

Forefront Research Center

Overview

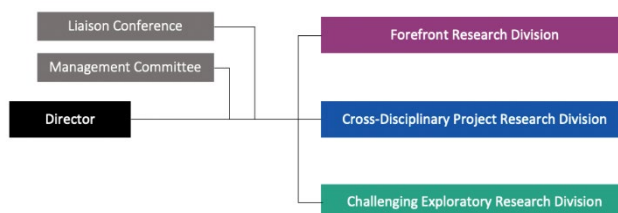
The Forefront Research Center (FRC), Graduate School of Science, Osaka University, was established on April 1, 2022, through a reorganization of the Project Research Center for Fundamental Sciences (PRC).

The PRC was established in October 2011 to carry out cutting-edge research projects led by faculty members of the Graduate School of Science. The aim was to promote intensive and dynamic research in cooperation with other academic fields. In the decade since its founding, the PRC has conducted 16 large-scale cross-disciplinary projects involving multiple departments and graduate schools. In addition, three joint industry–university research projects, which were previously rare for the Graduate School of Science, have been launched, thereby strengthening the ties between the university and the corporate world and opening the door to new possibilities for research. In 2015, we established the Challenging Exploratory Research Division with the aim of promoting challenging and emergent individual research, but only one specific theme was undertaken and sufficient results could not be obtained. In addition, there was insufficient support for obtaining large competitive grants and it was difficult to launch and complete new research projects involving multiple departments within the graduate school and across divisions within the university.

Therefore, to overcome this problem and promote cutting-edge research in the Graduate School of Science, the newly established FRC operates using a system in which several individual researchers are selected from each department and exempted from most non-research duties so they can devote themselves to research for about three years. In addition to achieving research results, we aim to develop new research areas, improve the level of research for the entire Graduate School of Science, and enhance the research reputation of Osaka University. Furthermore, research projects that contribute to cross-disciplinary research are selected based on proposals from outstanding project leaders and the FRC provides active support.

In this way, the FRC will promote the advancement of cutting-edge research and develop an environment to facilitate the highest level of original basic research.

Organization



Forefront Research Division

Advanced Mass Spectrometry Research Group

Cross-Disciplinary Project Research Division

Immune Regulation Project: Collaborative Research between NIBIOHN and Graduate School of Science, Osaka University

Molecular Basis of Cell Surface, Research Center for Lipids and Glycans in Biomembranes

Material Intelligence: Exploiting Intrinsic Learning and Optimization Capabilities for Intelligent Systems

Core for Collaborative Research: RIKEN and Graduate School of Science, Osaka University

Core for Medicine and Science Collaborative Research and Education (MS-CORE)

Theoretical Joint Research (TJR) Project

Project for sustainable polymer science

MS open innovation project in JEOL YOKOGUSHI Research Alliance Laboratories

Precise Multi-wavelength Space Observation Project

Development of isotope enrichment technology and its application to radiation detectors

Project [light x Mass Spectrometry]

Advanced Muon Science

Challenging Exploratory Research Division

Development of an accurate fIRST-principles calculation method on the basis of the wave-function theory

Development of ultra-fine mass spectrometry imaging by precise fluid control of pico-liquid

Project on establishing a research platform for environment friendly polymeric materials

Molecular Mechanism of Gross Chromosomal Rearrangement

Glycochemical biology Research Group

Home Page

<http://www.frc.sci.osaka-u.ac.jp/en/>

Advanced Mass Spectrometry Research Group

Research Themes

1. Development of the most advanced mass spectrometers
2. Interdisciplinary research using the developed mass spectrometers

The division aims at new interdisciplinary research beyond the framework of major disciplines, departments, or universities. The Graduate School of Science created Japan's first mass spectrometer apparatus in the latter half of the 1930s, and has continued since that time in developing a number of globally leading and original spectrometers. In particular, the multi-turn time-of-flight mass spectrometer (MULTUM) developed recently represents a compact apparatus that nonetheless is capable of an extremely high mass resolution. The MULTUM signifies an opportunity for on-site high-resolution mass spectrometry, previously an impossibility. Scientists across the globe look forward to tremendous advancements in this undeveloped domain.

