CHEMISTRY

Department of Chemistry,
School of Science,
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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, electronic 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 exploit 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 imaging 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**

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; epitaxial thin films, single crystal, and 1D or 2D coordination polymers. This material shows photoinduced phase transition from colorless to a black or red colored phase by visible light or heat. From this point of view, we have synthesized various photochromic materials including organic metal complexes and oxide materials which exhibit magnetization changes by the light/electromagnetic wave absorption. We have discovered that magnetic phase transition and optical absorption occur simultaneously. We have developed heat storage materials which use the phase transition of metal oxides or magnetic materials. As a result of continuous research, we have developed a novel magnetic oxide heat storage ceramic which can store heat by photoirradiation. This material shows a large heat energy storage density and is very economic and environment friendly. We have also discovered that metal oxide nanoparticles can be used as heat storage materials for solar thermal power generation systems or for efficient utilization of waste heat from factories.

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 designability of the molecular structure, and therefore, they are useful for developing novel magnetic materials. We have synthesized various metal complexes with different magnetic and optical properties. For example, we have synthesized a metal complex that exhibits both ferroelectricity and ferromagnetism. We have also synthesized a porous magnet that responds to solvent vapor, and so on. Recently, we have pioneeredly reported various novel functionalities, for example, a magnet exhibiting two compensation temperatures, a humidity-sensitive magnet, a ferromagnetic thin film 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.

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 photochromic materials using metal complexes and observed novel phenomena including photoinduced magnetic pole inversion and photoinduced magnetization, in which paramagnetism and ferromagnetism are reversibly photoinduced. Recently, we have observed light-induced spin–crossover ferromagnetism and 90°-optical switching of the polarization plane of second harmonic light. Furthermore, we could control light using the magnetic materials that we developed. We focus on nonlinear magneto-optical effects and have reported the second example of magnetization-induced second harmonic generation (MSSHG) in a bulk ferromagnet, the first example of MSSHG in a chiral ferromagnet, and the first observation of magnetization-induced third harmonic generation (MTHG) in a ferromagnet. Furthermore, from recent studies on photon observations by terahertz light, we observed low-frequency oscillations of Co+ ions in a Prussian blue framework and also a new developed Co-detection method using terahertz light.

Study of novel magnetic oxides with electromagnetic environmentally protective function

Magnetic materials, represented by iron oxides, have been used in our lives for their chemical stability and insulation properties. We have been studying the synthesis of novel magnetic oxides by chemical approaches and have succeeded to isolate a new kind of magnetic oxide, epsilon-iron oxide, ε-Fe₂O₃, 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.

Titanium oxides containing Ti⁴⁺ 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-TiO₂). This material shows photoinduced phase transition from colorless to black colored lamellar phase (metallic conductor) to brown colored beta phase (β-TiO₂) (semiconductor). Moreover, the reverse phase transition was also observed by photoirradiation. This is the first example of a metal oxide which shows photoresponsive properties at room temperature. Since λ-TiO₂ is very economical and environmentally friendly material and is obtained as nanopowder, λ-TiO₂ is expected as a next generation high-density optical storage material. Additionally, λ-TiO₂ 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 3 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.

References
Recent advances in laser technology made it possible to generate an ultrashort-pulsed intense laser field whose field intensity is as high as $10^{19} \text{ W/cm}^2$, which is comparable to 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 processes are strongly 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.

In Figure 1, we show 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 the 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 molecules are formed. These multiply charged molecules dissociate into fragment ions having large released kinetic energies by the Coulomb repulsion among fragment ions. This decomposition process of molecules into fragment ions with 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 “coincidence momentum imaging” method, which records the momentum vectors and distributions of fragment ions generated through the Coulomb explosion in intense laser fields, (2) “laser-assisted elastic electron scattering” for investigating ultrafast electron dynamics within atoms and molecules in intense laser fields and “laser-assisted electron diffraction” for probing ultrafast variation of the geometrical structure of molecules with the femtosecond temporal resolution, (3) “attosecond spectroscopy” in which photoelectrons and photo-ions are detected after molecules are ionized by high-order harmonics generated using few-cycle laser pulses, (4) elementary excitation processes of atoms and molecules in laser-induced plams, which are formed by focusing intense laser pulses into gaseous media, and (5) development of theory for describing atoms and molecules in intense laser fields and theoretical studies of dynamics of atoms and molecules in intense laser fields.

![Figure 1: Molecular dynamics in intense laser fields](image1)

**Molecular dynamics in intense laser fields studied by using coincidence momentum imaging**

By using the coincidence momentum imaging (CMI) technique, we revealed that a triatomic hydrogen molecular ion, $\text{H}_2^+$, is produced from a hydrogen molecule exposed to an intense laser field, and that hydrogen and/or protons migrate extremely rapidly within the molecular ion. From a pump-probe CMI measurement of methanol, $\text{CH}_3\text{OH}$, we revealed that hydrogen atoms are transferred within a molecule on a femtosecond time scale induced by an intense laser pulse. This phenomenon is called ultrafast hydrogen migration. In addition, we found the slower hydrogen migration (~150 fs) proceeding after the laser irradiation. These two types of hydrogen migration were interpreted by referring to the potential energy surfaces obtained by quantum chemistry calculations shown in Figure 2.

