homogeneous catalysts for flow asymmetric hydrogenation of enamides. Moreover, this method could be applied for the immobilization of chiral Lewis acid catalysts. We also developed chiral heterogeneous Ni catalysts supported inside the mesopore of MCM-41 for asymmetric 1,4-addition reactions. On the other



Catalytic asymmetric 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



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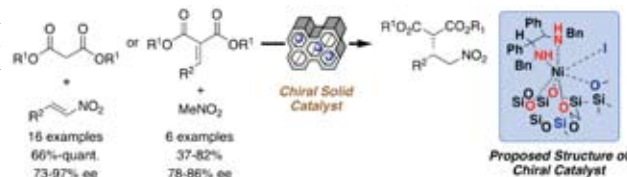
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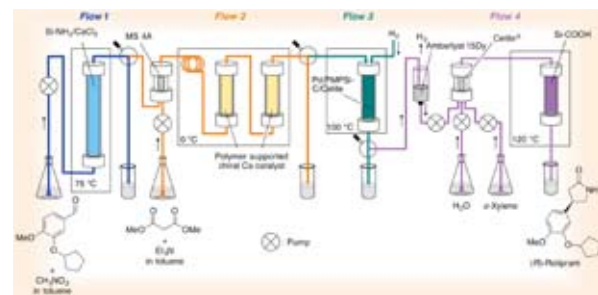
hand, we developed highly active immobilized Rh catalysts using silica-organic polymer composites with core-shell structure as support. The catalyst demonstrated higher activity than homogeneous catalysts for asymmetric 1,4-addition of boronic acids.



Heterogeneous chiral nickel complex immobilized in mesoporous silica catalyzed asymmetric 1,4-addition reactions.

Organic synthesis in the next generation with continuous-flow reactions

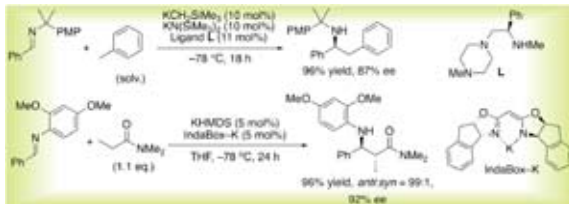
Flow reactions can synthesize molecules continuously by pumping substrate solutions into a reactor. Organic synthesis utilizing flow reactions has many advantages compared with conventional batch synthesis in terms of efficiency, safety, and environmental compatibility. Among them, flow reactions with 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, Rolipram, Donepezil, Venlafaxine, and Tamsulosin, and agrochemicals.



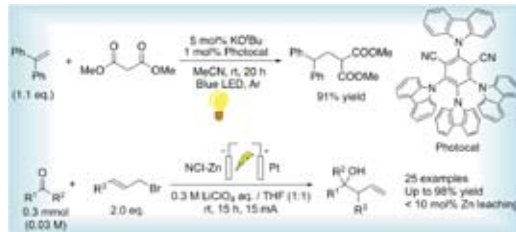
Total synthesis of optically active drug, Rolipram, using multi-steps continuous flow reaction system was achieved.

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. Recently, we have been focused on 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 developed catalytic asymmetric addition reactions of alkylarenes such as toluene with imines and Mannich reactions of weakly acidic simple amides. Moreover, we have been focusing on development of photo reactions and electrolytic reactions, and realized efficient catalytic carbon-carbon bond forming reactions.



Chiral alkaline metal strong Brønsted base-catalyzed asymmetric addition reactions of weakly acidic materials



(Top) Catalytic addition reactions of malonate with alkene using Brønsted base-photo catalyst hybrid system. (Bottom) Electrochemical allylation of carbonyl compounds using nitrogen-doped carbon-incarcerated zinc electrodes

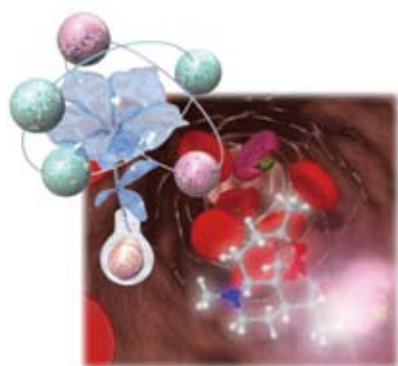
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Natural Products Chemistry

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. 1–3)

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.

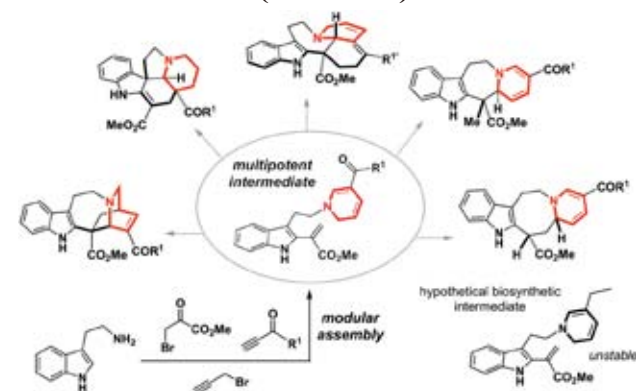


Fig. 1. Biogenetically inspired synthesis of skeletally diverse indole alkaloids.

Redesigning Biosynthetic Process: Chemo-enzymatic Hybrid Synthesis (Ref. 4–5)

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.

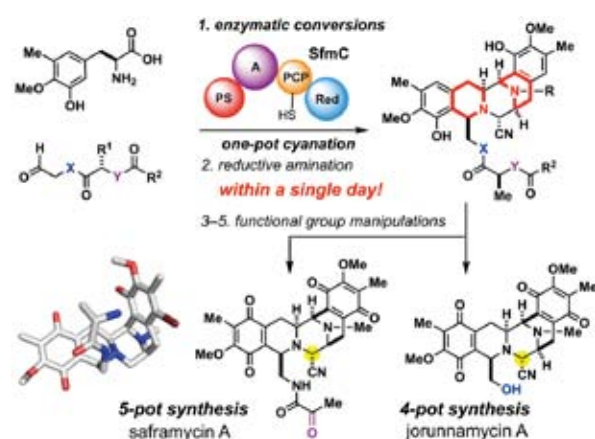


Fig. 2. Chemo-enzymatic hybrid synthetic process.



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Chemical biology utilizing covalent ligands (Ref. 6–8)

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.

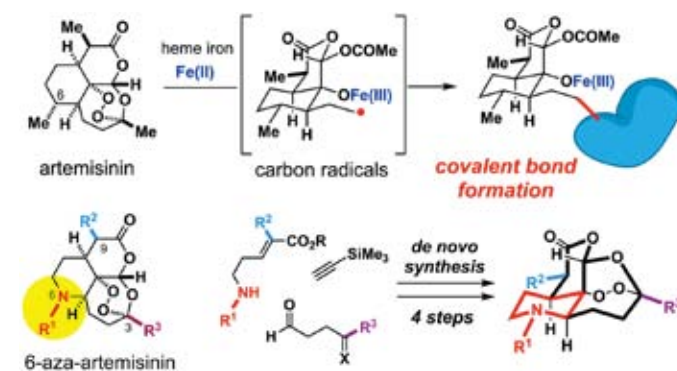


Fig. 3. Mode of action of artemisinin and modular *de novo* synthesis of 6-aza-artemisinins.

Supramolecular assemblies of natural product-based scaffolds (Ref. 9–10)

In efforts to generate self-assembling nanostructures, we paid attention to the precise molecular recognition capabilities of natural products with dense arrays of sp^3 stereogenic centers and various functional groups. The C_2 -symmetric alkaloidal skeleton has been demonstrated to be a versatile chiral scaffold for supramolecular chemistry, capable of generating configurational variations of the sp^3 stereogenic centers and thereby customizing the conformational flexibility, chiroptical property and self-assembling behavior (Fig. 4). We are developing the natural product-based versatile scaffolds that project multiple functional units with systematic diversification of the spatial arrangements. Supramolecular assemblies of the synthetic mid-sized molecules will be investigated to improve their sensing functions.