The Division of Interdisciplinary Science develops compact, lightweight, original mass spectrometers and associated

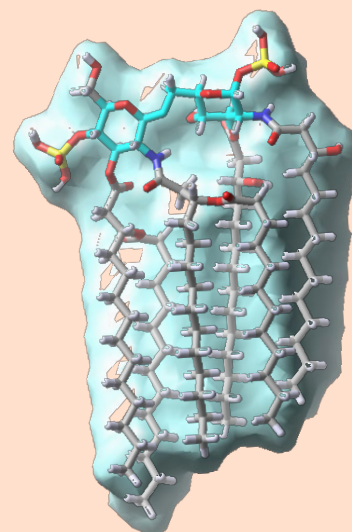
technologies for purposes of greenhouse gas monitoring, detection of hazardous or illegal substances, medical diagnostics, deployment to planetary probes, etc.; leads interdisciplinary research across different fields of research through collaborative efforts among division members, faculty members belonging to the Graduate School of Science, researchers at other departments or other universities, and industry; and aims to promote new scientific inquiry.



Immune Regulation Project: Collaborative Research between NIBIOHN and Graduate School of Science, Osaka University

In recent years, the field of chemical biology, which aims to elucidate biological phenomena at the molecular level using chemical methods, has become more and more important as the molecular basis of various biological phenomena has been unveiled. The National Institute of Biomedical Innovation, Health and Nutrition (NIBIOHN) and Graduate School of Science will promote the research on immune regulation based on chemical biology. The development of vaccines and adjuvants is becoming increasingly important. NIBIOHN has investigated to develop innovative pharmaceuticals including vaccines and adjuvants and to improve the health of the Japanese. Therefore, this collaborative project will promote joint research on drug development and improvement of public health, focusing on immune regulation research.

To achieve immune functional regulation at the molecular level, we will conduct the basic scientific research; chemical synthesis and immune functional analysis of bacterial glycoconjugates, functional analysis of host immunoreceptor proteins, development of novel immunomodulation technology using host-derived glycans. Furthermore, based on the molecular basis of immunoregulation, we will develop innovative non-toxic vaccine adjuvants, which will be applied to the development of vaccines for diseases with high social needs. Furthermore, this project is expected to contribute to society in areas related to health and disease, such as drug development.



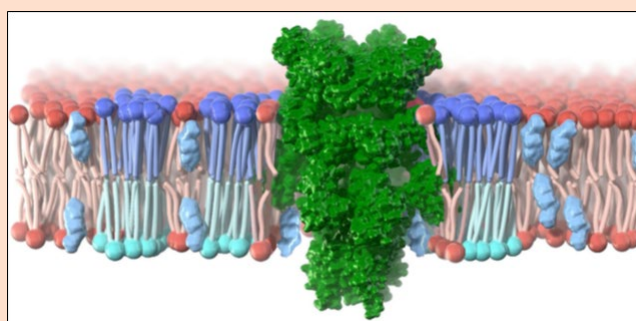
Molecular Basis of Cell Surface, Research Center for Lipids and Glycans in Biomembranes

Research Themes

1. Elucidation of lipid recognition mechanism by chemical approach
2. Structure-function relationships of lipid molecules in the quadruple layer of biological membranes including hydrated layer

Research on biomembranes has lagged behind that on membrane proteins, which has made remarkable progress in recent years, and the formation mechanism and role of domain structures (lipid rafts) caused by the localization of membrane lipids are not well understood. In order to solve this problem, it is desirable to create model membranes that functionally reproduce biological membranes. However, homogeneous artificial membranes of simple composition have not been able to reproduce the domain structure unique to biological membranes, which is localized and short-lived. In order to solve this problem, it is necessary to accurately understand the interactions between the outer and inner leaflets of biomembranes, which have different lipid compositions, and between them and the hydration layer.

In this project, we will reproduce the asymmetry of the outer and inner leaflets, the localization of phospholipids and glycolipids, and the molecular interactions at their interfaces, and compare them with those of biological membranes. By extracting the unique features of biomembranes and elucidating the molecular picture of lipids, we aim to understand biomembranes essentially.



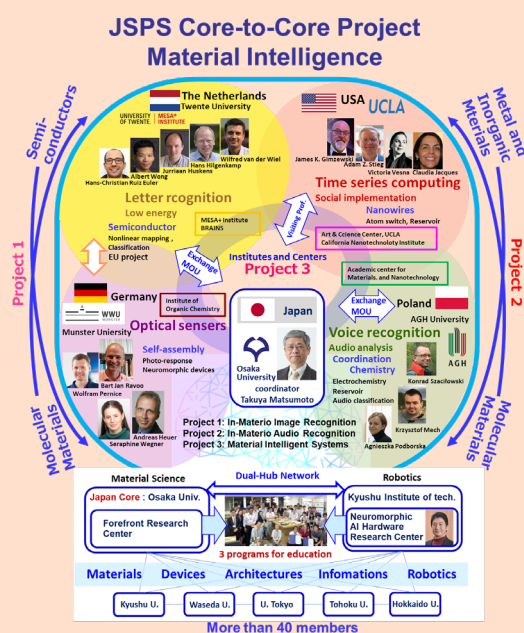
Material Intelligence: Exploiting Intrinsic Learning and Optimazation Capabilities for Intelligent Systems