We also developed an experimental setup in which the momentum images of fragment ions and the CEP of the few-cycle laser pulses are recorded in coincidence as shown in Figure 3. By using this setup, the CEP dependence of fragmentation pathways of acetylene induced by few-cycle laser pulses was investigated.

![Figure 2: The adiabatic potential energy surface of the electronic ground state of neutral methanol, $\text{CH}_3\text{OH}$ (lower) and that of the electronic ground state of methanol cation, $\text{CH}_3\text{OH}^+$ (upper). The arrow on the upper surface shows a trajectory leading to the ultrahigh hydrogen migration](image2)

![Figure 3: Experimental setup for the coincidence measurement of CEP and the momentum image of fragment ions](image3)

**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 high kinetic energy by multiples of the photon energy if the electron is a phenomenon called laser-assisted elastic electron scattering (LAES). By using the LAES process induced by an ultrashort laser pulses as an ultrafast shutter for the measurement of electronic excitation and dynamic of molecules, ultrafast dynamical change of molecules can be probed with the extremely high temporal resolution (Figure 4). By this laser-assisted electron diffraction (LAED) method, we recorded the electron diffraction pattern of carbon tetrachloride, $\text{CCl}_4$, at the moment of the irradiation of femtosecond laser pulses. Because the temporal resolution of the LAED method is limited only by the laser pulse duration, the temporal resolution of this method can be better than 10 fs.

![Figure 4: The schematic of the laser-assisted electron diffraction](image4)

**Development of theories to describe molecular dynamics in strong laser fields**

For describing multi-electron dynamics in atoms and molecules interacting with an intense laser field, we developed a first-principle quantum theory called multi-configuration time-dependent Hartree-Fock (MCTDHF) model. The variation of the spatial distribution of the electron density within atoms and molecules induced by an external light field can be treated by the MCTDHF method. We further extended this MCTDHF theory so that not only the dynamics of electrons but also the dynamics of protons within a molecule can be described, and discussed the quantum nature of the multi-proton dynamics involved in the ultrafast hydrogen migration process (Fig. 5).

We also developed a first-principles molecular dynamics method to investigate chemical bond breaking and formation processes. By analyzing the nuclear trajectories in the $H_2^+$ emission process from methanol, $\text{CH}_3\text{OH}$, we found that an $H_2^+$ moiety appears within the dication, and then, abstracts a proton from the remaining dication moiety, $\text{CHO}^+$, resulting in the formation of $\text{H}_2$ and $\text{CHO}^+$ as the fragment ions (Fig. 6).

![Figure 5: The logarithmic plot of the proton probability density in methanol, $\text{CH}_3\text{OH}$](image5)

![Figure 6: The neutral $\text{D}_2$ moiety appearing in the process of the emission of $\text{HD}^+$ from $\text{C}_2\text{HD}^+$](image6)

**References**

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 geometric 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 protected by ligands such as thiocyanates (RS), phosphines (PR₃), and alkynes. Our method yielded a series of clusters, such as Au₆(SR)₃, Au₈(SR)₅, Au₁₁(SR)₅, Au₁₃(SR)₅, Au₁₆(SR)₅(PR₃), and Au₁₈(SR)₅(PR₃)₂Cl₂, 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 stabilities and structures of the ligand-protected Au clusters.

Precise 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 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).

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


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

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

Figure 3. Activation of CO₂ by Cu cluster anions and a new activation route of the C=O bond of CH₂ by Au.

Figure 4. Controlled synthesis of supported Au-based clusters and the effects of the structural parameters on catalysis.
Dissecting Life with Organic Chemistry and Devising Methods to Control at Will

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

**Development and application of artificial ribozymes**

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

"Flexizyme" is one of the most successful ribozymes developed in our laboratory. Flexizyme is a short RNA molecule consisting of 46 nucleotides and it catalyzes the aminolysis of tRNA with a wide range of natural and unnatural amino acids. Flexizyme exhibits broad substrate tolerance, it accepts arbitrary RNA 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 flexizyme with a reconstituted E. coli translation system. Flexizyme allows us to prepare diverse nonproteinogenic aminoacyl-tRNAs quickly and easily to synthesize polypeptides with the freedom to incorporate various non-proteinogenic amino acids. (Fig. 2). For this purpose, we have developed "Flexizyme" is one of the most successful ribozymes developed in our laboratory. Flexizyme is a short enzymatic activity in order to validate the concept of the RNA world. In other words, development of nonstandard peptides has thus far been haphazard and a systematic method of discovery has not been established due to the limited availabilities of nonstandard peptides. On the other hand, the FIT system enables us to freely design and create such nonstandard peptides. We have already developed various methodologies for the macrocyclization of translated peptides and the synthesis of natural product-like nonstandard peptides using the FIT system. Now, we are trying to develop new systems for producing more complicated and pharmaceutically useful peptides.

**Drug discovery using the nonstandard peptide library**

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

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### References


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*Fig. 1 Three-dimensional structure of flexizyme (yellow) and tRNA (red). The flexizyme core is docked onto tRNA![](image-url1). *Superimposing the minihelix on the tRNA from Nature Chemical Biology (2009) showing our research project “Keys to translation.”