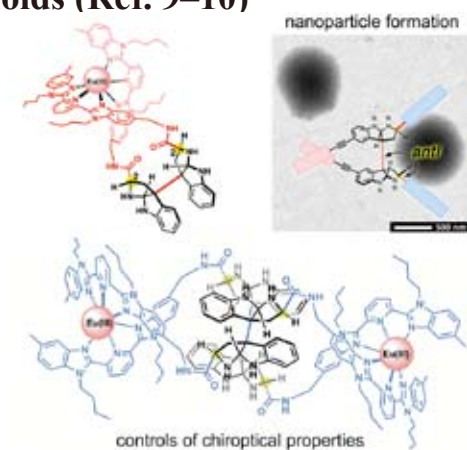


Fig. 4. Supramolecular assembly exploiting the chiral C_2 -symmetric alkaloidal scaffolds.

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Physical Organic Chemistry

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 nanotubes and their application in 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).

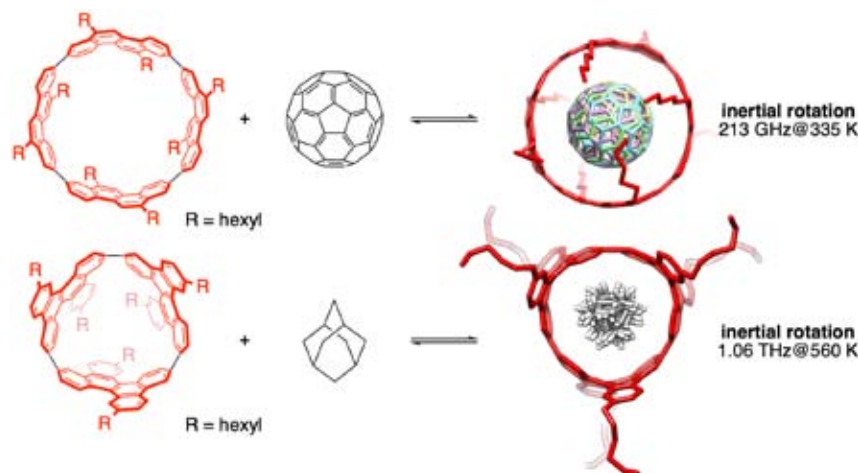


Figure 1. Molecular bearings composed of finite carbon nanotube molecules and their inertial rotation

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).

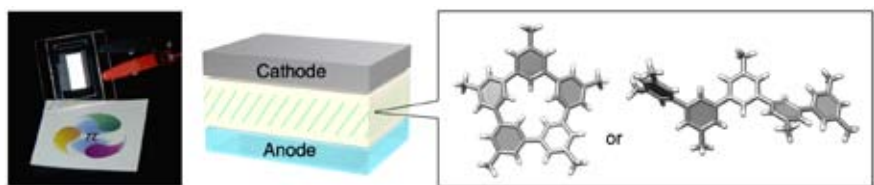


Figure 2. Highly efficient, single-layer organic light emitting devices



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Gigantic nanocarbon molecules, "phenine nanocarbons"

Recent years have witnessed an ever-growing interest in the bottom-up synthesis of nanocarbon molecules. Although elaborate synthetic methods have been devised for each molecule, they are generally "one-off" methods specified for individual targets. We have recently devised a versatile method for the design of gigantic nanocarbon molecules. The method adopts "phenine (1,3,5-trisubstituted benzene)" as basic trigonal planar units to create a series of nanometer-sized nanocarbon molecules. Based on this phenine design, we succeeded in the synthesis of a 3-nm sized nanotube molecule, *i.e.*, phenine nanotube, bowl- and saddle-shaped nanocarbon molecules and their nitrogen- and metal-doped variants (Figure 3, Reference 3). With various large phenine nanocarbon molecules, we are trying to reveal the uniqueness and anomalies of nanocarbon molecules.

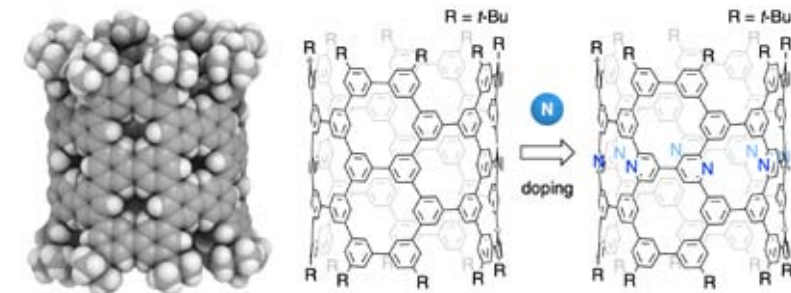


Figure 3. Phenine nanotubes (hydrocarbon and nitrogen-doped variants)

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 sp^3 carbon atoms, which led them to a discovery of a diamond twin. The diamond twin is a hypothetical network of sp^2 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.

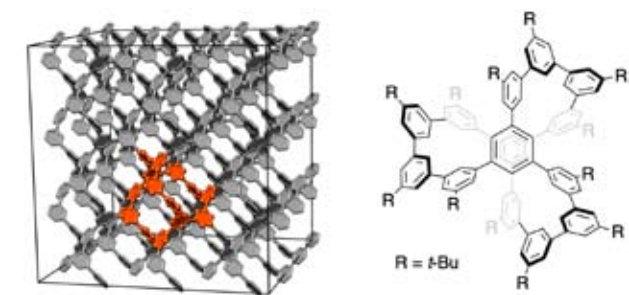


Figure 4. Phenine pollux and its minimal cage, phenine polluxene

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Engineering and directed evolution of protein-based tools

Proteins are versatile biomolecules that serve as the nano-machines and nano-structures necessary for all life on Earth. The range of functions for naturally occurring proteins is very broad. For example, proteins can be highly efficient catalysts, exquisite reagents for molecular recognition, building blocks of 3-dimensional structures, and even the basis of animal color. However, there are limits to that range of protein functions observed in Nature, since proteins evolved for the sole purpose of ensuring survival of their host species. Fortunately, some of these proteins also happen to be very useful tools for research, medical, and industrial processes. Our research is focused on making them even better! By mimicking the process of evolution in the laboratory we develop proteins that are better tools than their naturally occurring homologs. We also develop proteins that have unnatural functions and are unlike anything that is known to occur in Nature.

■ Introduction: Fluorescent proteins enable biologists to “see” the invisible world

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

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 (PhoCI) as a fundamentally new class of optogenetic tool to control protein function with light (4). PhoCI can be used light-activated transcription, gene recombination, manipulation of protein localization, and activation of enzyme activity.

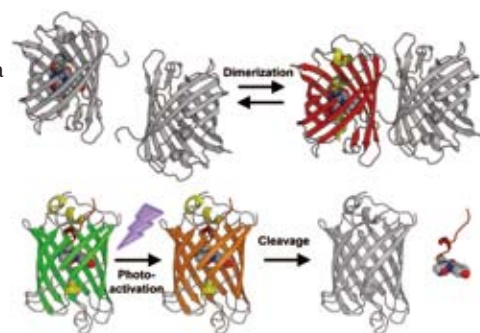


Figure 1. Novel class of optogenetic tools -ddFP & PhoCI.
Directed evolution produced novel fluorescent proteins as a new class of optogenetic tool (Upper: ddFP, bottom: PhoCI). They enabled us to detect protein-protein interactions and control protein functions with light.

■ 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

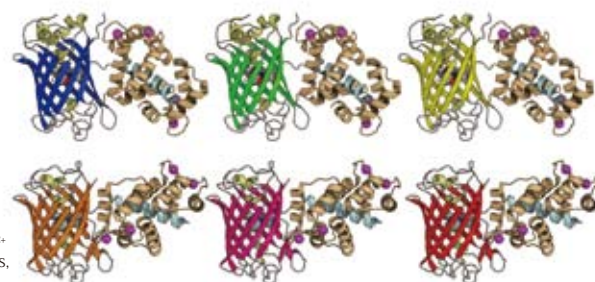
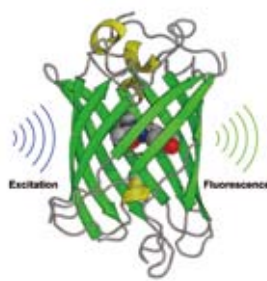


Figure 2. GECO series
Campbell group is a world leader of the development of genetically encoded Ca^{2+} indicators. To date, we have engineered genetically encoded Ca^{2+} indicators, designated as GECO series, with a range of color and Ca^{2+} affinity.

