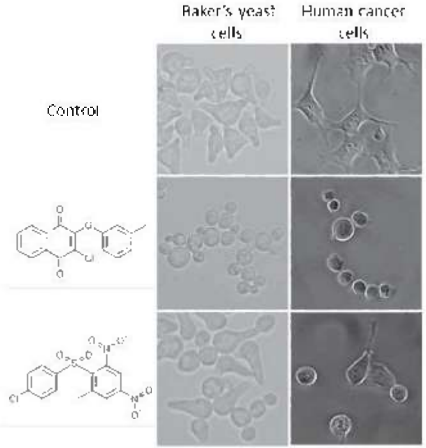
Genetic Engineering in Yeast and Human Cells

Our laboratory is unique in the world because we are studying both **baker's yeast** and **human cells** in the same way. Yeast is well known as a microorganism for bread making, alcohol fermentation, and recombinant protein production. It is also known as a model eukaryotic organism for molecular biological studies, allowing **advanced genetic analyses** for human genes. Equally, human culture cells isolated from cancer tissues are useful for medical research and also industrial protein production. Our research aims to develop simple gene manipulation methods in yeast and human cells. The various target genes include disease genes, hormones, enzymes, therapeutic peptides, and synthetic genes. Genetic engineering can create gene-manipulated yeast cells useful for understanding the cause of **human diseases** and for producing therapeutic proteins. Similarly, gene-manipulated human cells are used for industrial protein production and medical research. For the sake of advanced analysis, we made it possible to analyze genes in yeast cells and also in human cells. Genetic engineering methods that allow for freely transferring desired genes between yeast and human cells developed in our lab can solve clinical and social problems in human life.



Screening of drugs by genetically-engineered yeast and mammalian cells

About Researcher

AKADA Rinji, Ph.D.

Ph.D., 1988, Hiroshima University

WEB ≫ http://genetic.eng.yamaguchi-u.ac.jp/

Revealing Crystallisation Using in-situ Observations

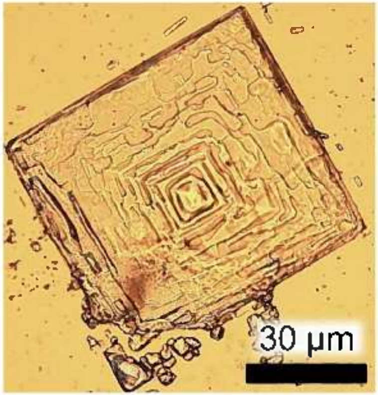
We study the **crystallisation of inorganic/organic crystals**, which are needed in industry, using an **in-situ observation/measurement method**. In particular, we focus on the crystallisation of carbonate crystals, zeolite crystals, polymer crystals and colloidal crystals. The details of these studies are described below.

1) Carbonate crystals: Because many types of carbonate crystals show poor solubility, they could to be used as containers for radioactive materials. To obtain large carbonate crystals, we investigate the growth kinetics of carbonate crystals grown from aqueous solutions.

2) Zeolite crystals: Zeolite crystals are a crucially important material for catalysts. We perform in-situ observations of the crystallisation of zeolite crystals under hydrothermal conditions. In this way, we can determine the fundamentals of crystallisation under hydrothermal conditions.

3) Polymer crystals: We are studying crystallisation from liquid crystal-like structures, which are thought to be the precursors of polymer crystals.

4) Colloidal crystals: Colloidal crystals are expected to be used as photonic crystals. We are searching for the proper conditions for recrystallisation to obtain large colloidal crystals.



A norsethite crystal $BaMg(CO_3)_2$ grown from an aqueous solution.

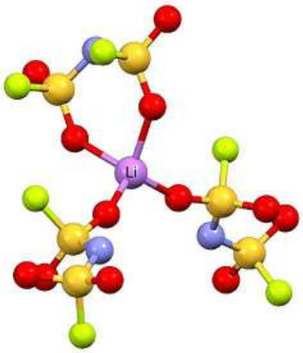
About Researcher

ASAKAWA Harutoshi,Dr.Eng.

Dr. Eng., 2012, Kyoto University

Electrolyte Solution Chemistry for Novel Electrochemical Devices

Our laboratory is exploring the thermodynamics and structure of electrolyte solutions and gel systems for electrochemical devices (e.g., Li and Mg batteries and capacitors). In the field of **solution chemistry, we research** solvation, intermolecular interaction, and the dynamics of solutes, especially metal ions in non-aqueous electrolyte solutions, ionic liquids and polymer gels at the molecular level. We focus on the following research subjects: (1) **Solvation** of metal ions in **electrolyte solutions** through the use of vibrational spectroscopy, X-ray/neutron scattering, and computer simulations; (2) Development of high-toughness **polymer gel electrolytes** with low polymer concentration and their application to electrochemical devices and carbon dioxide separation membranes; (3) The structural and thermodynamic properties of **room-temperature ionic liquids** and their metal ion solutions. We are also interested in soft matter science such as solvation, conformation, and phase transition in polymer solutions, as well as self-organizing aggregation (micelle and reverse micelle formation) in solutions with non-scale inhomogeneity.