*Fig. 2 Example of genetic code reprogramming.*

*Fig. 3 Ribosomal synthesis of cyclic N-peptide.*

*Fig. 4 Cover page of Nature Chemical Biology (2009) showing our research project “Keys to translation.”*
Synthetic organic chemistry is the science of "making" chemical products. Our laboratory is not only continuing and expanding upon the traditional synthetic organic role of creating compounds and new drugs, but also exploring the 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 production environmentally friendly. 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, and to solve recent energy problems from the viewpoint of synthetic 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 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

All living things, including human being, are made up of water. A number of chemical reactions performed in a living organism made up its metabolism, maintaining chemical and ionic gradients (homeostasis). Most enzymes provide a sequestered and somehow hydrophobic environment to exclude water, where chemical reaction is regulated tightly. To force this to happen in a non-microbial or non-biological systems, organic reactions have been long deemed to be conducted in organic solvents, owing to the compatibility and immiscibility between water molecules and many reagents or reactive species. Most organic solvents are, however, harmful to human body and environment, which urged chemists to seek "greener" solvent alternatives (non-toxic, inexpensive, and benign to environment). We believe that water is the most attractive candidate up to now. In addition, water sometimes provides us with a potential to achieve unique reactivity and selectivity that cannot be observed in conventional organic solvents. Our group has extensively engaged in the development of multilayer catalytic systems that are water-compatible. One of our fruits, Lewis Acid-Surfactant-Combined Catalyst (LASC) is regarded to be a highly efficient catalyst that works in water, forming hydrophobic micelle along with Lewis acidic site.

### Development of highly efficient and environmentally friendly polymer-immobilized metal catalysts

Although metal catalysts are essential tools in organic synthesis, these species are often toxic and harmful to humans and the environment. In addition, metals are precious and limited resources on the Earth, and they should be recovered and reused without forming any waste. Our "Micro-encapsulation" technique is a novel approach to convert metal nanoparticles into polymeric particles or polymers, which can be directly synthesized from two different metal salts by polymerization or covalent connection. This metal particle-encapsulated polymer catalyst can be directly synthesized from different metal salts by polymerization or covalent connection. This metal particle-encapsulated polymer catalyst can be readily activated by transition metal complicate, which achieve high catalytic activity compared to bulk metals, but these nanoclusters can be easily deactivated due to aggregation. Our polymer-based immobilization methods were shown to stabilize metal nanoclusters. We also demonstrated that alloyed metal nanoclusters consisting two different metals could be prepared by using the MC or PI method, and these catalysts showed higher reactivity and selectivity than single metal nanoclusters. Moreover, these catalytic reactions are carried out in both liquid and solid phases, and these reactions can be directly synthesized from two different metal salts by polymerization or covalent connection. This metal particle-encapsulated polymer catalyst can be directly synthesized from different metal salts by polymerization or covalent connection. This metal particle-encapsulated polymer catalyst can be readily activated by transition metal complicate. We also realized the use of Au-Pd alloyed nanocluster.

### Total synthesis of optically active drug, Rhodipin, using multi-step continuous flow reaction system

Asymmetric carbon-carbon bond formation reaction is one of the key reactions to prepare metal nanoparticles as heterogeneous catalysts. Asymmetric 1,4-addition of aryl boronic acid to α,β-unsaturated alkenes is a powerful method for the formation of carbon-carbon bonds. We reported the development of highly efficient catalytic asymmetric 1,4-addition reaction of aryl boronic acids with α,β-unsaturated alkenes to form carbon-carbon bonds using chiral Lewis acid integrated with single-walled carbon nanotubes (SWCNTs). In addition to the enhanced reactivity, the asymmetric performance and long-term stability were demonstrated in asymmetric catalytic addition reactions of aldehydes to female aldehydes with excellent enantioselectivity and efficiency. The application to various Lewis acid-catalyzed reactions is expected to open up new opportunities and novel modes of catalysis.
The food chain and a body defense against marine toxins

Okadaic acid (OA), a polyether marine toxin first isolated from the sponge Halichondria okadai in the 1970s, is deemed a product of a microbial symbiont that inhibits the host body, or an accumulated product of food origin. Exhibiting its toxicity as an inhibitor of protein phosphatases (PPs), OA is thought to be highly toxic, even to the host sponge. Assuming a complex formation for OA with okadice acid binding proteins (OAABPs) in sponge cells to inhibit its binding to PPs, binding affinity guided fractionation afforded OAABP2, a novel protein of 189 amino acid residues lacking PP activity. Although cell separation experiments suggest that the majority of OA may be present outside the sponge cells, the questions to be answered concerning whether OAABP2 simply masks the OA having entered the cells, or mediates its transport to the outside of the cells, seem to increase. It is hoped that our new findings will lead to the elucidation of mechanisms behind symbiotic host selectivity in sponges and other organisms, and hence mechanisms for habitat segregation in multicellular organisms on sea bottoms, in the context of marine chemical ecology.