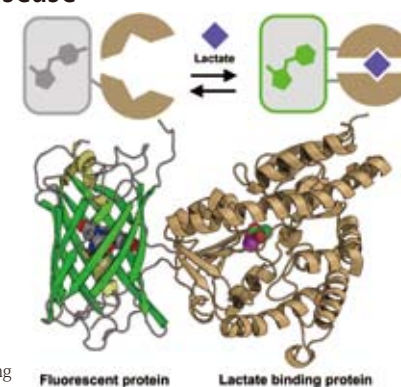


red fluorescent indicators from labs worldwide (6, 7). Versions of R-GECO1 are freely used by hundreds of research groups around the world to address a diverse range of biological problems. Our most recent addition to the GECO series is near-infrared (NIR)-GECO1 (8). The Campbell lab also developed several other classes of red-shifted neural activity indicators. For example, we developed the near-infrared (NIR) fluorescent QuasAr-series of voltage indicators (9,10), the red fluorescent FlicR1 voltage indicator, and a red fluorescent glutamate indicator (11).

■ Current Theme 1: Investigating the role of biological energy usage in disease

A healthy cell is like a well-organized city that keeps its citizens healthy and happy due to a steady supply of delicious foods being transported into the city from the surrounding countryside. If the supply of food was to be cut off, or the food was changed to less delicious alternatives, the health and happiness of the citizens would decrease. Similarly, 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 the first high-performance indicator for extracellular lactate (12).

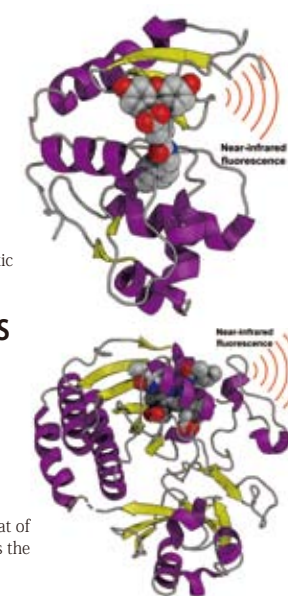
Figure 3. Genetically encoded green fluorescent lactate indicator (iLACCO)
Lactate plays a critical role in metabolism. Campbell group has developed iLACCO using directed protein evolution. Upper: schematic illustration, bottom: X-ray crystal structure.



■ Current Theme 2: Indicators based on hybrid chemi-genetic fluorescent proteins

A very promising approach for expanding the range of colors for multiparameter imaging, particularly in the near-infrared (NIR) region of the spectrum, are chemi-genetic FPs. A chemi-genetic FP is a hybrid system in which a synthetic dye fluorogen is designed to covalently attach to a specific protein expressed in the cell or tissue. The Campbell lab has started converting chemi-genetic FPs into a new generation of high performance indicators. This is an unexplored and exciting research frontier! We are also working on another design of chemi-genetic indicators using FPs and synthetic ligands.

Figure 4. Chemi-genetic fluorescent protein
Chemi-genetic fluorescent protein is a “hybrid” molecule that contains synthetic small fluorescent molecule (the filling model in the figure) and protein.



■ Current Theme 3: Expanding the color palette of near infrared 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. The Campbell lab is pioneering the development of genetically encoded indicators that absorb and fluoresce in the NIR window. These indicators will be ideally suited to multiplexed imaging applications with existing visible wavelength indicators and optogenetic tools. These indicators will enable researchers to perform functional in vivo optical imaging deeper inside model animals than has previously been possible!

Figure 5. Near-infrared fluorescent protein
Near-infrared fluorescent proteins have much different structure from that of jellyfish-derived fluorescent protein such as GFP. Filling model represents the chromophore, a heme metabolite biliverdin.

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Solid State Chemistry



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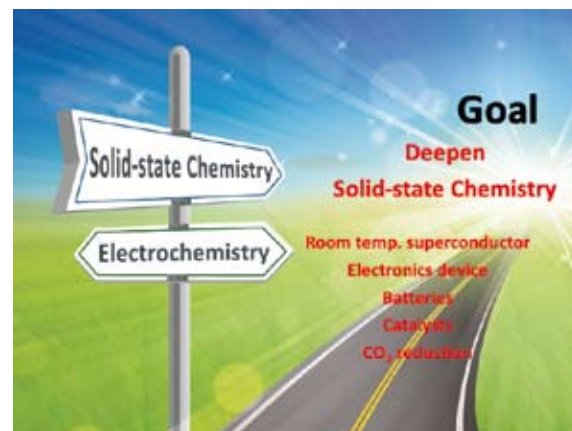
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Crossroad of solid-state chemistry and electrochemistry

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.

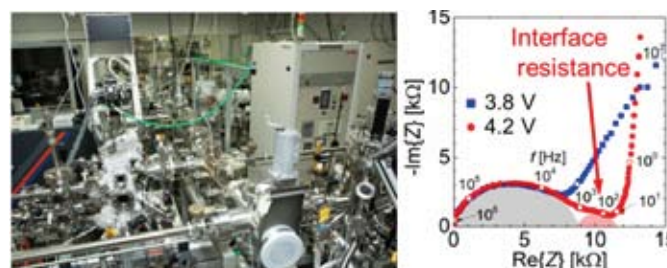


Major Direction of Research

Research on All-solid-state Li battery

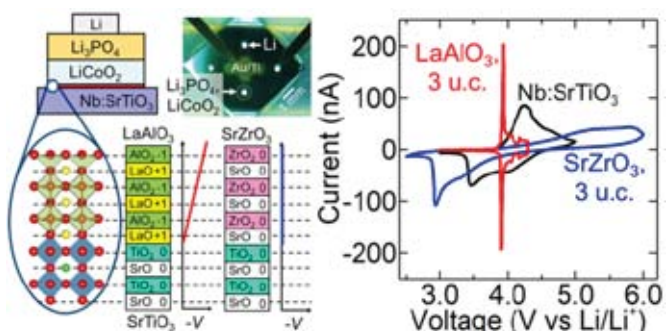
The development of high-voltage, high-capacity batteries is critical toward the advent of a sustainable society. Among the existing battery types, the all-solid-state Li batteries promise to realize the next-generation batteries by replacing the organic electrolytes used in conventional Li-ion batteries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

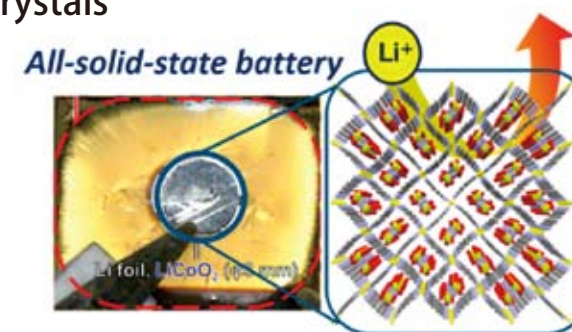
Right: The world's smallest interfacial resistance has been achieved.



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

Accelerating 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

Opto-bioanalysis Inspired by Chemistry and Biology

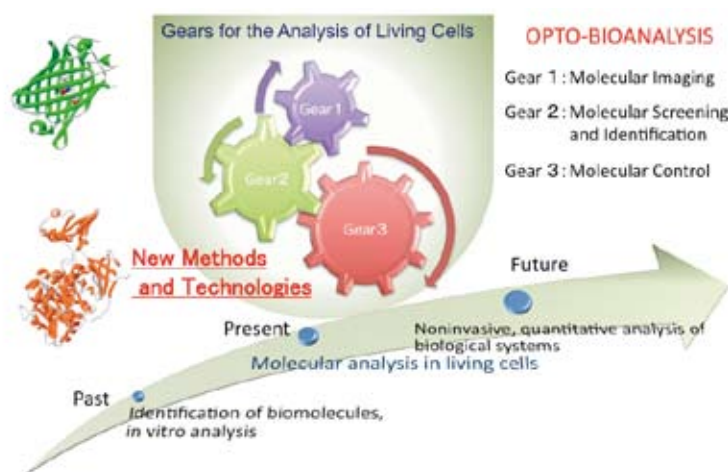


Fig. 1. Major three themes in the analytical chemistry laboratory.

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.

