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.
Goda Lab is aimed at developing innovative laser-based molecular imaging and spectroscopy technologies together with multidimensional 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.

**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.

**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 explore new applications based on the imaging methods. Prominent examples of Goda Lab's previous efforts for high-speed imaging include STEAM and STAMP.

**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.

**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.

**References**

Solid State Physical Chemistry

We are working on the development of novel functional materials responding to light and electromagnetic waves 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, c-FeO₂, showing huge coercive field and high-frequency millimeter wave absorption, and lambda-titanium oxide, λ-TiO₂, 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 design 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 aromatic metal complexes 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 pioneeredly 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.

Study of novel magnetic oxides with electromagnetic environmentally protective function

Metallic 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 c-FeO₂ for the first time, c-FeO₂ shows a large coercive field (Hc) over 20 kOe even at room temperature, which is the largest Hc value among magnetic oxides. Recently, we succeeded to enlarge the Hc value and achieved a gigantic Hc value of 35 kOe in a metal substituted c-FeO₂. This Hc value is comparable to those of rare-earth magnets. We have also observed that c-FeO₂ and metal substituted c-FeO₂ show the highest frequency electromagnetic wave absorption in the millimeter wave region, and thus, proposed an application 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.

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

Titanium oxides containing Ti³⁺ are colored black and have electron spins. We have investigated black titanium oxide by nano-scale chemical synthesis, and discovered a new type of metal oxide, lambda type trititanium pentoxide λ-TiO₃. This material shows photoinduced phase transition from black colored lambda phase (metallic conductor) to brown colored beta phase (β-TiO₃) (semiconductor). Moreover, the reverse phase transition was also observed by photoirradiation. This is the first example of a metal oxide which shows photoinduced phase transition at room temperature. Since λ-TiO₃ is very economical and environmentally friendly material and is obtained as nanoparticles, λ-TiO₃ is expected as a next generation high-density optical storage material. Additionally, λ-TiO₃ 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 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 use of industrial heat generated from furnaces.

References

Recent advances in laser technology made it possible to generate an ultrashort-pulsed intense laser field whose field intensity is as high as $10^{15-10^{16}} \text{W/cm}^2$, which is comparable with or even larger than the Coulombic field within atoms and molecules. In such an intense laser field, electrons in atoms and molecules are influenced by a highly order-generating pulse, (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 in their intense laser field,” (8) “quantum computing applied to atomic and molecular problems,” and (9) “material processing by the extreme ultraviolet femtosecond laser pulses.”

In these decades, our group has been investigating the following research subjects; (1) “ultrafast hydrogen molecule in hydrogen-carbon molecular ions by the ‘coincidence kinetic imaging’ method, which records momentum vector distributions of fragment ions generated through the Coulomb explosion in an intense laser field,” (2) “pump-field-ultra-high-resolution Fourier-transform spectroscopy,” (3) “laser-assisted elastic electron scattering,” (4) “investigate ultrashort electron dynamics within atoms and molecules in an intense laser field and ‘laser-assisted electron diffraction’ to probe ultrafast variations of the geometrical structure of molecules with the femtosecond temporal resolution,” (5) “ultrafast spectroscopy in which photoluminescence and photo-ion signals are detected after molecules are ionized by high-order harmonics generated using few-cycle laser pulses,” (6) “laser-assisted electron diffraction in laser-induced molten,” 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 in their intense laser field,” (8) “quantum computing applied to atomic and molecular problems,” and (9) “material processing by the extreme ultraviolet femtosecond laser pulses.”

When a hydrogen molecule is exposed to an intense laser field, associated with the ionization, hydrogen atom ions ejected rapidly and a triatomic molecule, $\text{H}_2^+$, is produced. By a pump-probe coincident momentum imaging measurement of methanol, CH$_3$OH, we revealed that the yield of the $\text{H}_2^+$ periodically oscillates as a function of the delay time and that the period of the ultrafast dynamics (38 fs) obtained by the Fourier transform corresponds to the period of the C-O stretching vibration. By extending the delay time range of the Fourier-transform spectroscopy, we determined the vibrational band of $\text{D}_2$ to a precision of 10 cm$^{-1}$ (Fig. 2). By this method of strong-field ultra-high-resolution Fourier-transform spectroscopy with an extreme laser field delay range of 500 ps, we determined the spin-orbit splitting energies of rare gas atoms to a precision of 0.01 cm$^{-1}$.