Chemical synthesis of polyether ether skeletons

Ladder-shaped polyether marine toxins, represented by ciguatoxin, a neurotoxin first isolated from edible fish as the cause of food poisoning in coral sea areas, are produced by dinoflagellate in unusual propagation. Assuming that these toxins are difficult to obtain from nature, and their production is a discipline that studies small molecules from organisms. Genes, proteins and other biopolymers that play key roles in biological phenomena are generally ubiquitous in all organisms, whereas low-molecular natural products are diversified throughout different biological species and environments. Because of their high mobility, most low-molecular natural products are responsible for information transmission among the cells of individual multicellular organisms, or among the organisms in ecosystems. We are working to develop new methodologies based on organic and spectroscopic chemistry with a focus on small molecules produced and accumulated by marine organisms that constitute ecosystems through chemical communication via the aequous mediums, and to elucidate their actions in living organisms and ecosystems.

Recognition principle of polyether ether compounds and membrane-bound proteins

Most membrane-bound proteins are activated by stimulation from outside of the cells, producing a series of intracellular physiological changes due to enzyme activity alterations and inorganic ion inflows. However, because they return to the static state upon completion of signal transduction, this activation is only transient under physiological conditions; the obtainable information on three-dimensional structural changes associated with the activation is no more than estimation. We are working to acquire and analyze information on the three-dimensional structure of membrane-bound proteins by extending the longevity of their activated state using exogenous molecules such as natural toxins that exhibit high affinity for the activated state, so as to elucidate the structural mechanisms for the activation of membrane-bound proteins. Hence, our research focuses on (1) the procurement of ligand molecules by organic synthesis, which allows us to introduce markers for acquisition of structural information, including isoforms, and (2) the development of a methodology for acquiring information on the structures of complexes in lipid bilayers with the use of these ligands if available. To accomplish aim (1), with synthetic preconvenience in mind, we synthesize ligand molecules by joining non-natural polyether ether units by permutations-and-combinations and Suzuki coupling with a number of components, on the assumption of non-specificity in the mutual recognition of membrane-bound proteins and polyether ether molecules having molecular lengths equivalent to the thickness of biomembrane. Out of the membrane-bound proteins with which these molecules form complexes, those suitable for structural research are chosen; their general roles in the assumed molecular recognition are clarified, and the mechanism behind the onset of specificity in the recognition is explored. Aim (2) can be accomplished using a complex of ciguatoxin and voltage-sensitive sodium channel protein, which is deemed the target cell component in the onset of the toxicity of the toxin molecule which is the subject of the research. Our scheme comprises four steps: (1) identification of the binding site of the protein using photoaffinity labeling and mass spectrometry analysis, (2) isoform labeling of both the identified transmembrane site and the ligand molecule, (3) preparation of the complex by reconstitution into membrane, and (4) acquisition of information on labeling site distance by NMR. If structural evidence is thus obtained for the activation of membrane-bound proteins by polyether ether, the findings will lead to the designing and creation of molecules that are capable of specifically controlling the functions of particular membrane-bound proteins.

Visualizing cells and marine ecology by precision chemistry

The generic term natural products refers to a group of substances excluding artificial products, and the chemistry of natural products is a discipline that studies small molecules from organisms. Genes, proteins and other biopolymers that play key roles in biological phenomena are generally ubiquitous in all organisms, whereas low-molecular natural products are diversified throughout different biological species and environments. Because of their high mobility, most low-molecular natural products are responsible for information transmission among the cells of individual multicellular organisms, or among the organisms in ecosystems. We are working to develop new methodologies based on organic and spectroscopic chemistry with a focus on small molecules produced and accumulated by marine organisms that constitute ecosystems through chemical communication via the aequous mediums, and to elucidate their actions in living organisms and ecosystems.

Natural Products Chemistry

References

2. Determination of the WTXII motif using nicotine acetylcholine receptor from a complex of ciguatoxin and voltage-sensitive sodium channel protein, which is deemed the target cell component in the onset of the toxicity of the toxin molecule which is the subject of the research. Our scheme comprises four steps: (1) identification of the binding site of the protein using photoaffinity labeling and mass spectrometry analysis, (2) isoform labeling of both the identified transmembrane site and the ligand molecule, (3) preparation of the complex by reconstitution into membrane, and (4) acquisition of information on labeling site distance by NMR. If structural evidence is thus obtained for the activation of membrane-bound proteins by polyether ether, the findings will lead to the designing and creation of molecules that are capable of specifically controlling the functions of particular membrane-bound proteins. 13
Creation of new molecular architectures that lead to development of functional materials supports the progress and growth of our society. Fundamental materials for the next generation are therefore awaited in various fields, such as nanoscience, materials science and life science, and there arises growing expectation on "organic chemistry". Here in this group, we are exploring new π-rich molecules that hold the key to the discovery of ground-breaking principles and functions by employing organic synthesis together with the power of physical organic chemistry.