Solvation structure of a lithium ion in an ionic liquid-based electrolyte for lithium-ion batteries

About Researcher

FUJII Kenta, Ph.D.

Ph.D., 2006, Kyushu University

WEB ▸ http://elechem.chem.yamaguchi-u.ac.jp/hp_sol/solchem/top.htm

High Performance Ceramics and Spectroscopy

Our research group develops high performance ceramics used in the fields of energy and medicine. We approach their development from a structural point of view through such methods as x-ray diffraction, solid state NMR, and Raman spectroscopy. Current research topics include (1) hydrogen energy, (2) bioceramics, and (3) perovskite compounds.

For (1), we promote the use of **hydrogen** to reduce carbon dioxide discharge. Fossil fuels are presently a primary source of hydrogen, and carbon dioxide is emitted in the process of producing this hydrogen. As a fuel for the future, water should replace fossil fuels as a fuel completely free of carbon dioxide emissions. There are three main activities we pursue to achieve this purpose: (a) We study photocatalytic activities, with particular attention to crystal structures, to develop high performance photocatalysts. (b) We perform experiments that assess the viability of solar radiation to synthesize photocatalysts while producing zero carbon emissions. (c) We evaluate the heat resistance of **ultra high-temperature** ceramics for the development of hydrogen turbines that can reach maximum temperatures of over 2000℃, something not easily achieved by normal furnaces.

For (2), we investigate calcium phosphates like **apatite**, which are used in tissue engineering, with a focus on the relation between biocompatibility and crystal structures. This involves the use of simulated body fluids and NMR.

For (3), we study synthesis and engage in **Rietveld analysis** of perovskite compounds, including sodium bismuth titanate, which is an environmentally-friendly lead-free ferroelectric.

Xenon arc image furnace. A simulated solar furnace capable of attaining maximum temperatures of over 3000℃

About Researcher

FUJIMORI Hirotaka, D.Sc.

D.Sc., 1997, Tokyo Institute of Technology

WEB ≫ http://www.cera.chem.yamaguchi-u.ac.jp/

Improvement and Evaluation of Micropous Crystals for Radioactive Waste Treatment Materials

GTS-type **microporous** titanosilicates have a three-dimensional tunnel structure. In this structure, four edge-sharing TiO_6 octahedra form a Ti_4O_4 cubic cluster. They are linked through SiO_4 tetrahedra, forming an interconnected framework with a three-dimensional pore system of 8-ring channels occupied by the alkali-metal ions and adsorbed water molecules. The crystal structures of Na-GTS ($Na_4[(TiO)_4(SiO_4)_3]\cdot 6H_2O$) and K-GTS ($K_3H[(TiO)_4(SiO_4)_3]\cdot 4H_2O$) show rhombohedral symmetry ($R3m$, $\alpha = 7.812$ Å, $\alpha = 88.79°$) and cubic symmetry ($P43m$, $\alpha = 7.764$ Å), respectively. We have thoroughly researched the ion-exchange properties of **GTS** for Cs^+ or divalent ions (Co^{2+}, Sr^{2+}, etc.) for application to radioactive waste treatments. However, the ion-exchange properties for trivalent ions have not yet been reported in GTS, although their optical and catalytic properties are interesting. In this study, we researched lanthanide **ion-exchanged** forms of GTS.

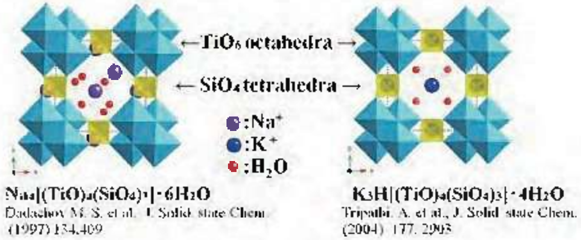


Fig.1 A polyhedral representation of the crystal structure of $Na_4[(TiO)_4(SiO_4)_3]\cdot 6H_2O$ and $K_3H[(TiO)_4(SiO_4)_3]\cdot 4H_2O$

About Researcher

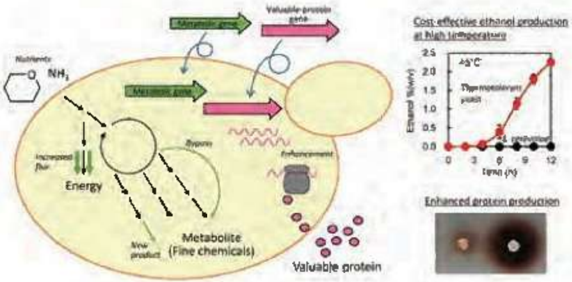
FUJIWARA Keiko, BPharm.