Research Themes

1. Emergence of in-materio neuromorphic function.
2. Information processing using nanomaterials.

Based on precise physical property measurements made by the Graduate School of Science and Institute of Scientific and Industrial Research (SANKEN) at the atomic and molecular level, we are building a nanoscale network that has neural characteristics, including nonlinearity and hysteresis. In cooperation with the Department of Information and Physical Sciences of the Graduate School of Information Science and Technology, we are also mathematically analyzing the behavior of electrons and ions with the aim of collaborating with the Kyushu Institute of Technology to implement robots and other applications as perceptual arithmetic devices that can be useful to society

The Forefront Research Center will be run as the core of the international research base for the Japan Society for the Promotion of Science, which consists of dozens of researchers from the Netherlands, the USA, Germany, Poland, Italy and Japan.



Core for Collaborative Research: RIKEN and Graduate School of Science, Osaka University

Research Topics

1. Studies of host-guest interaction by means of nuclear magnetic resonance (NMR)
2. Studies of structural analyses as well as molecular dynamics of lipids, glycolipids, and glycoproteins by means of NMR

This project examines frontier scientific researches by combining both techniques accumulated in Riken and graduate school of science, Osaka University. Riken has developed a huge frontier NMR facility in Yokohama and elucidated many protein structures. These results have been applied not only to the elucidation of protein functions but also to basic researches. In addition to these NMR methods have contributed to the development of pharmaceutical drugs. Researchers in graduate school of science, Osaka University have demonstrated isolation, chemical syntheses and structural analyses of valuable natural molecules and novel functional derivatives, e.g. specific binding experiments between novel macromolecular gels

modified with unique host and guest molecules, syntheses of glycolipids concerned with our immune system, antibiotics interacting with cell lipid bilayer and glycoproteins. The collaboration of Riken's NMR techniques and chemical approaches by graduate school of science, Osaka University will open up a new avenue to elucidate the functions and molecular dynamics of natural and new functional compounds in detail.

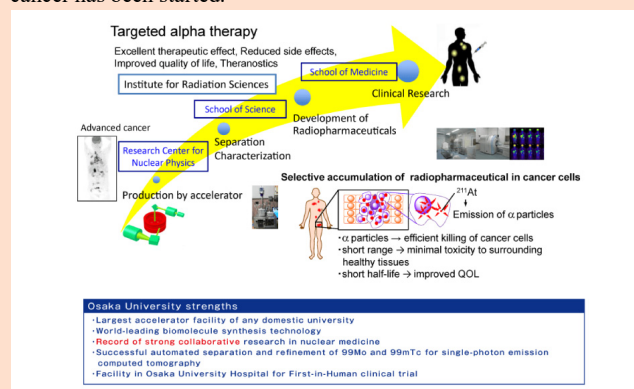


Core for Medicine and Science Collaborative Research and Education (MS-CORE)

Cooperation among the Core for Medicine and Science Collaborative Research and Education (MS-core), the Institute of Radiation Sciences, the Research Center for Nuclear Physics, the Graduate School of Medicine, and the Radioisotope Research Center has now led to a joint engagement in the development of a new targeted α -particle radiotherapy for treatment of intractable cancer, the development of the high-temperature superconducting Skeleton Cyclotron with high beam strength and reduced power consumption, and methods for producing alpha-emitting radionuclide in quantity and the automatic separation of generated nuclides. Further engagements will include the production of radiopharmaceutical candidates by bonding radionuclides with cancer-targeted agents and investigating the resulting therapeutic efficacy and side effects in order to determine the potential for clinical trials and treatments involving targeted α -particle radiotherapy.

In an effort centered at the Medicine-science-nuclear physics Collaboration Center Anteroom located in the MS-core, "Formation of International Therapeutic Core for Intractable Cancer Therapy by Medicine and Science Collaboration" has achieved good progress.