**Finite carbon nanotubes and their application in nanoscience**

Carbon nanotubes are fascinating materials that possess characteristic curved π-electron systems. However, carbon nanotubes produced by current (physical) methods lead to a wide range of structures with different properties, and such heterogeneous mixtures are insufficient for advanced applications. They are not "molecular entities" but "chemical species". Bottom-up organic synthesis, on the other hand, has allowed in-depth study of structure-property relationships and facilitated the creation of new, discrete molecular entities. In 2011, our group was the first to demonstrate the bottom-up synthesis of finite helical single-wall carbon nanotube molecules (Figure 1a, Reference 1). Since then, a variety of finite carbon nanotube molecules were prepared by state-of-the-art organic synthesis. Using the belt-shaped/belt-persistent molecules, we are exploring the nanoscience of 

**Triazole-linked analogue of nucleic acids**

Replacement of internucleoside phosphodiester linkages of DNA or RNA with non-natural structures would generate intriguing oligonucleotides with functions that could explore the field of medicinal chemistry, chemical biology and materials science. The Nature's choice of phosphate for the internucleoside linkage is so divine that allows the connection and cleavage of the oligonucleotides at will. When chemists wish to explore the tailor-made variants, sophisticated design of molecular structures is required: an easy synthetic access to the monomeric units, efficient elongation processes and duplex-forming strands. Our group recently introduced the new analogue of triazole-linked DNA and RNA (TLDNA and TLRNA) using copper-catalyzed Huisgen cycloaddition reaction for the elongation reaction (Reference 5). The robust method supported the concise synthesis of oligonucleotides with triazole-linkages and development of their functions in biomolecular and materials chemistry (Figure 3, Reference 6).

**References**


6. Triazole-linked Analogues of DNA and RNA using copper-catalyzed Huisgen cycloaddition reaction for the elongation reaction (Reference 5). The robust method supported the concise synthesis of oligonucleotides with triazole-linkages and development of their functions in biomolecular and materials chemistry (Figure 3, Reference 6).
Biomolecular Chemistry Laboratory

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 receptors 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 purposes. 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 homologues. 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 chromosome within their structure. Amazingly, the DNA that encodes a FP can be introduced into practically any animal and be properly expressed, making the tissues of the animal fluorescent. Genetically encoded fluorescence has revolutionized many areas of cell biology because it enables researchers to use fluorescence microscopy to “see” structures and cellular processes that would normally be invisible.

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

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

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

The Campbell research group has expanded the toolbox of color-coded FP variants for use in a wide variety of application areas, including the construction of FP-based indicators. For example, Ai (Ph.D. 2008) and Hoi (Ph.D. 2012) developed cyan, yellow, and green-to-red fluorescent proteins (GFPs) that increase their brightness when they form a heterodimeric complex (3). This technology provided a powerful new approach for developing protein-protein interactions in live cell. In more recent work, Zhang (Ph.D. 2017) developed a photoactivatable protein (PhoCi) as a fundamentally new class of optogenetic tool to control protein function with light (4). PhoCi uses light-activated transcription gene recombination, manipulation of protein localization, and activation of enzyme activity.

Past Highlights 2: Engineering a palette of visible fluorescence neuroactivity 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 to occur in Nature.

The GECO series was further extended by Wu (Ph.D. 2014) and Shen (Ph.D. 2014) (6, 7). Versions of R-GECO are freely used by hundreds of researchers around the world to address a diverse range of biological problems. Our most recent addition to the GECO series is near-infrared (NIR)-GECO (8), developed by Qian (Ph.D. in progress). The Campbell lab also developed several other classes of red-shifted neural activity indicators. Zhao developed the near-infrared (NIR) fluorescent QuasA-series of voltage indicators (9, 10), Abdel-Rahman (Ph.D. 2016) developed the red-fluorescent Fluo1 voltage indicator, and Wu developed a red-fluorescent glutamate indicator (11).

Future 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 source 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 at The University of Tokyo will develop high performance indicators for cell metabolic pathways and enable the full metabolism of a cell to be visualized for the first time!

Future 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 fluorophore is designed to covalently attach to a specific protein expressed in the cell or tissue. Over the coming years, the Campbell lab at The University of Tokyo will work to convert chemi-genetic FPs into a new generation of high performance indicators. This is an unexplored and exciting research frontier!

Future 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 ~1300 nm. The Campbell lab at The University of Tokyo will pioneer the development of genetically encoded and hybrid chemi-genetic 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!

Solid-state compounds including metal elements involve various electronic states, resulting in diverse electronic functionalities such as electronic, magnetic, and optical properties. However, ordinary synthesis process only produces thermodynamically equilibrium phase, hampering materials exploration of new compounds. Our group is trying to break down this barrier by using pulsed laser deposition (PLD). PLD is a thin film growth method, in which high energy laser deposits solid evaporation sources on atomically flat substrates. This method is a non-equilibrium growth process enabling to synthesize metastable compounds. Atomic layer-by-layer growth is also possible to engineer newly designed compounds.

**Electronic functionalities of oxynitrides**

Transition metal oxides show a variety of electronic functionalities such as conductivity, ferromagnetism, ferroelectricity, and superconductivity. So far, their electronic functionalities have been mainly designed and controlled by carbon substitution. Currently, we are developing a new strategy for exploration of novel electronic functionalities by synthesizing transition metal oxynitrides, in which the oxygen is partially substituted with nitrogen. An example is perovskite oxynitrides $AORN_x$ that have been studied as pigments or photocatalysts and their electric properties have been scarcely known due to difficulty in synthesis of high-quality bulk crystals. Recently, we succeeded in synthesizing epitaxial thin films of perovskite $A0TaN_x$ ($A = Ca$ or Sr) by plasma-assisted pulsed laser deposition technique. The obtained $Sr0TaN_x$ thin film showed room temperature ferroelectricity (Fig. 2) as well as visible light absorption due to the narrow band gap. Such features are usually not concomitant in oxides and originate from metastable trans-type anion coordination of $TaO_6$ octahedra in the crystal, which was stabilized by epitaxial strain from the substrate. We also succeeded in synthesizing nanoscale $TaO_N$ for the first time, and demonstrated that it is a promising semiconducting material with high electron mobility and high refractive index. Amorphous oxynitrides are another class of interesting materials. For example, amorphous $ZnO_N$ exhibits extremely high electron mobility over 200 cm$^2$/V-s, almost twice as high as those of amorphous oxide semiconductors.