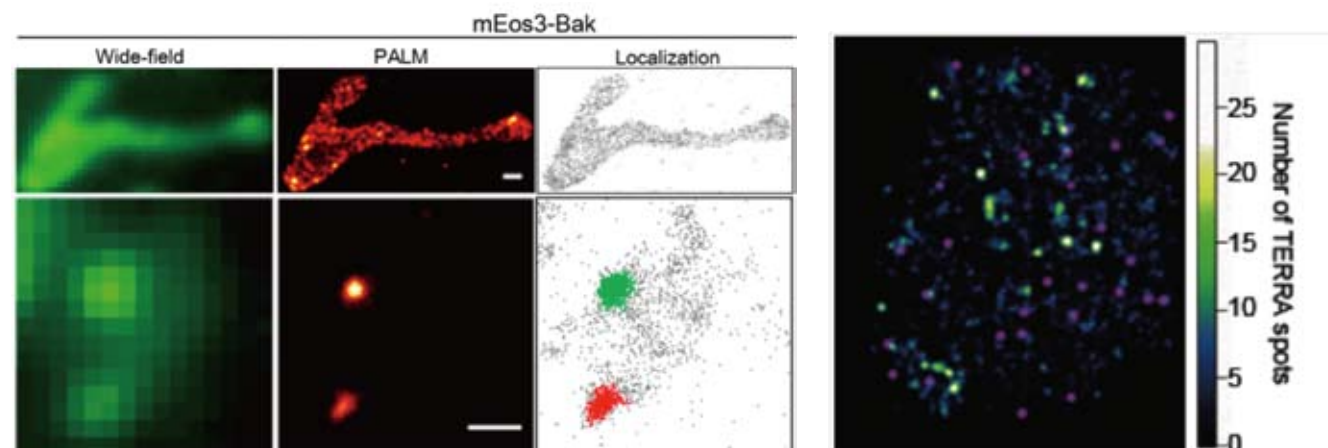


Figure 2. Left: Superresolution single molecule images (PALM) of Bak proteins on the mitochondrial membrane. Right: Localization of Telomeric RNAs. Purple dots indicate telomere regions in the nucleus.



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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.

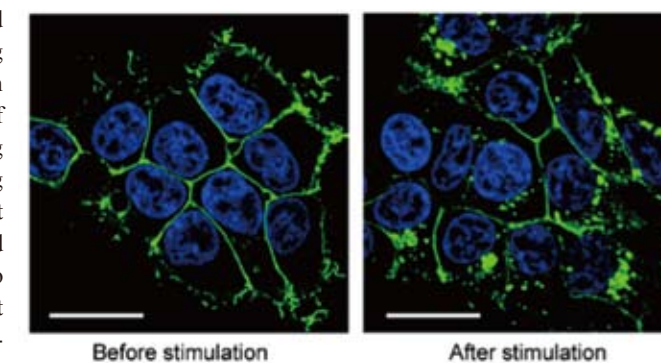


Fig. 3. Localization alteration of GPCR (somatostatin receptor) (green). Stimulation with somatostatin induces GPCR- β arrestin interaction, results in internalization of the GPCR.

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 oligomerization of a plasma membrane receptor (DCC) to control the direction of neuronal axon elongation (Figure 4). These light-driven controlling system promises to revolutionize our understanding of intracellular signaling and cellular communications in living animals.

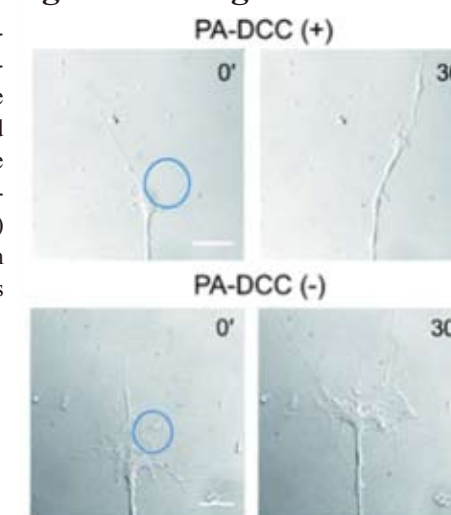


Fig. 4. Photo control of the direction of neuronal axon elongation. The axon of neurons expressing photo-activatable DCC (PA-DCC) are guided to elongate to the photo-irradiated direction (blue circles).

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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 with thermo-responsive molecular science

Thermocell is a group of thermoelectric devices that utilizes the thermal shift of redox equilibrium and featured by the cheap materials (1/5 watt-cost compared to conventional semiconductors and even half compared to solar cells) and relatively-high Seebeck coefficient (voltage per unit temperature difference). We are trying to make a paradigm shift of these thermocells by introducing various thermo-responsive molecular science into it.

First, we are introducing supramolecular chemistry into thermocells. A thermocell consisting of redox equilibrium of triiodide (I_3^-) and iodide (I^-) was introduced cyclodextrin (CD). The CD encapsulates I_3^- at the cold side and release it with elevated temperature, and as a result, the Seebeck coefficient of the thermocell was improved. The theoretical relation between the host–guest interaction and the Se was derived, which has grown up to the novel method for evaluating the host–guest entropy and enthalpy. Some CD derivatives, starch, and polymers were also effective.

The improvement of Se is associated with the connection of thermal response and redox reaction, and the concept can be generalized. For example, Se was improved by the precipitation and dissolution equilibrium. We are trying to introduce various thermo-responsive chemistry or physics and change the world of thermoelectric conversion, as well as the inverse phenomena.

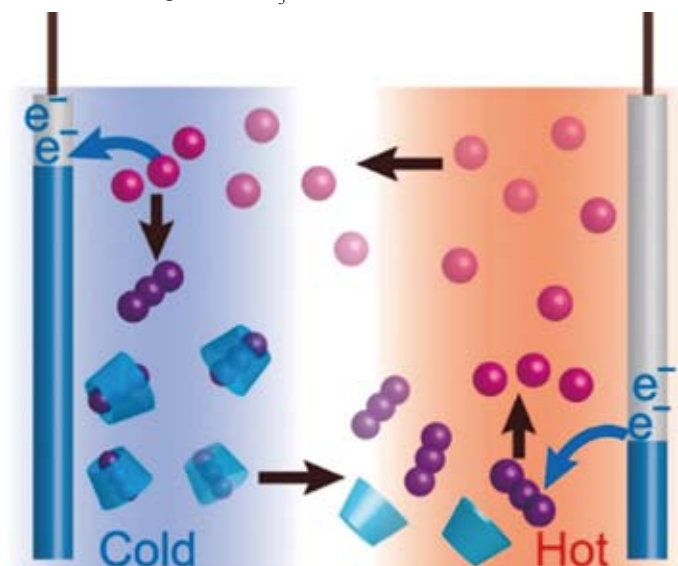


Fig. 1 Schematic illustration of a thermocell with thermo-responsive molecular science. The encapsulation of triiodide anion by cyclodextrin causes the shift of the redox equilibrium between iodide and triiodide. Oxidation reaction at the cold side of the cell was accelerated and as a result, an improved Seebeck coefficient was observed.

Design of novel nanospace, investigation of ionics in the nanospace toward novel energy devices

The motion of ions directly connected to electric energy.

Thanks to the development of coordination chemistry, organic synthesis, and self-assembly science of them, we live in the era of at-will design of nanospace that can recognize a single molecule. Our laboratory focuses on the behavior of redox-active molecules and ions (ionics) in such nanospace. We found that a melting point or diffusion coefficient of a material, which are statistical parameters molecular populations, could show a drastic shift from that of bulk material by confining

them into nanospace. The shape, size, or the packing fashion of molecules are controlled by the nanospace and anisotropic diffusion coefficient or peculiar rotational motion are investigated.

Through the development of the nanospace ionics, we aim to invent new energy devices. New battery, mobile energy sources are a part of the targets.

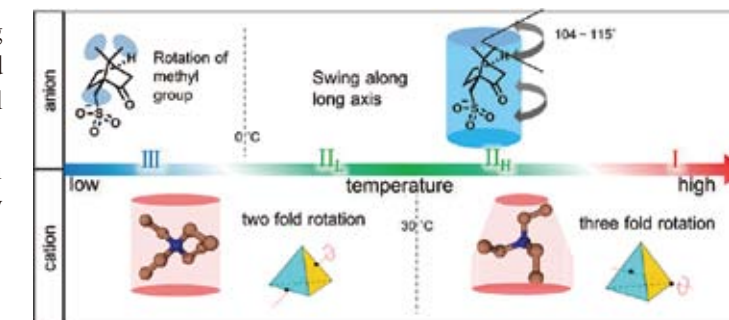


Fig. 2 Phase behavior and ionics of chiral plastic ionic crystals (tetraethylammonium-d20 d-10-camphorsulfonate). Tetraethylammonium cation changes its rotational mode from three-fold to two-fold rotations by temperature.