We also developed an experimental setup for the coincidence measurements of the carrier-envelope phase (CEP) of few-cycle laser pulses and the momentum images of fragment ions revealed the CEP dependence of the fragment pathways of acrylate ions (43) and methanol (53).

The scattering cross-section of the atom in the presence of very large molecules that can be treated by classical interaction and that, by the interaction with the laser field, the population in the $\Sigma^+$ state of N$_2$ is transferred to the first electronically excited A/$\pi$ state, which further increases the extent of the population inversion between the $\Sigma^+$ and $\Sigma^-$ states.

Ultrafast molecular dynamics in intense laser fields

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 ultrafast dynamics of molecules, ultrafast geometrical changes of molecules can be probed with extremely high temporal resolution. As a laser-assisted electron diffraction (LAED) method, we recorded an electron diffraction pattern of carbon tetracloride, CCl$_4$, at the moment of the irradiation of femtosecond laser pulses [7]. We also developed a reduced multi-state contracted variational quantum eigensolver (RMC-VQE) method and calculated the Fermi resonance vibrational-energy levels of CO, and the corresponding wave functions, which is strong-field ultra-high-resolution Fourier-transform (SURF) spectroscopy with an extended delay time range of 500 ps, we determined the spin-orbit splitting energies of rare gas atoms to a precision of 0.01 cm$^{-1}$.

We also developed an experimental setup for the coincidence measurements of the carrier-envelope phase (CEP) of few-cycle laser pulses and the momentum images of fragment ions revealed the CEP dependence of the fragment pathways of acrylate ions (43) and methanol (53).

References


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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).

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 with diameters smaller than 2 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.

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 2 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.

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.

References

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

Development and application of artificial ribozymes
The "RNA world" hypothesis is based on the concept that life on Earth originated as RNA molecules without the participation of the DNA and/or protein components that are integral to modern life. As early as the 1960s, Crick and Orgel had already proposed the basic concept of the RNA world hypothesis, but this early hypothesis could not be widely accepted due to a lack of experimental evidence. The discovery of RNA molecules with enzymatic activities called ribozymes in the 1980s drastically changed this situation. However, in the modern world, very few natural ribozymes exist and they are limited to the catalysis of RNA modifying reactions such as cleavage and ligation of RNA. These limited functions are apparently insufficient to support life, that is, ribozymes would need to have been responsible for more varied enzymatic functions if the RNA world really existed. It is possible that over the course of 4 billion years of evolution the catalytic activity of proteins was favored and thus ribozymes with more diverse functions have been lost, so that just a trace of the real RNA world can be seen in nature today. Therefore, one of the themes of our lab is to artificially create ribozymes with novel catalytic activity in order to validate the concept of the RNA world. In other words, development of artificial life consisting entirely of ribozymes is one of our ultimate goals. “Flexizyme” is one of the most successful ribozymes developed in our laboratory. Flexizyme is a short RNA molecule consisting of 46 nucleotides and it catalyzes the aminoacylation of tRNA with a wide range of natural and unnatural amino acids. Flexizyme exhibits broad substrate tolerance; it accepts arbitrary RNA body sequences and various amino acids regardless of their side-chain structures. Therefore, flexizyme is a powerful tool for genetic code reprogramming and translation of nonstandard peptides as discussed below.