Osaka University established the Institute for Radiation Sciences to promote unique radiation-related research and education such as new medical innovations in 2018. MS-core has collaborated with the Institute for Radiation Sciences to promote the interdisciplinary researches, such as targeted α -particle radiotherapy, between nuclear physics, nuclear chemistry, biomolecular chemistry, nuclear medicine, and radiology. In fiscal year 2021, an investigator-initiated clinical trial for targeted α -particle radiotherapy targeting thyroid cancer has been started.



Theoretical Joint Research Project (TJR)

Gather theoretical researchers, Nurture new joint research.

The purpose of this project is to break through the current state of modern science, which has become fragmented, and to improve the openness of the theoretical sciences in the Faculty of Science so that new research directions can be found. We will create a place where researchers and students of theoretical sciences from Osaka University and outside the university can interact by holding cross-disciplinary talks and seminars. We will explore new paradigms through pioneering research that transcends hierarchies in nature and existing fields from the perspective of theoretical science.

We also host the "*Nambu Colloquium*," named after the Nobel Prize winner in Physics, Dr. Yoichiro Nambu (Distinguished Professor, Osaka University).

Outlook for the Future -- Fostering new scientific joint research

The TJR will provide a place for researchers to gather and nurture the seeds of new science at Osaka University. We will continue to host the Nambu Colloquium, as well as topical meetings of each research branch. We will employ and maximize the merit of the collaborative agreement for joint research with RIKEN iTHEMS, and create a place where researchers from in and out of Osaka University will gather. We aim to develop this project so that Osaka University, where Yoichiro Nambu and Hideki Yukawa used to work, will become a melting pot of science.

Theoretical Joint Research Project

Nambu Colloquium

Early Universe, Higgs, Baryogenesis

Atomic Nucleus, Quarks, Nucleosynthesis

Mathematical Structure of Gauge Theory, Gravity, and String Theory

Plasma x Astrophysics

Electron Correlation, Superconductivity, Topological Matter

Theory of Universal Biology

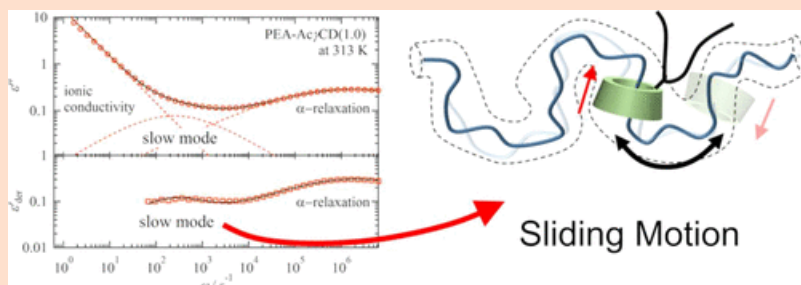
Deep Learning, Universe, Life, Computation

Project for Sustainable Polymer Science

Research Themes

1. Creation of functional polymer materials using bio-based materials.
2. Development of planar cell scaffolds that exhibit elastic modulus changes using stimuli-responsive polymeric materials.
3. Physical analysis of supramolecular cross-network materials by reversible and mobile cross-linking.

Development of new sustainable polymer materials: Nowadays, polymers, such as plastics, are combined with organic, inorganic, and biological materials, as well as metals. They are implemented in society in various aspects and consumed in large quantities. However, these polymer materials sometimes cause various environmental issues. Therefore, novel polymer materials are needed, as discussed in International Chemical Summit in 2019. In this project, researchers with various background of polymer science work together. We aim to advance the basic science of polymers and contribute to construction of a sustainable and resource-recycling society through the development of new sustainable polymer materials.



Sliding motion of mobile cross-links understood from polymer science

MS open innovation project in JEOL YOKOGUSHI Research Alliance Laboratories

This project was launched as an MS open innovation joint research laboratory in April 2017. Then it was integrated / reorganized with other joint research projects in April 2018 that were underway between Osaka University and JEOL as a project of the JEOL YOKOGUSHI Research Alliance Laboratories. In addition to mass spectrometry-related research, we are working with the mission of developing new application and instrumental fields in collaboration with JEOL's core technologies such as electron microscopy and nuclear magnetic resonance.

Missions

1. Promotion of technological development and applied research related to mass spectrometry
2. Promotion of science education
3. Joint business / cooperation with external organizations / companies

In this project, we have three missions, as described above. As the first mission, we are developing on-site diagnostic equipment and analytical methods for periodontal disease as a research and development theme.