**Topotactic synthesis of mixed anion compounds in epitaxial thin film form**

Introduction of hydroxide ($OH^-$) and fluorine ($F^-$) anions into transition metal oxides has recently become possible through topotactic synthesis, where guest species can be doped into a host crystal structure by destabilizing the initial cation framework. This synthesis can be further extended by using thin film samples because of their high reactivity compared with bulk. Furthermore, single-crystalline samples can be obtained through topotactic reactions of epitaxial thin films, which could provide direct information about amorphous electronic/bonding natures. We are exploring novel mixed anion compounds with intriguing chemical or physical properties in single-crystalline thin film form by utilizing topotactic reactions (Fig. 3).

**Electronic states of oxide thin films by using synchrotron radiation spectroscopy**

Evaluation of electronic states is indispensable to understand the various electronic properties of transition metal oxides. We investigate their electronic states by using synchrotron-radiation X-ray photoemission (PES) and absorption spectroscopy (XAS). Core level and valence band spectra are obtained by PES, and conduction band spectra are investigated by XAS. In addition, resonant PES (R-PES) can reveal partial density of states of a resonant element in the valence-band region. The valence band spectra of $TaO_N$ thin films were measured by 2p-$3d$ R-PES (Fig. 4). By oxygen annealing, the density of states at the Fermi level originating from $Ta 3d$ states was decreased, while the intensity of the bonding energy of $-3.0$ eV derived from $O 2p$ states was increased. This result corresponds to the reduced carrier concentration by oxygen annealing, suggesting that the carrier generation in anatase $TiO_2$, thin films strongly depends on interstitial oxygen.

**Computational material design with the first-principle study**

Recent advance in computational science enables us to calculate microscopic structure of functional materials. Intensive efforts have been devoted for the density functional theory (DFT) based calculation of doped oxides. We are surveying the electronic structure of transparent conducting oxides (TCO) promoted simultaneously with experimental study. Their physical properties are significantly affected by different combinations between mother compounds, dopants, and the crystal structure. Such theoretical prediction is important. Recently, we exemplified a significant effect of non-stoichiometry and impurity complex on the electronic properties. We also demonstrated the necessity of proper treatment for electronic spin states and self-interaction error (SIE) in DFT approach (Fig. 5). Currently, we are pursuing the calculations of doped materials and ionic transport at interface, aiming at a rational computational material design and a discovery of new functional materials.
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.

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

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 can lead to the destruction of cells or tissues before detection of a target molecule. The true physiological functions of biomolecules cannot be elucidated if their functions and dynamics are 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 activities with external light. We are also developing Raman microscopic system for noninvasively investigating biomolecules without any labeling techniques.
Creating molecules that alter their structures and properties in response to external stimulation and assembling them in precise combination would lead to the development of functional molecular systems based on a totally new concept. We are working to create new molecular systems that sensitively respond to light, electric fields, magnetic fields, and/or chemical environments to change their structures, properties, and functions in various states, such as single molecules, single crystals, clusters, polymers and complex systems, and to build molecular devices by arranging them in interfaces of electrode substrates and metal nanoparticles in a controlled way. We are also developing new catalytic reactions making use of the characteristics of transition metal complexes and nanoparticles.

**Creation of materials**

One-dimensional π-conjugated polymers, also called “conducting polymers”, not only possess high electronic conductivity, but also exhibit a variety of other characteristics, including chromism and luminescence. We are engaged in creating new materials by fusing the conductive polymers with transition metal characteristics, including chromism and luminescence. We have synthesized a variety of hetero-metal cluster complexes using the new method. Now we are comprehensively exploring the correlation between their crystalline structures and optical characteristics, electronic characteristics, and chemical reactivity.

**Chronic metal complexes**

We are working on design and synthesize metal complexes of ligands containing organic photochromic molecules such as azobenzene, spiropyran, and diarylethen, in search of new materials and phenomena. Our achievements include the discovery of reversible isomerization by means of metallothermochromism and redox control in azobenzene-conjugated bipyrinium cobalt complex and ferrocenyleneazobenzene, the reversible conversion of the triple stable state using trichromatic light in a platinum complex coupled with two azobenzene units, the construction of a photosignal-conductive redox molecular wire possessing an extremely high capacity for electron transport.

**Building a biomolecular device**

We have developed a photosensing device consisting of an in vivo photoreceptor component, a molecular wire, gold nanoparticles, and a transistor by extracting a photosystem 1 (PSI) from a heat-resistant cyanobacterium, replacing its vitamin K1 (VK1) unit with gold nanoparticles, previously structurally modified with an artificial VK molecule, and chemically immobilizing the PSI onto an FET gate.