Creation of Functional Organic Compounds Base on Group 14 Elements

New molecular designs and synthetic strategies are also investigated to synthesize functional materials based on group 14 elements. Palladium-catalyzed cyclization 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 intensity 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.

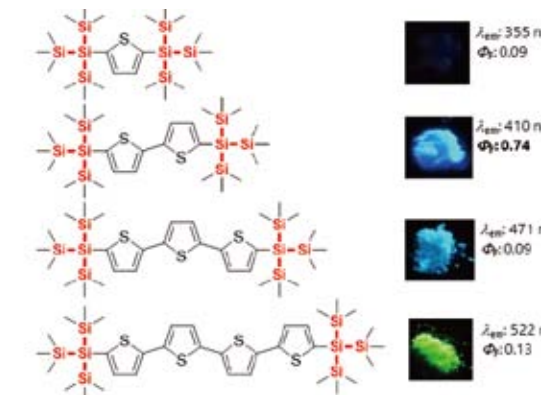
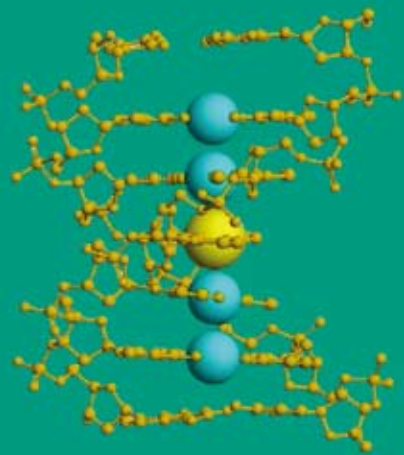


Fig. 3 Structures of aromatic oligosilanes and their luminescence under UV irradiation. These compounds show intense emission in the solid-state.

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Bioinorganic Chemistry



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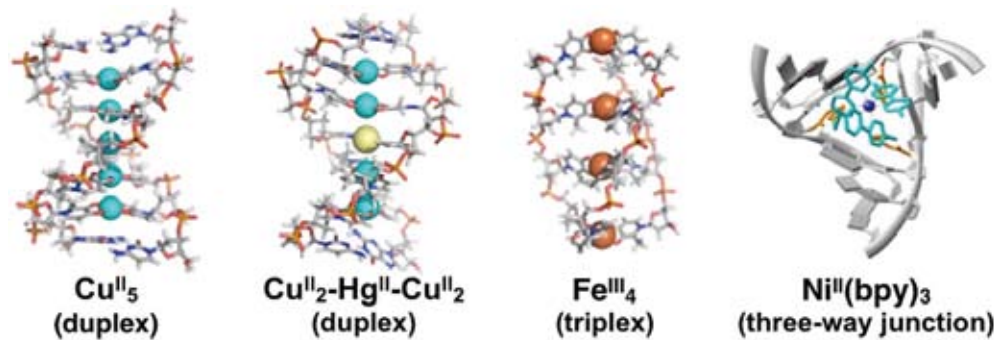
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Bio-inspired construction of designer supramolecular architectures

Construction of supramolecular architectures requires the following factors in general: 1) precise design and synthesis of basic chemical components, 2) control of dynamic bonding behaviors between chemical components, and 3) initial setting of chemical environment that determines molecular association processes. Our group is aiming to create nano to submicrometer-size, bio-inspired supramolecular architectures directed towards elaborate molecular systems and functions.

Artificial metallo-DNAs (Refs. 1-4)

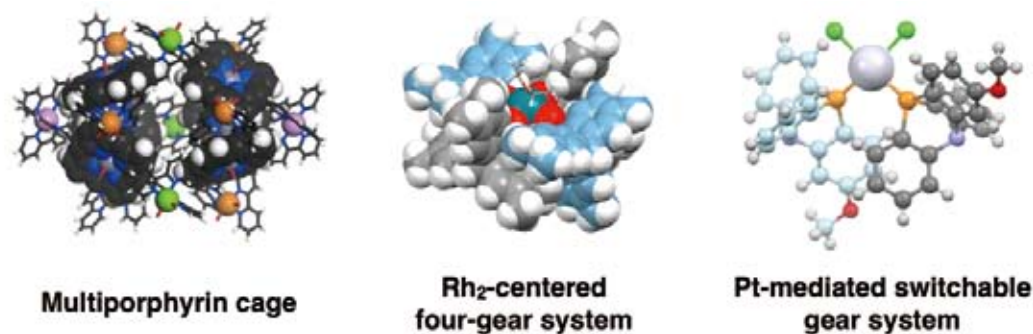
DNA, which governs genetic information, has a structural basis to arrange functional building blocks into a one-dimensional sequence in a programmable way. We have developed artificial metallo-DNAs, in which hydrogen bonds between natural nucleobases are replaced by metal coordination bonds between a central metal ion and a pair of artificial ligand-type nucleobases. The metal-mediated base pairing allows metal-dependent thermal stabilization of DNA duplexes and triplexes. Moreover, one-dimensional, homologous or heterologous metal arrays can be constructed within DNA helices in a manner whereby the number and sequence of the metals are programmable. Indeed, some of these metallo-DNAs exhibit characteristic physical properties in terms of magnetism and electrical conductivity. Another structural motif of artificial metallo-DNA is a metal-mediated three-way junction structure. This structure is thermally stabilized by the formation of a tris(bipyridine) metal complex that crosslinks the three strands. Structural transformation is also possible between DNA duplexes and three-way junctions in a metal-responsive manner. Recently, enzymatic synthesis of ligand-bearing DNA strands has been accomplished directed towards facile preparation of metallo-DNA systems. Thus, metal-based artificial DNAs have a great potential for bio- and materials-oriented functions.



Metal-mediated supramolecular architectures (Refs. 5-8)

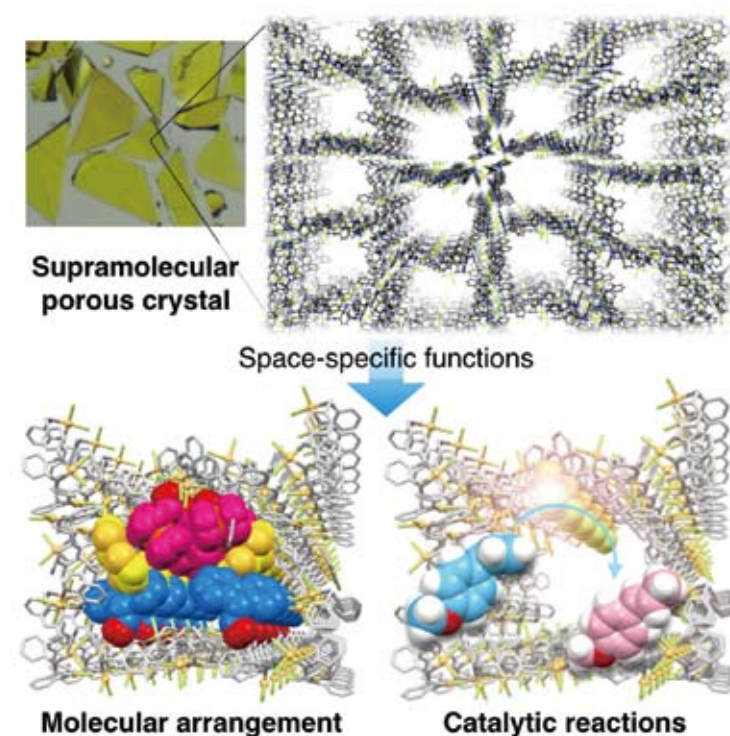
Dynamic natures of metal coordination and designer metal ligands can possibly provide stimuli-responsive, metal-mediated supramolecular architectures. For instance, zincporphyrin ligands tethered by four bipyridine ligands and Zn(II) ions form a hexameric cage with a rugby ball-shaped nano-cavity, which can accommodate electron-deficient guest molecules.

Metals can also act as a hub of dynamic molecular functions. We have developed two types of metal-centered triptycene-based molecular gears. The first example is a molecular gear box composed of a lantern-type dirhodium complex as a stator and four hexamethyltriptycene carboxylates as meshing rotors which are arranged circularly around the dirhodium center. The rotational rates of the four rotors are affected by the two axial ligands with different coordination ability and bulkiness. We also constructed another organic gear box molecule, in which six triptycene gears circularly arranged around a benzene ring are meshed with each other. The rotational motion of the gears was highly restricted by binding of a [Cp*Ru]*complex to a phenylene ring of one gear. The other example is a molecular system with a switching function based on coordination isomerism on a Pt(II) ion. Two molecular azaphosphatriptycene rotors are meshed in the *cis* form (see the rightmost figure), but under photo-irradiation they become disengaged due to the isomerization of the Pt(II) center. This process is photo- and thermally driven reversibly by the *cis-trans* isomerization.