BPharm., 1979, Daiichi University of Pharmacy

WEB ≫ http://seigyo.amse.yamaguchi-u.ac.jp/

Genetic Engineering of Yeast Cells to Produce Valuable Substances

Cells synthesize various kinds of substances from simple nutrients. In other words, cells can be compared to a living factory. Some of these substances can be used for industrial and medical purposes. For practical use, although it should be possible to efficiently produce these substances in large quantities, it is often difficult to produce sufficient quantities of these valuable substances. **Genetic engineering** seeks to design cells for practical biological substance production. I am currently interested in creating yeast cells to produce energy, fine chemicals and valuable proteins by combining genetic engineering and traditional techniques. **Metabolic engineering and synthetic biology** are approaches in order to produce energy and fine chemicals. Traditional breeding is also effective. Protein synthesis is specific and unique ability for the cells. It is natural function, and therefore theoretically seems easy. However, **recombinant protein production** is a big challenge in practice. Transcription, translation, quality control, intracellular traffic, and protein modifications are targets to enhance protein production. Efficient, convenient, simple and systematic methods for genetic manipulations are also being developed.



Metabolic engineering and recombinant protein production using yeasts for industrial and medical applications

About Researcher

HOSHIDA Hisashi, Ph.D.

Ph.D., 1998, Kyoto University

Development of Green and Sustainable Science and Technology Using Organic Chemistry

Synthetic organic chemistry has unlimited potential. This potential includes creating unprecedented molecules that are expected to play a key role in the scientific and technological innovations modern society desires. This is the power of organic synthesis. It not only covers synthesis of novel molecules, but also presents innovative solutions and concepts regarding environmental problems. The wide range of applications of organic synthesis provides lateral approaches to green and **sustainable technology**, in addition to the invention of novel molecules. Our research achievements in synthetic organic chemistry include novel **syntheses of bioactive molecules**, such as Tamiflu. We also have proposed new earth-conscious methodologies for the chemical conversion of plastics and biomasses using ionic liquids and supercritical fluids, which will make an important contribution toward global sustainable development. In the course of our research, we have collaborated with a number of scientists around the world, and have established good international relationships in the communities of various research fields. We are always working hard to advance our research in organic chemistry to find and create innovative molecules and chemical methodologies.

We have developed 2-sulfanylhydroquinone dimer,
a new fluorescent dye being turned on and off by chemical reaction.

About Researcher

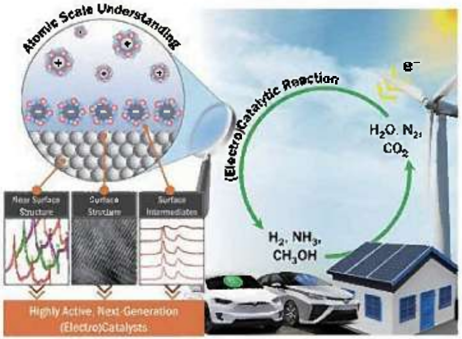
KAMIMURA Akio, Ph.D.

Ph.D., 1987, Kyoto University

WEB ⇒ http://perkin.chem.yamaguchi-u.ac.jp/

Probing Reaction Dynamics on (Electro)catalyst Surfaces

(Electro)catalysis provides exciting opportunities to address some of the impending global changes of the 21st century, ranging from energy and the environment to food and chemical production. Noble metal-based catalysts are the gold standard for catalytic processes at the heart of electrochemical energy storage and conversion devices (for example in the oxygen evolution reaction in water electrolyzers and oxygen reduction reaction in fuel cells). While highly active and state-of-the-art, their high cost and scarcity necessitates the development of alternative (electro)catalysts. The unique catalytic activity of metal/-metal oxide stems from its distinctive electronic structure, which can be tuned to facilitate numerous (electro)catalytic process on the surface, including adsorption, conversion, and desorption of reactant and product molecules in aqueous media. Although electrocatalytic activity has been improved by tuning the electronic structure of the electrode materials, there has been little focus on engineering the **electrode/electrolyte interface**. Furthermore, little is known about molecular processes and interactions that govern reaction activity, stability, and selectivity, limiting the design of new functional electrode/electrolyte interfaces. Therefore, there are immense opportunities for fundamental research into electrode/electrolyte interfaces to identify governing parameters that dictate the complex interactions at interfaces. Our group aims to connect the understanding of **surface reaction mechanisms** obtained by **in situ spectroscopic techniques** to the activity and stability of the catalysts, as well as to establish novel design principles for designing electrode/electrolyte interfaces.



Surface (electro)catalytic processes are explored using in situ spectroscopic techniques in order to establish a catalyst design strategy, enabling radical innovation for energy storage/conversion devices

About Researcher

KATAYAMA Yu, Ph.D.