Currently, we are developing an analytical method that can be analyzed in a shorter time, and at the same time, developing metabolite analysis technology to know the underlying pathological condition. We are also developing new high-sensitive soft-ionization technology, cell detection / identification technology, and method.

As the second mission, we are carrying out activities with the promotion of science education, accepting trainees and short-term international students from overseas, and conducting practical training using mass spectrometers. In addition, we cooperate with events for high school students in the Kansai area, and conduct observation and analysis using an electron microscope as experiential learning at the university.

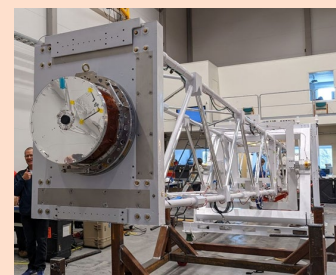
The third mission is to promote joint business and cooperation with external organizations and companies. As an example, we regularly hold the "Wai-Gaya Kai" as a place for researchers and engineers involved in mass spectrometry to discuss topics that are rarely discussed at academic societies. In 2021FY, it was held 12 times as a WEB event.

Precise Multi-wavelength Space Observation Project

We are aiming to develop observational instruments by using state-of-the-art technologies and to operate them for actual observations by ourselves. For cosmic X-ray observation, we are developing a new X-ray CCD camera for the next X-ray satellite XRISM. We are also developing a new type of high-angular resolution X-ray imaging instrument which utilizes the Talbot effect. We participate in the FORCE project and the XL-Calibur project. Both of them are international projects and we are developing X-ray telescopes for them. Main targets of FORCE and XL-Calibur are black holes and neutron stars, and the growth mechanism of massive black holes and physics in ultra-strong magnetic fields of neutron stars are expected to be clarified.

In the field of infrared astronomy, we are leading the PRIME project. This project is an international collaboration between Osaka University, JAXA, NASA, University of Maryland, South African Astronomical Observatory, and so on. We are constructing a new 1.8-m wide-field telescope with a large-area near-infrared camera in the Republic of South Africa, and we will search for exoplanets in the near-infrared band by observing gravitational microlensing

phenomena. We also participate in the MOA project, which is another exoplanet search project using a wide-field 1.8m telescope in New Zealand. We are also leading the Japanese contribution to the Nancy Grace Roman Space Telescope project of NASA. This project will pursue to investigate the structure of the universe including the dark energy and dark matter, formation histories of galaxies, stars, and exoplanets.



XL-Calibur project

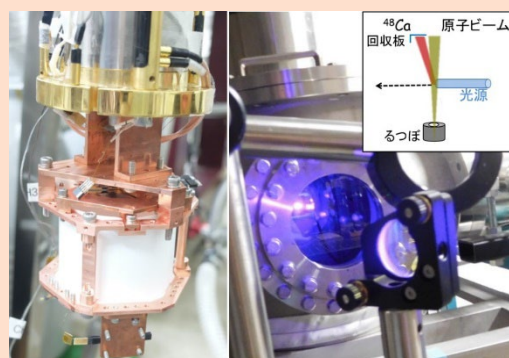
Development of isotope enrichment technology and its application to radiation detectors

Research Themes

1. Development of isotope enrichment technology
2. Application to ultra-sensitive radiation detectors for rare event measurement

We have been developing isotope enrichment methods based on laser enrichment and electrophoresis, and have successfully verified the principle of enrichment techniques for specific isotopes (^{48}Ca and ^6Li) based on our research. The design of the next generation enrichment system, which will realize large volume isotope enrichment, is under study with the aim of practical application. We are aiming to increase the natural abundance of ^{48}Ca isotopes (0.19%), to more than 50% by laser enrichment method, and to establish mass production technology by developing a high-power laser in collaboration with researchers from different fields (nuclear engineering and optical engineering). We are also trying to fabricate high-purity scintillator crystals. An extremely low background environment is essential for rare event searches, and we are developing an ultra-high purity (<10 nano-Bq/g) crystal with extremely low radioactive impurities.

To dramatically improve the energy resolution of radiation detector, we are developing a bolometric detector that operates in a cryogenic temperature (~ 10 mK). The essential development is high sensitive phonon detections using various types of superconducting sensors. Although these sensors have been used in radiation detectors for only very limited purposes, the sensitivity of various types of detection can be dramatically improved if the signal readout technology can be generalized and used in radiation detectors for a wider range of research tasks.