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

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

Drug discovery using the nonstandard peptide library
For high throughput screening of bioactive nonstandard peptides, we have integrated the FIT system with an in vitro display method called mRNA display, with the combined system referred to as the RaPID system (Random Peptide Integrated Discovery system). Currently, we are applying the RaPID system to drug development projects with the intention of isolating nonstandard peptide inhibitors of various pharmaceutical targets. In the near future, by establishing this system as a fundamental technology of next generation drug discovery and being the first nonstandard peptide drug discovery institution to originate from Japan, we aim to deliver many achievements for the benefit of society.
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 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 resources of the Earth. We are also interested in developing highly efficient catalytic asymmetric reactions for the purpose of supplying fine chemicals, like drugs, that demand to solve recent energy problems from the viewpoint of synth. organic chemistry. The goals of the natural sciences are to seek universal 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 the 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” is systemizing. Our group has extensively engaged in the development of multifunctional 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 high solubility of the metal catalysts was modelled to address the inherently low Lewis acidity of metal catalysts, 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 1,4-addition of boronic acids. To date, we have developed asymmetric hydroxylamination, Michael addition, and protonation reactions. Furthermore, we have highlighted the halogen-metal, 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 allylmetal compounds with imines and Mannich reactions of weakly acidic simple amides. Moreover, we have been focusing on development of photo reactions and electrolytic reactions to address the energy crisis. In our recent work, a homogenized combination of nickel-based LASCs and carbon-incarcerated zinc electrodes is shown to be effective in water, the reaction failed to give the desired adduct completely under neat (solvent-free) conditions.

**Development of high-performance heterogenous 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 nanoparticle catalysts, which demonstrate high 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 arenas. More recently, we have developed a cooperative catalytic system by the combination of nanoparticle catalysts and Lewis acid catalysts. On the other hand, we have developed N-doped carbon incorporated (NC) earth-abundant metal catalysts such as Cu and Co. These metal catalysts are highly active than precious metal catalysts, however, we have developed highly active heterogeneous catalysts by the precise design of support. We have also developed a novel immobilization method of chiral metal complexes utilizing noncovalent interactions without chemical modification of chiral ligands. We have found that immobilization of Rh catalysts have comparable activity and selectivity as original homogeneous catalysts for flow asymmetric hydrogenation of enamides. Moreover, this method could be applied to the immobilization of chiral Lewis acid catalysts. We also developed Ni catalysts supported inside the mesopore of MCM-41 for asymmetric 1,4-addition reactions. On the other hand, we developed highly active immobilized Rh catalysts of silico-organic polyoxometalates with core-shell structure as support. The catalyst demonstrated highly efficient hydrogenation catalysis for various 1,4-addition of boronic acids.

**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 syntheses in terms of efficiency, safety, and environmental compatibility. Among them, flow-through catalysis enabled fully multiphase reaction without the isolation of reaction intermediates. Our laboratory has achieved continuous-flow multiphase synthesis of fine chemicals utilizing catalytic transformations with heterogeneous catalysts. Particularly, we have focused on reactions with high added value, such as addition reactions and reduction with hydrogen gas. We have reported the continuous-flow synthesis of various kinds of fine chemicals, including important intermediates such as chiral oxazolidines, chiral nitrogen-containing compounds, chiral oxindoles, and chiral oxazoles.

**Development of new synthetic methods directing higher efficiency**

Our group has a long standing interest in developing more efficient catalytic reactions and organic asymmetric reactions that provide only the desired enantiomer in high yield. We have reported many highly functionalized metal catalysts for various asymmetric carbon-carbon bond forming reactions. Recently, we have focused on proton transfer catalysis for realizing high aluminon-homocatalysis and developing catalytic addition reactions of less reactive materials using alkylmetal strong Bronsted bases. We have developed catalytic asymmetric addition reactions of alkylsilane 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.

**References**

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 skeletal diversely 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 variations toward the creation of functional substances based on the generation of diverse molecular scaffolds.

**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 sterogenic 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 variations, we will streamline concise synthesis, screening, and identification of the covalent complexes composed of the synthetic ligands and biomolecules. These efforts are expected to facilitate the development of lead candidates for the treatment of infectious diseases and cancers.

**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 and coordination properties of sp² stereogenic centers and various functional groups. The C₇-symmetric alkaloidal scaffold has been demonstrated to be a versatile chiral scaffold for supramolecular chemistry, capable of generating configurational variations of the sp² stereogenic centers and thereby customizing the conformational flexibility, chirotrophic property and self-assembly behavior (Fig. 4). We are developing the natural product-based versatile scaffolds that project multiple functional units with systematic diversification of the spatial arrangement. Supramolecular assemblies of the synthetic mid-sized molecules will be investigated to improve their sensing functions.
Aromatic molecules have played a pivotal role in organic chemistry since the discovery of benzene 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 explored 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).