Porous supramolecular crystals with a functional nano-space (Refs. 9-12)

Porous crystalline materials such as zeolites and coordination polymers (or metal-organic frameworks) have attracted much attention because their nano-sized pores are capable of exhibiting space-specific functions such as molecular storage, separation, transportation, and catalysis. We have newly developed a metallomacrocyclic-assembled porous crystal whose pore surface provides five enantiomeric pairs of molecular binding pockets. The unique feature of the pore structure has allowed several ways of molecular arrangement; site-selective arrangement of functional molecules, diastereoselective arrangement of chiral molecules, and simultaneous arrangement of multiple different molecules. Recently, acid-immobilized porous crystals have been developed for a size-specific heterogeneous catalytic reaction. Furthermore, *in situ* crystallographic analyses can visualize a stepwise arrangement process of a chiral molecule on the pore surface. Based on the findings, we are currently approaching to supramolecular enzymes in which multiple functional groups are assembled to build-up an active center of catalytic reactions with high efficiency and selectivity.



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Presidential Endowed Chair for “Molecular Technology Innovation”

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.

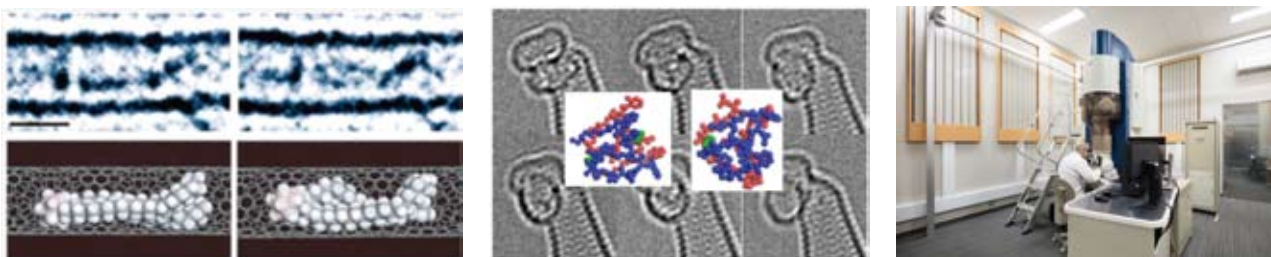


Figure 1. Electron microscope and dynamic molecular images. a. World's first video of molecular movement. b. Motions of daptomycin dimer. c. Electron microscope in the Molecular Life Innovation Building

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).

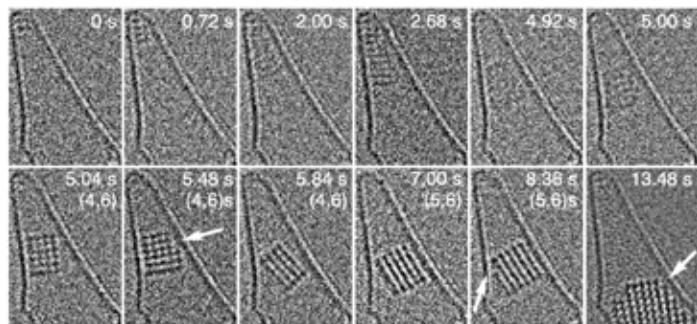


Figure 2: A nanocrystal of salt suddenly appears at the tip of a carbon nanotube in a vacuum (at 5.04 sec)

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).

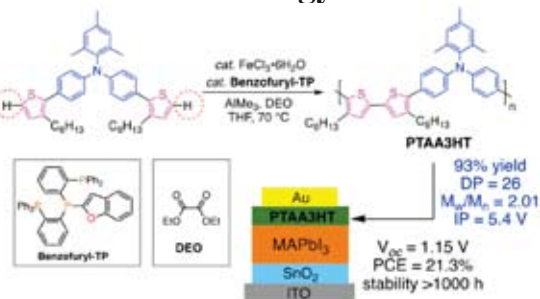


Figure 3: Iron-catalyzed polymerization by C–H bond activation as the key reaction.



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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.

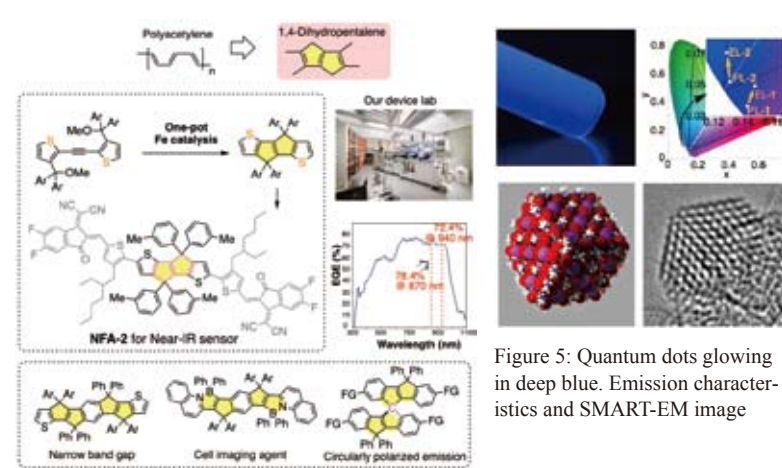


Figure 4: Iron-catalyzed synthesis of planar conjugated molecules and application to near-infrared detectors

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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Linking cutting-edge chemistry to building a sustainable society

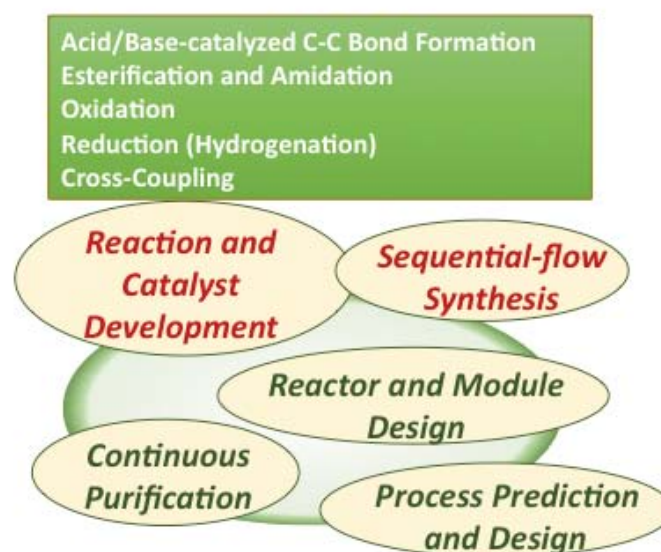
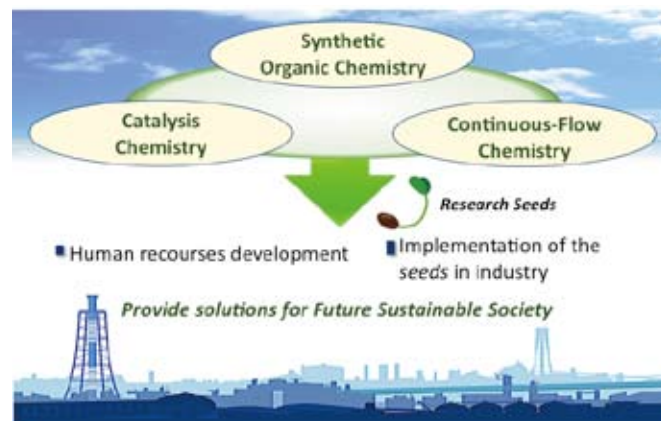
Green Sustainable Chemistry (GSC) Social Collaboration Laboratory was established with supporting of collaborative companies, with the aim of conducting practically oriented research and development on environmentally friendly low-load chemical processes and fostering human resources who will lead the GSC field. GSC is the ideal attitude of chemistry to build a sustainable society and is an important concept for modern society and the 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.