Ph.D., 2017, Kyoto University

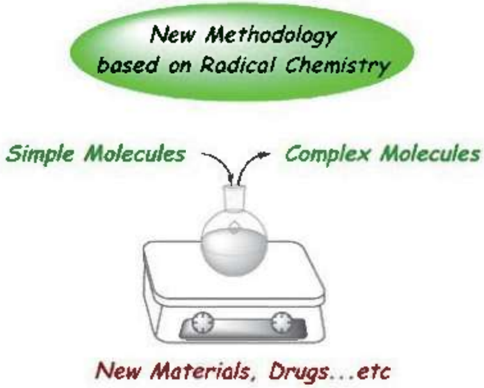
WEB Search ≫ Tsutsumi lab Yamaguchi

New Methodology Based on Radical Chemistry

Our research interest is in discovering **new methodologies** based on **radical chemistry**. Radical reactions are one of the most useful tools in organic synthesis, particularly for the formation of carbon-carbon bonds in intra- and intermolecular processes. Radical reactions do not require harsh conditions, and are thus well-suited to the synthesis of complex molecules such as materials and drugs. Research now underway in our group is focused on unique radical reactions, namely the following five topics:

1) Construction of carbon-carbon bonds via cascade reactions
2) Cleavage of carbon-carbon bonds and reconstruction of carbon-carbon bonds
3) Synthesis of organoboron compounds
4) Utilization of carbon dioxide for organic synthesis
5) Photo-induced electron transfer reactions

We are also interested in the development of **green synthetic reactions** without using ordinary organic solvents.



Our research concept

About Researcher

KAWAMOTO Takuji, Ph.D.

Ph.D., 2014, Osaka Prefecture University

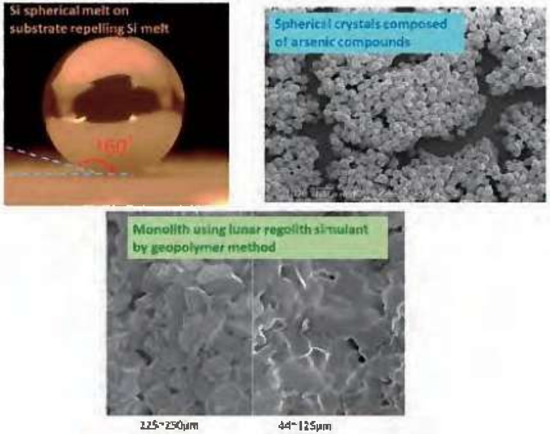
WEB ≫ http://perkin.chem.yamaguchi-u.ac.jp/en/

Development of New Effective, Low-Cost Methods for Crystal Growth

The formation of crystals plays a central role in the fields of materials science, metallurgy, geology, industrial technology, and life sciences. Understanding the nucleation and further growth of crystals is therefore a highly relevant issue.
We have been conducting research aimed at developing a new effective, low-cost crystal formation process based on the growth behavior of the crystal. Research now underway in our laboratory is focused on the following three fields:

1) Development of new crucible material repelling Si melt (Fig.1 indicating 160° contact angle between the Si melt and the crucible);
2) Development of new arsenic compound with hardly water-soluble (Fig.2);
3) Development of new preparing method of lunar base using lunar regolith (Fig.3)

Although these research fields are remarkably wide —spanning environmental problems to space exploration, as well as a solar Si crystal wafers—we contribute to the development of these fields through a study of the crystal growth.



Recent research results

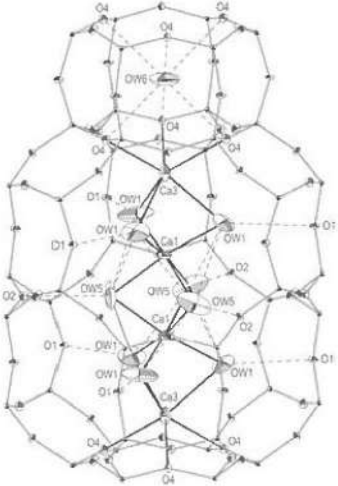
About Researcher

KOMATSU Ryuichi, Dr.Eng.

Dr.Eng., 1996, Tohoku University

Crystal Chemistry of Functional Inorganic Materials

Our research interest is in **crystallography and crystal chemistry** of **functional inorganic materials** such as garnet-, perovskite-, spinel-type compounds and microporous materials (e.g., zeolites). The macroscopic properties of these materials are closely related to their microscopic structural properties, including the atomic arrangements and atomic thermal vibrations. From this viewpoint, we aim to elucidate the relationship between physical properties and crystal structures of these compounds using **precise structure analysis** based on a **single crystal X-ray diffraction** technique.
As an example, a portion of the crystal structure of chabazite, a natural zeolite with strong potential for use as a heat absorbant, is shown in the figure. We determined the crystallographic configurations of water molecules and exchangeable cations in the structural cavities, which had been unclear. On the basis of this result, we examined hydrogen bonding and other such interactions between water molecules and their adjacent atoms, and elucidated the relationship between the interatomic interactions and the heat-exchange capability of chabazite.