**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 ones. Among various kinds of design principles being explored, our simple molecular design adopting two basic elements, carbon atoms, and double bonds, 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 multiplicity has realized highly efficient OLEDs in novel single-layer architectures. (OLEDs), and such multiplicity has realized highly efficient OLEDs in novel single-layer architectures (Figure 2, Reference 2).

**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.

**Diamond twin**

As the key features of the beauty of diamonds, mathematicians disclosed the presence of "maximal symmetry" and "strong isotropy" in the network of sp3 carbon atoms, which led them to a discovery of a diamond twin. The diamond twin is a hypothetical network of sp2 carbon atoms with identical geometrical features, although its existence has been theoretically questioned due to the strained structure composed of decagon-shaped carbon rings. As the key features of the beauty of diamonds, mathematicians disclosed the presence of "maximal symmetry" and "strong isotropy" in the network of sp3 carbon atoms, which led them to a discovery of a diamond twin. The diamond twin is a hypothetical network of sp2 carbon atoms with identical geometrical features, although its existence has been theoretically questioned due to the strained structure composed of decagon-shaped carbon rings.

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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 fluorescent proteins has revolutionized all 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), 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 applications, 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 (dFPs) 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 photoactivatable protein (PhoCl) as a fundamentally new class of optogenetic tool to control protein function with light (4). PhoCl can be used light-activated transcription, gene recombination, manipulation of protein localization, and activation of enzymatic activity.

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 Ca²⁺ indicators known as the GECO series (5). We initially engineered a variety of colors of Ca²⁺ indicator, including the red fluorescent R-GECO1 which has served as the basis for many other 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. In addition to the GECO series, near-infrared (NIR)-GECO (8). The Campbell lab also developed several other colors 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 FlcR1 voltage indicator, and a red fluorescent glutamate indicator (11).

Current Theme 1: Indicators on hybrid chemi-genetically 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 fluorophore 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.

Current Theme 3: Expanding the color palette of near infrared indicators

Expanding the color indicator palette into the NIR will create a variety of new opportunities for multiplexed and decentralized data analysis (12), where new approaches are required to expand the fluorophore palette. 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.

References

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Solid State Chemistry

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.

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.

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 ions of molecular crystals by introducing our knowledge of inorganic-materials design. Our group has already used this approach on the Li$_2$SAASN, 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.

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—or to construct the new perspective on materials science.

References

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 analytical 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.

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.

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

References
which are statistical parameters of molecular populations, could show a drastic shift from that of bulk material by confining them into nanospace. The shape, size, or the packing of molecules are controlled by the nanospace and anisotropic diffusion coefficient or peculiar rotational motion is 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.

**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 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 Seebeck coefficient, 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 See 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.

**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 show 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 of molecular populations, could show a drastic shift from that of bulk material by confining

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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-mediated base pairing allows metal-programmable way. We have developed artificial metallo-DNAs, in which hydrogen bonds between natural nucleobases are replaced by metal DNA, which governs genetic information, has a structural basis to arrange functional building blocks into a one-dimensional sequence in a 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 directed towards elaborate molecular systems and functions.

**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 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-liquidified 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.

References


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 with organic 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 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.

Organic Synthesis without Relying on Searing 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 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).

Organic Electronics 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. Polycarbazole, 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-dihydropyrene 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 indole unit, and this 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.

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.

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

References

Green Sustainable Chemistry Social Collaboration Laboratory was established 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.

**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.

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2. bench-scale continuos-reactor system of 100 g/h - 1,000 g/h continuous synthesis. 300 mL of CRs 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.
4. Green Sustainable Chemistry Social Collaboration Laboratory

**Linking cutting-edge chemistry to building a sustainable society**
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 brightness 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.