Development of continuous process for energy-saving chemical manufacturing

Although the production of value-added chemicals is considered to be the key of Japan's economic growth, the lack of equipment and manpower for small-lot, large-item production, and the by-product and wastes including carbon dioxide emissions disturb its progress. To overcome this and improve the international competitiveness of the Japanese chemical industry, it is necessary to shift the current production manner of value-added chemicals to a continuous production manner. In this laboratory, we are developing reactions and catalysts to realize the "core 5 reactions" that are often used in the synthesis of functional chemicals by a continuous-flow method with heterogeneous catalytic reaction. By developing the reactions and catalysts developed in this laboratory in a joint industry-government-academia project and combining them with reactor modules and separation/purification module, an on-demand production of wide variety of value-added chemicals can be realized.



The Core 5 Reactions for Continuous Production of Value-added Chemicals



Project Associate Professor

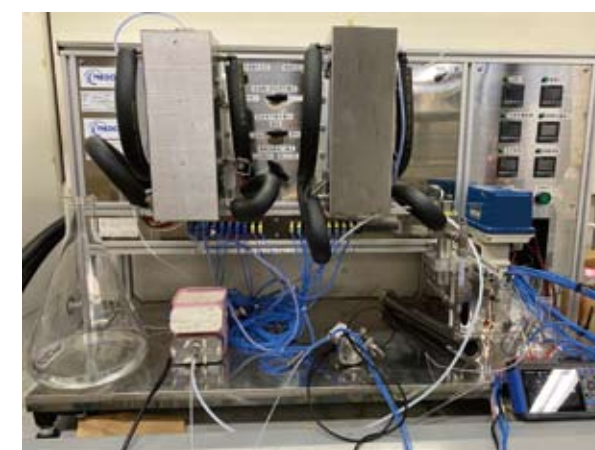
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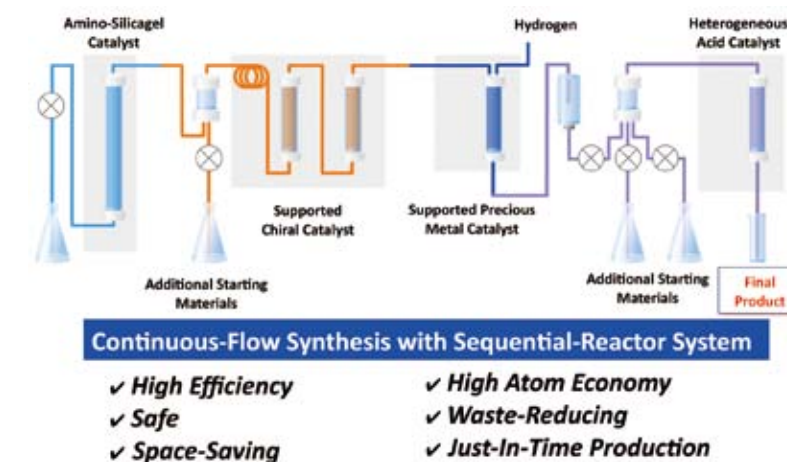
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Bench-scale flow reactor system of 100 g/h - 1,000 g/h continuous synthesis. 300 mL Of reactors are housed in the two metal boxes on the front, and by connecting them in a series, two-step sequential continuous reactions can be performed.



Sequential and Continuous-flow Synthesis of Active Pharmaceutical Ingredients Rolipram.

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.



Relationship of GSC with other areas

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Research Center for Spectrochemistry

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 CoFe₂O₄ 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 Bi₂Se₃ 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.

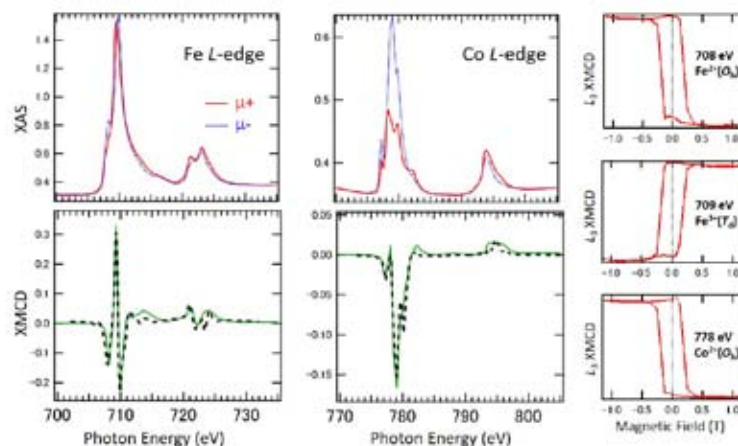


Fig. 1, XMCD of CoFe₂O₄ with ligand field theory calculation and element-specific hysteresis curves.

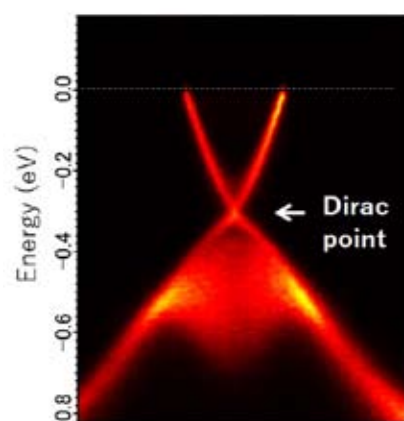


Fig. 2, ARPES image of surface states in topological insulator Bi₂Se₃.



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Ultra-rapid spectroscopy and its biological application

Understanding biological functions require cell measurements in wide temporal and spatial range with molecular specificity. To this end, we develop spectroscopic methods based on ultrafast laser technology that enable rapid and detailed analysis of biomolecules in vivo. We have developed a rapid-scan Fourier-transform coherent anti-Stokes Raman scattering (FT-CARS) spectrometer (Fig. 4), which enables acquisition of 24,000 broad Raman spectra in one second, and applied it to large-scale label-free flow cytometry (Fig. 5). With using the developed method will be useful both in basic life science and medical science. We specifically apply the method to metabolic engineering by sorting highly productive microalgal cells and cancer diagnosis by detecting circulating tumor cells in the blood.



Fig. 3, The rapid-scan Fourier-transform coherent anti-Stokes Raman scattering spectrometer



Fig. 4, Vibrational spectral acquisition from flowing single cells



Fig. 5, Various applications of the developed large-scale label-free single cell analyzer

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. 6 , Examples of the instruments in RCS available for common use. ESR, NMR, FT-IR, and XRF.

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Center for Attosecond Laser Science

Promoting Attosecond Laser Science, Capacity Development of Young Researchers,

In April 2022, the Center for Ultrafast Intense Laser Science (CUILS) was restructured as the Center for Attosecond Laser Science (CALS) aiming to further development of laser technologies and measurement techniques in attosecond laser science based on the previous development of ultrafast intense laser science research field. CALS promotes the frontiers in the interdisciplinary research field of ultrafast intense laser science through international research cooperation and developing an educational program in photon science by industry-academia collaboration.

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.

Promotion of international research cooperation

CALS is dedicated to promoting international research cooperation in the interdisciplinary field of ultrafast intense laser science and attosecond laser science. We have supported the 17th AMO Symposium (Online, July 18th and 19th, 2021), which is an international workshop in ultrafast intense laser science and advanced photon science in 2021.

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 so that they will be researchers at forefront of advanced 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 so that students could learn fundamental concepts in photon science and acquire the knowledge and skills needed to explore the frontiers in photon science. In the CORAL program, researchers and engineers from 22 photonics-oriented companies and professors from the School of



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and International Exchange in Photon Science

Science and the School of Engineering at the University of Tokyo, the University of Electro-Communications, and Keio University 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).