Crystallographic configurations of water molecules (OW) and exchangeable cations (Ca)

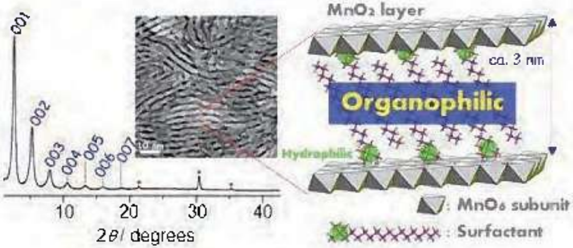
About Researcher

NAKATSUKA Akihiko, Ph.D.

Ph.D., 1997, Osaka University

Design of Electrode Materials for Energy and Environmental Applications

We are involved in research and education relating to energy and environmental science, the specific topics of which are: (1) electrosynthesis of metal oxides for electrode materials, (2) development of next-generation energy devices (e.g., **supercapacitors**), (3) recovery of rare resources and removal of pollutants from the aqueous phase, and (4) recycling of waste silicon. We work to identify issues that might be interesting and address them by means of various approaches, where the approaches should be energetically favorable and environmentally-friendly. The products of our research should also contribute to the supply and storage of clean energy. The latest research focuses on the **electrochemical synthesis** of layered inorganic/organic nanohybrid materials in a thin film form and their applications in charge-storage, sorption, and electroanalysis. Our newly developed layered manganese oxide sandwiched with cationic surfactants, which we named "**organo-manganese oxide**", can selectively and effectively capture iodide anions from seawater into its interlayer space. The anions accommodated between manganese oxide layers can be desorbed by applying an external electric field without using any reagents, and the interlayer restored to the original state.



Organo-manganese oxide fabricated by an electrochemical route

About Researcher

NAKAYAMA Masaharu, Ph.D.

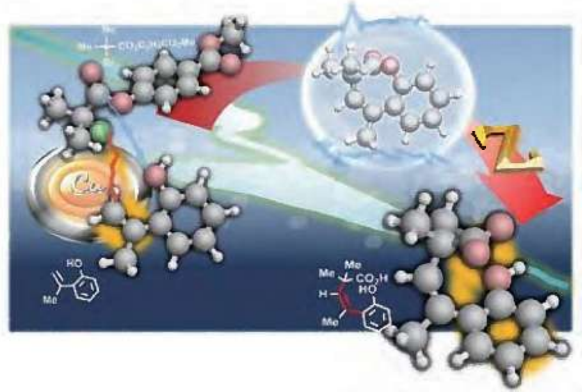
Ph.D., 1998, Yamaguchi University

WEB ≫ http://web.cc.yamaguchi-u.ac.jp/~nkymm/web/en/index.html

The Development of Efficient Transition Metal-Catalyzed Olefin Transformations

The discovery of new organic reactions is one of the most important areas of research in the formation of carbon-carbon and carbon-heteroatom bonds. New organic reactions enable the efficient synthesis of complex molecules, including useful bio-active compounds and materials. The discovery of such ideal reactions would shorten the synthetic protocols, reduce the costs of useful molecule syntheses, and realize an environmentally benign process. To accomplish the above, we have focused on the following research: 1) designing **new transition metal complexes** for a catalyst; 2) designing a **new catalytic reaction** for an efficient molecule transformation; and 3) synthesizing useful molecules using our reactions.

Our current interest is focused on the development of **new transformations of olefins** in the presence of a copper catalyst, including tertiary-alkylations and Z-olefinations, as well as the accurate synthesis of cyclic compounds. A key to success here is controlling "reactive intermediates" using designed catalysts.



We recently published this reaction image in an international journal. It depicts a Z-alkylation reaction, in which a copper catalyst (Cu) connects two different molecules in the Z-direction through the controlled reactive intermediate, shown in the bubble.

About Researcher

NISHIKATA Takashi, Ph.D.

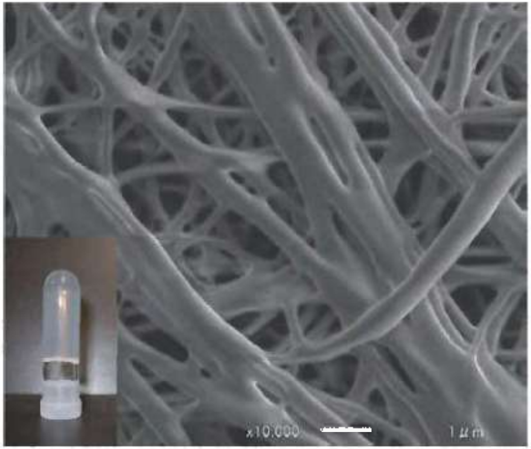
Ph.D., 2005, Hokkaido University

Synthesis and Development of Advanced Organic Materials

Our research interests lie in **advanced organic materials** and related fields including liquid crystalline materials and organogels with a low molecular weight compound. They are used in electrochemical devices such as display devices, batteries, and capacitors. Research now underway in my laboratory is focused on the following five fields:

1) Synthesis of **low molecular weight organic gelators** and their application;
2) Synthesis of **liquid crystal materials** and their application;
3) Development of organogel electrolytes with high ionic conductivity;
4) Application of ionic liquid gels in electrochemical and environmental materials;
5) Investigation of molecular arrangements of liquid crystal materials using a polarized microscope, differential scanning calorimetry, and a small-angle X ray diffraction;

We have also researched the development of organogel electrolytes with high ionic conductivity using a new approach: adding a small amount of aprotic organic gelators to organic electrolytes.