Fig. 1 shows XAS and XMCD spectra, defined as the difference in absorption spectra excited by right and left circular polarized light, of ferrimagnetic CoFe\(_2\)O\(_4\) with perpendicularly magnetic anisotropy. Analysis of spectral shapes using the magnet-optical sum rules estimates spin and orbital magnetic moments separately, which becomes a powerful technique for clarifying mechanism of the functionalities of novel materials and molecules. Furthermore, we have developed x-ray magnetic linear dichroism (XMLD) technique to deduce quadrupole moment with ligand field theory calculation for clarifying novel magnetic anisotropy. Recently, we succeeded in Operando XMCD system to detect the control of orbital magnetic moments during applying external strain, which is utilized for interfacial physics and chemistry.

In order to detect the energy band dispersion around the Fermi level, we have developed high-resolution angle-resolved photoemission spectroscopy (ARPES). As an example, the band dispersions of topological insulator (TI) of Bi\(_2\)Se\(_3\) surface are shown in Fig. 2. Dirac point which originates from bonding states and electronic and magnetic structures. 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.

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).

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.

References
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, our 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 Physics, Chemistry, and Laser Engineering.

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

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.

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).

**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
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 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 materials, we must study various materials under high-pressure conditions in laboratory-based experiments. Along with high-pressure experiments, natural samples are also important to obtain information on the real Earth. We are investigating mineral inclusion 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 trigger a state of the Miura active fault zone. In addition to the researches above, our interest extends to diffuse degassing processes during long periods. 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 edifices, which is an indicator for volcanic unrests or eruptions.

**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 fields 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, planetesimal 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 analysis. 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-MS. Laser induced ions are extracted into a high-vacuum, and separated by mass. The newly developed system has blossomed to become a method of choice to provide the most precise chronological data by analyzing the年代定年層（ICP-SFMS）.

**Geochemical Research Center**

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

**Geochemical characteristics**

Volcanic gas is a mixture of volatiles degassed from magma and fluids from hydrothermal system. By monitoring chemical composition and flux of 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 pathways of volatiles through volcanic gas investigations using elemental and stable isotope measurements. For example, sulfur is an important element which is related to volcanic gas chemistry using a FT-IR spectrometry 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 above researches, our interest extends to diffuse degassing of volcanic carbon dioxide from volcanic edifices, which is an indicator for volcanic unrests or eruptions.

**Groundwater 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 Atogawa 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 technique in 2010. A radon monitor was installed in Nakasu observatory, which was used in our laboratory for 30 years, was replaced with the new one in 2010. This new monitor dramatically detected an abnormal radon concentration increase before the Tohoku earthquake in March 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 our geochemistry for aiming to investigate and monitor a cross-border phenomenon with these monitoring techniques in some years.

**References**

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 Co₃O₄ nanocrystals with different shape grown in aqueous solution through oxidation of CoCl₂ by H₂O₂. 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 NaBH₄ 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 nanoparticles, whose TEM image is shown in Figure 3 [2], have average particle size of 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.

**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 sonochemistry 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 CO₂ 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 cluster interacting with NH₃, NH₂, benzene and O₂ 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 O₂ 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].

**References**

History
1861 The Department of Manufacturing Chemistry in the Institute for Research of Foreign Books established by the Tokugawa Shogunate. Re-established at Yoshi Shiraisho Rikai Gakko and Tokyo Kaisei Gakko.
1877 Merged with Tokyo Igakk to form Tokyo Daigaku (Tokyo University), and the Department of Chemistry founded within the School of Science.
1880 Gakushu Kenkyukai (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
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 Greener Transformation (GAN)’ project commenced.

Facilities

Nuclear Magnetic Resonance Spectrometer

The Library of Our Department

Chemistry Experiment for Undergraduate Students

Auditorium

Map of Hongo Campus
(Chemistry Bldg.)
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E-Mail: kagaku@chem.s.u-tokyo.ac.jp
Homepage: http://www.chem.s.u-tokyo.ac.jp/

From Ueno Station: take Toei Bus #01 for Todai-Konai and get off at Konai Bus Stop.
From Ochanomizu Station: take Toei Bus #07 for Todai-Konai and get off at Konai Bus Stop.

Subway
- Hongo-sanchome Station (Tokyo Subway Line), 15 min walk
- Hongo-sanchome Station (Toei Subway Line), 15 min walk
- Nezu Station (Tokyo Metro Line), 10 min walk
- Todaimae Station (Tokyo Metro Line), 15 min walk