**References**

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 metal-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 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 meshed in the center. This process is photo- and thermally driven due to the isomerization of the Pt(II) complex into a phenylene ring of one ring. The other example is a molecular system with a switching function based on coordination isomerism on a Pt(II) ion. Two molecular arachphosphatritycenes rotate and 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 metallomacrocyclar-assembled porous crystal whose pore surface provides five enantiomeric pairs of molecular binding pockets. The unique feature of the pore structure has allowed several arrangements 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 crystallization analysis 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 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 assemblages 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.

A scientists’ dream: “Imaging single organic molecules in motion” is becoming reality

It has been the dream of scientists to observe the motion of single small organic molecules, ever since the concept of atoms and molecules was established a long time ago. We showed in a 2007 Science paper that this is no longer a dream, by studying using a high-resolution electron microscope to in situ record movies of the motions of small organic molecules trapped in carbon nanotubes (Reference 1). Figure 1a shows images of a saturated hydrocarbon molecule tagged with a ball-shaped boron marker in motion. Since then we reported movies of the conformational changes of a number of small molecules (Reference 2), and even performed kinetic analysis of chemical reactions by analysis individual reaction events one by one (Reference 3). We could also study for the aggregation of single organic molecules leading to nucleation and crystal growth (Reference 4). Once considered too futuristic, this research is seeing rapid development owing to a state-of-the-art atomic resolution electron microscopic microscope (Figure 1b) in full operation on the basement of the Molecular Life Innovation (MLI) building where our lab located.

Functional carbon clusters: Synthesis, assembly, function, and applications

π-Conjugated organic compounds possess unique electronic properties, and assemble to form functional materials. We have developed new carbon-rich π-conjugated materials (functional carbon clusters) and investigated their materials and biological applications. For example, when nanometer-sized [60]fullerene molecules are functionalized and aligned horizontally, water-tight fullerene bilayer membranes form and assemble into nanoscale structures. Figure 2 shows a vertically aligned fullerene bilayer vesicle with core-shell membrane structure.

Optoelectronic devices for solving energy issues: Contributions of synthetic organic chemists to new materials design

Solar cell manufactured using a low temperature solution process provides a promising solution to the energy problems in modern society. We have conducted fundamental research and practical applications of “organic thin-film solar cells” and “organic-inorganic hybrid solar cells” in the past 15 years (Figure 3). For example, with the understanding of the formation mechanism (Reference 9) of lead perovskite materials, we developed a polymer stabilization method for perovskite device fabrication (Reference 10) and tailor-designed new types of hole transporting materials to obtain perovskite devices with high operational stability and power conversion efficiency (Reference 11). We advantage of our expertise in microscopy (see above) to elucidate the mechanism of materials organization, and also explore modern organic synthesis (cataylsis) as a tool to create new conjugated molecules for materials science. We maintain close collaboration with companies in this research.

Foster scientists who can see their face from the world

Training next-generation world leaders in chemical science is an important mission of our laboratory. To this end, we have set up a long lasting program of sending Ph.D. students abroad for research experience, and of organizing Tateshina Seminar series twice a year to foster scientific curiosity and communication skill in science (Figure 5).
Green Sustainable Chemistry Social Cooperation Laboratory

Utilization of cutting edge chemistry for the construction of a sustainable society

Green sustainable chemistry (GSC) social cooperation laboratory was established in April, 2012 for the purpose of developing practical and environmentally-friendly chemical processes, and to educate international researchers who will lead this area, with the cooperation of several companies who agree with our intentions.

Promotion of GSC by industrial-academic-government cooperation

With the growing realization of the ever increasing environmental and energy problems, research and development in GSC area have expanded intensively for the construction of a sustainable society. In particular, the development of environmentally-friendly (= green) chemical processes is an essential aspect of GSC. However, realization of industrial processes is not trivial since many challenges, such as the development of innovative catalysts, recycling systems, green materials and products, and cost-reduction must be solved. These challenges can be met through systematic research and development by the cooperation between industry, academia, and government. Moreover, the education of international researchers, who will lead this area, is essential for the global realization and development of a sustainable society. Our laboratory aims to promote domestic and international GSC activities through research and education.

Top GSC technology toward industrial processes

The main focus of this laboratory is the promotion of GSC through industrial-academic-government cooperation. We plan to develop green chemical processes including the choice of starting materials, separation processes and recycle processes by utilizing cutting edge GSC technologies. In many developing nations, industrial wastewater is often discharged into large bodies of water (rivers, lakes, oceans) without appropriate treatment. It is important to maintain global leadership in GSC technologies and we must strive to continuously develop and discover new green chemical processes. Since we possess a variety of seed technologies for green chemical processes, we plan to seamlessly develop industrial processes by cooperating with our industrial partners. Catalyst technology, which is one of the most important key technologies in GSC, requires higher catalytic activity and longer lifetime of the industrial processes by cooperating with our industrial partners. Catalyst technology, which is one of the most important key technologies in GSC, requires higher catalytic activity and longer lifetime of the industrial processes by cooperating with our industrial partners. Catalyst technology, which is one of the most important key technologies in GSC, requires higher catalytic activity and longer lifetime of the industrial processes by cooperating with our industrial partners. Catalyst technology, which is one of the most important key technologies in GSC, requires higher catalytic activity and longer lifetime of the industrial processes by cooperating with our industrial partners. Catalyst technology, which is one of the most important key technologies in GSC, requires higher catalytic activity and longer lifetime of the industrial processes by cooperating with our industrial partners. Catalyst technology, which is one of the most important key technologies in GSC, requires higher catalytic activity and longer lifetime of the industrial processes by cooperating with our industrial partners.