The appearance of an organogel composed of a novel low molecular mass organic gelator and an SEM image of its xerogel

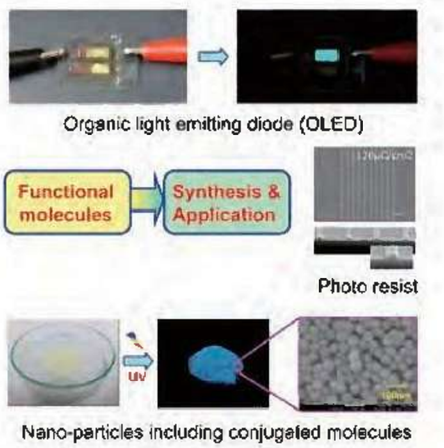
About Researcher

OKAMOTO Hiroaki, Ph.D.

Ph.D., 1995, Kyushu University

Materials for Organic Optical and Electronic Devices

Our group focuses on a variety of research projects in organic chemistry, organic semiconductors, **organic electronic devices**, **nano materials** and photoresist resins. We are interested in the development of materials for organic optical and electronic devices such as organic light emitting diodes (OLED), organic photovoltaic (OPV) cells, photoluminescent materials and nanoparticles. In order to realize such materials and devices, a set of basic technologies must be established:
(1) Create **conjugated molecules** with the desired molecular structure for organic electronic devices, (2) Develop organic electronic devices using the conjugated molecules with the desired optical and electronic properties, (3) Establish the fundamentals and applications of electrochromic devices using organic conjugated molecules, and (4) Synthesize nanoparticles, which includes conjugated molecules and their application. In addition, we are collaborating with a number of corporate partners in the research and development of new electronic devices and nanotechnologies.



Functional materials for photonic and electronic devices

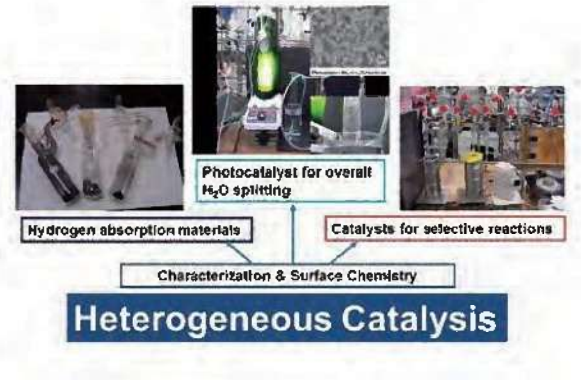
About Researcher

ONIMURA Kenjiro, Ph.D.

Ph.D., 1993, Kyushu University

Heterogeneous Catalysis, Surface Chemistry to Application

Our research subject is **the fundamental knowledge and application of heterogeneous catalysis**. Regarding fundamental knowledge, **the characterization of surface state and surface chemistry** over solid catalysts is performed by applying spectroscopic techniques. Research into the development of solid catalysts and related materials is also carried out. This includes the **development of solid catalysts** for selective reactions, efficient photocatalysts for overall H_2O splitting, and hydrogen absorption materials for hydrogen storage by utilizing the conceptions of catalyst preparation. Recent research targets are as follows: (1) Preparation and characterization of supported binary metal catalysts by electron microscopy and infrared spectroscopy, (2) Elucidation of reaction over the surfaces of oxide catalysts by infrared spectroscopy, (3) Development of new catalyst systems for selective reduction of carboxylic acids to aldehydes, selective hydrogenolysis of esters to aldehydes and alcohol, and selective dehydrogenation of alcohol to aldehydes or ketons, (4) Development of efficient photocatalysts and photocatalytic systems for artificial photosynthesis, including overall H_2O splitting, (5) Development of hydrogen absorption materials by utilizing mechanical alloying.



Our research subjects (heterogeneous catalysis and related fields)

About Researcher

SAKATA Yoshihisa, D.Sc.