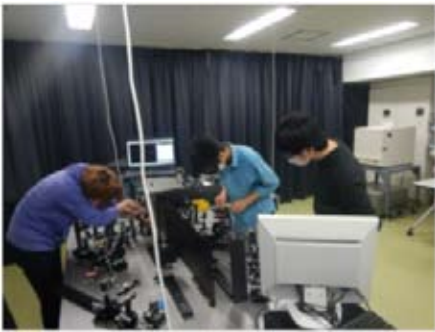


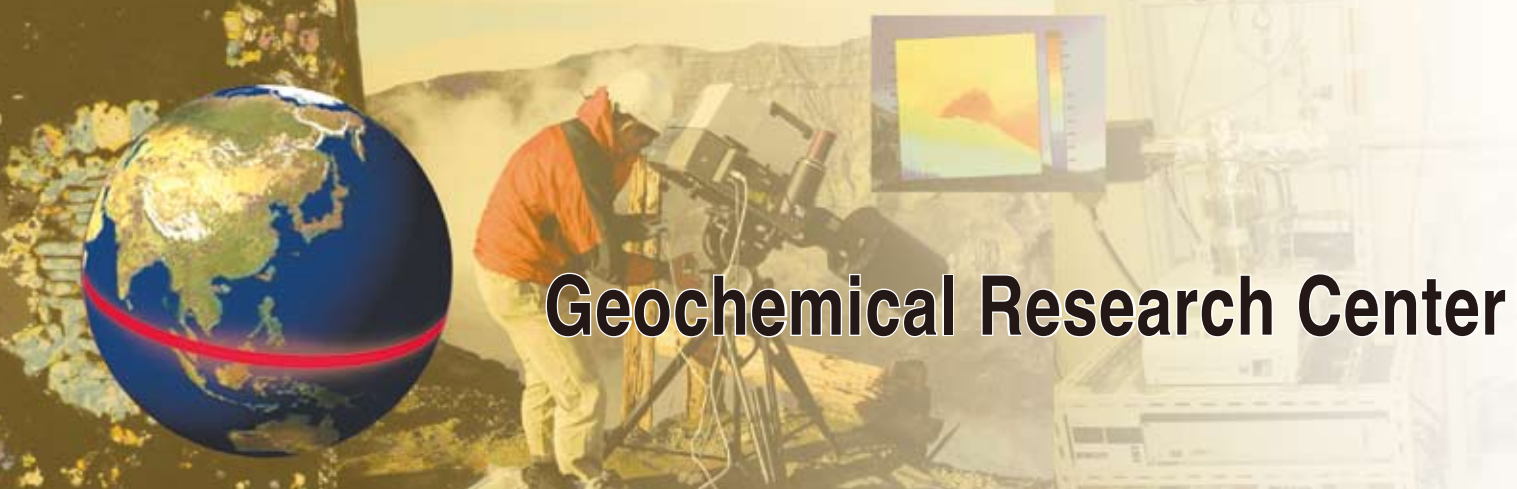
Figure 1. Laboratory courses of advanced optical science I/II in 2021.

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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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 CO₂. In future, we will estimate global circulation of volatile elements from surface environments to the deep Earth by synthesizing the obtained knowledge.



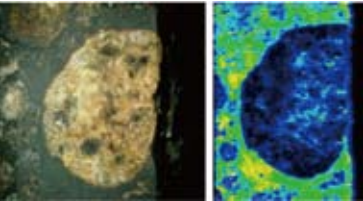
PLANET beamline at J-PARC.



Dense CO₂ 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.



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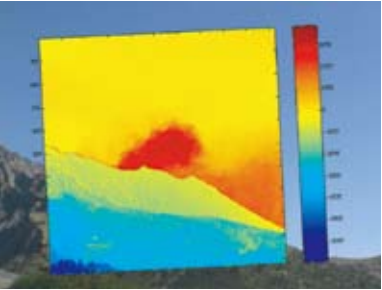
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Chemical composition and flux of volcanic gas as an indicator of dynamics of volcanic eruption

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.



SO₂ 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



Associate Professor

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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 °C). 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].

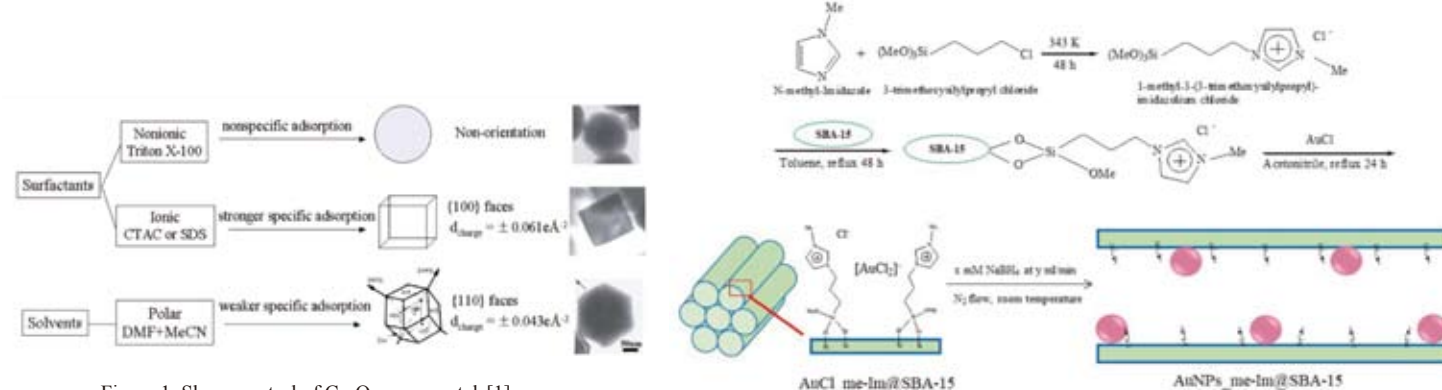


Figure 1. Shape control of Co_3O_4 nanocrystals[1]

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

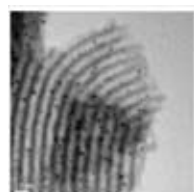


Figure 3 TEM image for Au nanoparticles supported on SBA-15 with immobilized imidazolium groups [2]



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].

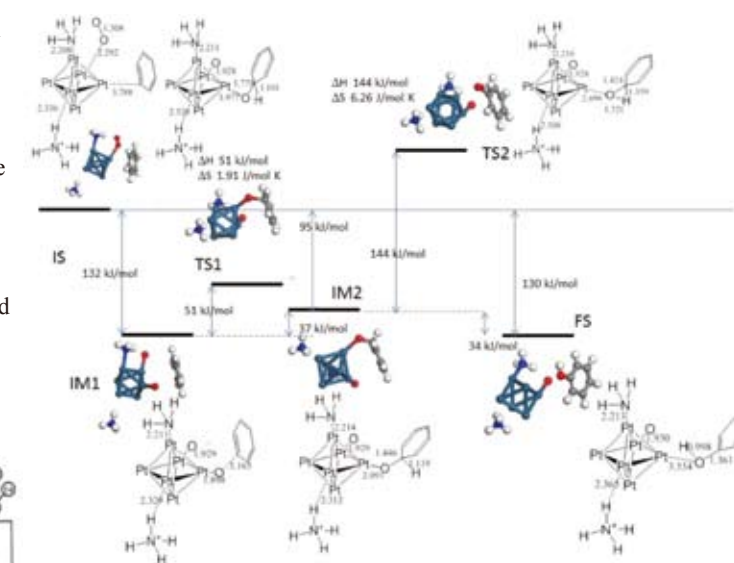


Figure 6. Energy diagram for the Pt_6 cluster interacting with NH_3 , NH_4^+ , benzene and O_2 leading to the formation of phenol [5].

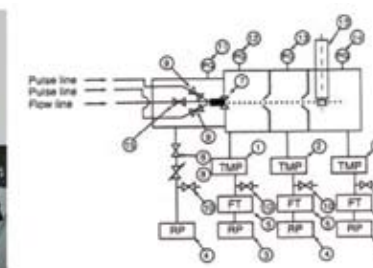


Figure 5 Photograph and diagram for TAP system.

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6. The mechanism of sorbitol dehydration in hot acidic solutions, T. Kondo, T. Sasaki and M. Shiga, *Journal of Computational Chemistry*, **2021**, 42, 1783.
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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 Yoshō Shirabeshō, 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 Kenkyūka (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

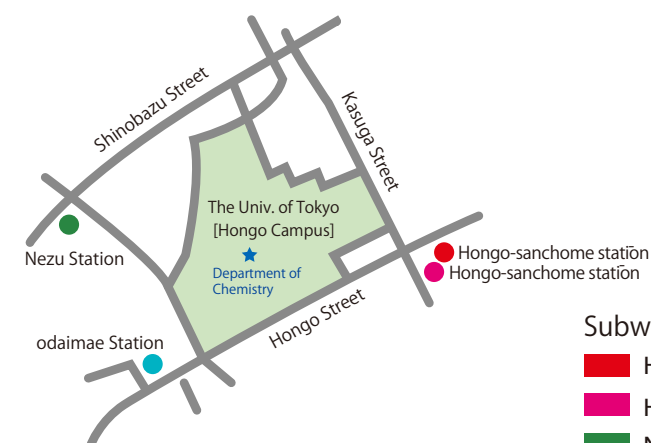
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Subway

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- 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