Systematic study of basic and top GSC

GSC not only relates to chemical and environmental studies, but also to energy, law, politics, and economy. Systematic study of GSC by the creative cooperation among these areas is critical for the development of GSC and the construction of a sustainable society. Our research will include systematic study of GSC towards the total development of the GSC field. Due to the rapidly proceeding regulation of chemical substances around the world, GSC should be considered the global standard. The evaluation of the total greenness of the lifecycle of chemical products is a necessary component in the development of green chemical processes. The standard of ‘green’ is mutable and depends on our current scientific knowledge and social conditions. The continuous discovery or development of novel technology and information is desired. We plan to observe GSC information from the world and develop new GSC.

We will contribute to the leadership of our country in the world and promote global GSC by cooperation, research and education. To achieve this purpose, we accumulate the technology and knowledge through industrial-academic-government cooperation and promote our activities.

References

Green chemical process. Catalysts and solvents should be recycled or used continuously.
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 [4-5] (Fig. 4), which enables acquisition of 24,000 broad Raman spectra in one second, and applied it to large-scale label-free flow cytometry [6] (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 microalgual cells and cancer diagnosis by detecting circulating tumor cells in the blood.

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, fluorescence spectroscopy, IR spectroscopy and microscopy, nuclear magnetic resonance (NMR), gas chromatography (GC), electron spin resonance (ESR), differential thermo analysis (DTA), and thermogravimetric analysis (TG).

References

The Center for Ultrafast Intense Laser Science (CUILS) aims to explore the frontiers in the interdisciplinary research field of ultrafast intense laser science through international research cooperation and to develop an educational program in photon science by university-company cooperation.

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 matters. However, recent ultrashort pulsed laser technologies enabled us to increase the intensity of light up to 100 million times as large as 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 in which we investigate such light-matter interactions is regarded as an attractive and promising interdisciplinary research field covering physics, chemistry, and laser engineering.

CUILS for promotion of international research cooperation

CUILS is dedicated to promoting international research cooperation in the interdisciplinary field of ultrafast intense laser science, and has been supporting the following international conferences and workshops in ultrafast intense laser science and advanced photon science:

- The 9th Shanghai-Tokyo Advanced Research Symposium on Ultrafast Intense Laser Science (STAR9) (Hotel Sunvalley Nasu, Tochigi, Japan in May 24th-27th, 2018)
- The 15th AMO symposium (Tohoku University, Miyagi, Japan in July 15th and 16th, 2018)
- The 18th International Symposium on Ultrafast Intense Laser Science (ISUILS2018) (Thermal Hotel Visegrád, Visegrád, Hungary in October 14th-19th, 2018)

CUILS for a university-company 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 CUILS 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 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 can 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 (*1) and professors from the School of 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 Courses of Advanced Optical Science I/II.” The educational activities in the CORAL program, originally established as a five-year program, was highly evaluated by Ministry of Education, Culture, Sports, Science and Technology (MEXT), and became a permanent program from 2011.

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 (*2).


*2 Ushio Inc., Sigma Koki Co., Ltd., Toshiba Corp., Nichia Corp., Hamamatsu Photonics K.K.
Geochemical Research Center

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

Geochemistry can derive the "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 6400 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, 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 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 minerals, which plays an important role to the global circulation of CO2. In future, we will estimate global circulation of volatile compounds from surface elements to the deep Earth by synthesising the obtained knowledge.

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 formation of the Earth's core.

Geochemical Research Center

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. The main targets to investigate the dynamics of volcanic activities through volcanic gas investigation are various optical remote sensing techniques. A remote measurement technique of volatile gas chemistry using a FT-IR spectrometer 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.

Groundwater gas geochemistry of fault zones

Dissolved gases 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 Aogashima 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 in Nakajima 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 change in major active fault zone and the Tachikawa active fault zone. Not just above investigations, we will start an air geochemistry for aiming to investigate and monitor a cross-border pollution with these monitoring technologies in some years.

References


Remote measurement of volcanic gas chemistry using FT-IR spectrometer.

SG: column amount image observed at Sakurajima volcano.

Gas emission is monitored under uniaxial compres- sion in a vacuum chamber.

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

Geochemical Research Center

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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 cube exhibiting (100) equivalent surfaces. Addition of polar organic molecules such as acetonitrile or DMF instead of surfactants gave rhombohedral crystal, 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 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) 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, NH4+, 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 on 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.

References

History

1861 The Department of Manufacturing Chemistry in the Institute for Research of Foreign Books established by the Tokugawa Shogunate. Re-established at Yosho Shirahesho, 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 Kenkyuukai (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 Ultrashort 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.

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