D.Sc., 1990, Tokyo Institute of Technology

Intersection of Polymer Chemistry and Electrochemistry

Our research interest is in **functional polymer chemistry** and related fields where a polymeric material is used in electrochemical devices such as batteries, capacitors, and medical or biochemical devices. Research now underway in our laboratory is focused on the following five fields:
1) Development of polymer electrolytes with high ionic conductivity; 2) application of nano or micrometer electrospun fibers in electrochemical and biomedical devices; 3) preparation of organic-inorganic (especially hydroxyapatite) composites and their application; 4) preparation of melt-electrospun sulfur fibers and their application; and 5) application of enzyme-modified electrodes for biosensors. We have researched the development of **polymer electrolytes** with high ionic conductivity using two approaches: adding functional conducting enhancers to polymer electrolyte matrixes and introducing new matrixes based on poly (oxetane) with a low glass temperature. We are also interested in an **electrospinning technique** for the preparation of nano or micrometer fibers using simple equipment.

Our research concept and related devices

About Researcher

TSUTSUMI Hiromori, Ph.D.

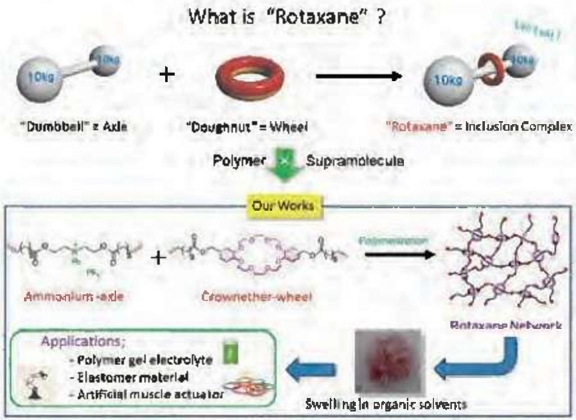
Ph.D., 1988, Osaka University

WEB ≫ http://ds0n.cc.yamaguchi-u.ac.jp/~tsutsulb/index_Eng.html

A Unique Inclusion Polymer — Collaboration Between Polymer Chemistry and Supramolecular Chemistry

We research the synthesis of and applications for functional inclusion materials. An "**inclusion complex**" consists of two key components: macrocyclic (wheel) and linear (axle) moleculars. The wheel has a specific environment, and selectively incorporates various axle molecules in a cavity through "guest-host interaction" such as hydrophobic interaction, charge transfer interaction, and hydrogen bonding.

However, inclusion complexes consisting of two components exhibit instability with respect to pH, pressure, temperature, and solvent quality. These external stimuli force the complex into disassociation. Inclusion complexes are stabilized by attaching bulky molecules called stoppers. The resulting structure, known as "rotaxane", has a unique shape wherein a "dumbbell" axle penetrates into a "doughnut" ring. Recently, "**three-dimensional rotaxane network polymer**" was successfully developed through the polymerization of an inclusion complex consisting of secondary ammonium salt and a crown ether compound. The rotaxane network has a strong affinity to organic solvents and is highly flexible as a result of the characteristic movement of crosslinking points (the Ring-moving Effect). The material shows promise in applications for polymer gel electrolytes, elastomers, and artificial muscle actuators.



Our research

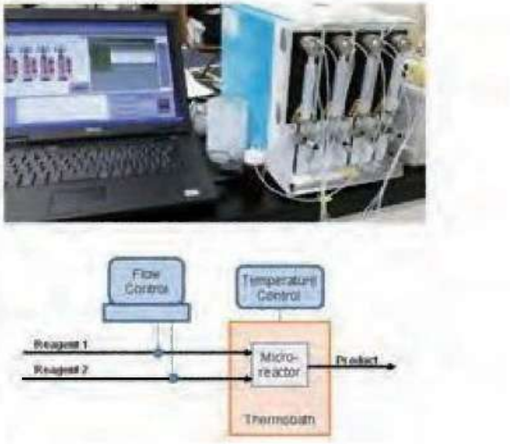
About Researcher

YAMABUKI Kazuhiro, Ph.D.

Ph.D., 2008, Yamaguchi University

Development of Continuous Flow Chemistry using a Microreactor

The traditional method for solution-phase synthesis is to mix several compounds in a flask or reactor and to stir this mixture while the container is cooled or heated. After the lapse of a certain length of time this process is stopped and the product can be isolated from the mixture. Recently, the **microreactor** (MR) has been regarded as a new device in organic synthesis. It is well known that reactions in an MR proceed with good efficiency in reactant mixing and thermal conduction, allowing for the easy control of the MR's reaction conditions. However, there have only been a few **kinetic studies** done on chemical reactions using MR. We suppose that experimental results based on MR under controlled conditions—which includes solvent effects as well as temperature and pressure—will be close to those of theoretical calculations. We are planning to calculate activation free energy for reactions in other solvents and use those values to determine the MR's reaction conditions.



Microreactor set

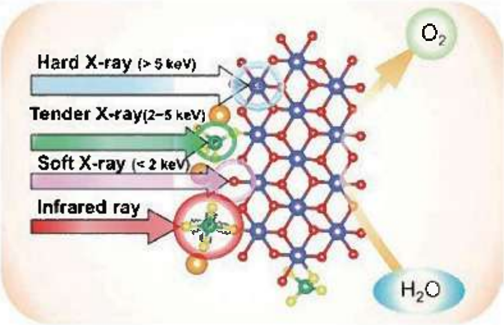
About Researcher

IWAI Shiho, M.Sc.

M.Sc., 2000, Yamaguchi University

Operando Observation for Water Splitting Catalysis

Recently, hydrogen production by electrochemical water splitting has been receiving a lot of attention with regard to achieving a sustainable society. For commercial applications, improving overall water splitting efficiency has been required for the development of highly active oxygen evolution electrocatalysts. However, we have not yet obtained enough detailed information about the oxygen evolution reaction. In this situation, we have developed a number of **operando observation techniques** for X-ray absorption spectroscopy (XAS) and infrared absorption spectroscopy using attenuated total reflection mode (ATR-IR) to observe the oxygen evolution electrocatalysts. For example, hard X-ray XAS can observe the electronic states and local structures of metal species in the catalysts. On the other hand, tender and soft X-ray XAS and ATR-IR can reveal the chemical states of light elements in the catalysts. Therefore, we are focusing on the investigation of the **reaction mechanism** for water splitting catalysis using various kinds of operando XAS and ATR-IR spectroscopy, and are planning to develop **highly efficient water splitting electrocatalysts** on the basis of the knowledge we have obtained from these operando spectroscopic techniques.



Schematic model of operando observation for water splitting catalysis using X-ray and infrared spectroscopy

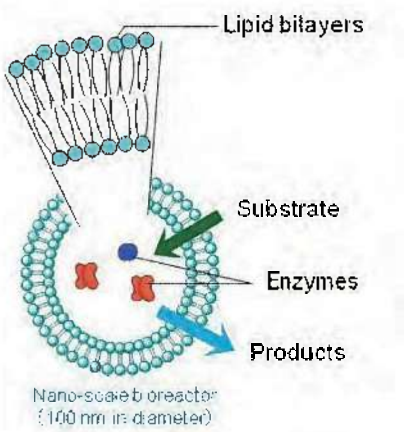
About Researcher

YOSHIDA Masaaki, Ph. D.

Ph. D., 2010, The University of Tokyo

Enzymatic Reactions in Liposomes and Bioreactors

Biocatalysts are applicable to developing biomedical sensors, diagnostic tools and environmentally benign processes. In living cells, a number of chemical reactions are controlled through the interactions with biomembranes. One of our research interests involves the fabrication of cell-mimicking reaction systems using phospholipid vesicles (**liposomes**). Liposomes offer ultrafine aqueous droplets where biomolecules including enzymes can be stably solubilized or compartmentalized. The enzyme-containing liposomes are useful for kinetically controlling enzymatic reactions on the basis of the mass transfer characteristics of lipid bilayers and for stabilizing the conformation and biological activity of enzymes. We are also interested in the emerging functions of biocatalysts induced by hydrodynamic properties such as liquid shear stress. In this regard, we examine the shear-triggered structural changes in liposomes and the catalytic performance of liposomal enzymes suspended in **gas-liquid contacting reactors** such as bubble columns. Our approach should prove useful for controlling enzymatic reactions for various biochemical and biomedical applications at multiple scales.



Liposome-based nano-scale bioreactors for controlled enzymatic reactions

About Researcher

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Chromatographic Purification of Biomolecules

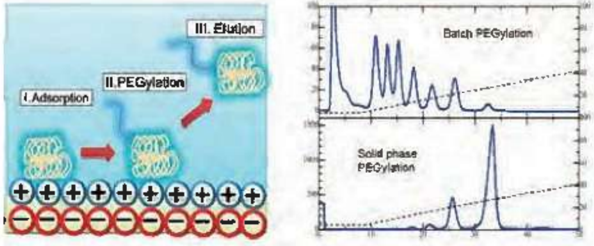
Our group has developed a chromatographic separation process for biopharmaceuticals such as antibodies and polymer-functionalized proteins, DNA, and virus-like particles. Our efforts are now mainly devoted to the following two topics:

1) PEGylated protein isoform separation processes

Protein PEGylation is a promising technique in the development of generic protein drugs. However, the PEGylation reaction is difficult to control due to consecutive competitive reactions with activated PEG, as well as native and PEGylated proteins. PEGylation produces positional isoforms and isomers which have different PEG chain numbers. We analyze the **retention behavior of these isoforms** based on the stoichiometric displacement model and strive to acquire a mechanistic understanding of the interaction between PEGylated protein and chromatography resin.

2) Solid phase PEGylation on chromatographic media

Both PEGylation reaction and separation are simultaneously performed on the chromatography column, where protein distribution on solid surfaces is controlled via electrostatic interaction. Therefore, in solid phase PEGylation, isoform formation is controllable on the basis of ligand type and size, as well as the pore diameter of the particles used in the stationary phase.



PEGylation and separation in ion exchange chromatography

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