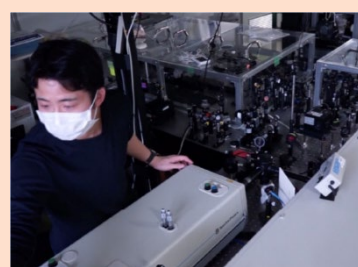


Project [light x Mass Spectrometry]

Osaka University has the only university-based mass spectrometry equipment development base in FRC. In the 21st century, the forefront of optical science has made great strides, but has not yet realized the potential of mass spectrometry. In this project, we will develop the forefront of analytical science by crossing and fusing both fields. Interdisciplinary and fusion of fields is a difficult task now since the specialization of research in each field has advanced to a high degree. In addition to accumulating dialogues between research groups, we will take on the challenge of creating a place for the creation of new research platforms through various attempts such as discovering and encouraging the small research and development based on free ideas that are not bound by the frame.

The following actions are planned with the aim of creating a model for the cross-sectional research platform. (1) Introduce a membership system and form a network. Utilizing the science caravan, we will expand the members in an event-driven manner. (2) Secure a room as a base (cradle) for exchanges and research design activities that ensure psychological safety.

- (3) Set up a core research project: At PRC, fusion research of super-resolution fluorescence imaging and mass imaging has already been started to develop. Furthermore, we will consider the introduction of advanced research such as phase-controlled coherent Raman spectroscopic imaging into the field of mass spectrometry. (4) Develop a system using a spectroscopic system such as a femtosecond laser transferred from VBL and a self-made mass spectrometer, and launch sprouting research subprojects. Involve undergraduate students in these sub-projects. (5) By participating in public engagement such as Science Festa, we aim to bring about a positive cycle in which researchers grow and play an active role, and their appearance attracts the next generation.



Advanced Muon Science

Research Themes

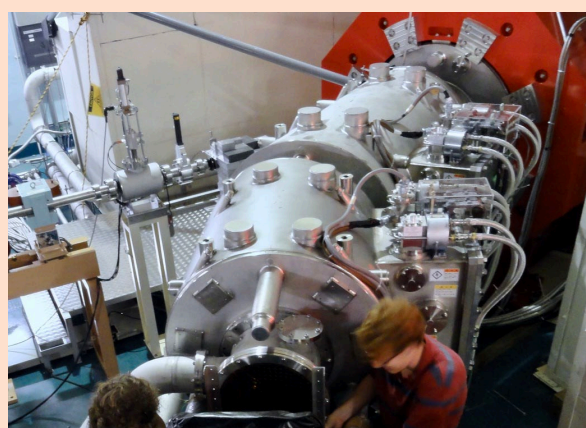
Pioneering new scientific and applied uses of muons

1. Development of new scientific and applied research using continuous muon beams and cosmic-ray muons
2. Development of new systems and measurement methods based on the latest radiation detection technology for nuclear and elementary particle physics

Osaka University plays a very important role in promoting fundamental and applied muon research. The University not only has Japan's only continuous muon beam facility, MuSIC, but also has many leading researchers who are pioneering research using muons and have already achieved a variety of results.

In this project, Osaka University's expertise and facilities will be coordinated and developed, and new measurement systems and methods will be developed in cooperation with academic institutions and private companies in Japan and abroad, applying the latest radiation detection technology.

In this way, Osaka University will take the leadership in pioneering and promoting scientific and industrial applications of cutting-edge muon technology.



Development of an accurate first-principles calculation method on the basis of the wave-function theory

Research Themes

1. Development of a new calculation method for solids
2. Theoretical study on strongly correlated systems

We develop a new theoretical method that can accurately describe the electron-electron interaction in materials.

A rich variety of materials properties originates from the complicated interactions among electrons and nucleus. Theoretical methods to solve their governing equation are called first-principles calculation. First-principles calculation is nowadays widely used for materials science, because it is a very effective and important method to know microscopic information of materials. On the other hand, it is very difficult to obtain materials properties by solving the governing equation while it is in principle possible. Therefore, first-principles calculations have many limitations in accuracy.

To overcome this problem, a theoretical framework that is different from the present calculation method has been actively developed.

We develop a new first-principles calculation method on the basis of the wave-function theory, for accurate description of the complicated and non-trivial materials properties.

We have developed our original computational code, and have applied it to electronic structure calculation of isolate atomic systems and solid systems. By analyzing computational results using this code, we have studied many problems, such as improvement of the accuracy and extension of the applicability of the method. Through these studies, we aim at establishment of the reliable first-principles calculation method.

Development of ultra-fine mass spectrometry imaging by precise fluid control of pico-liquid

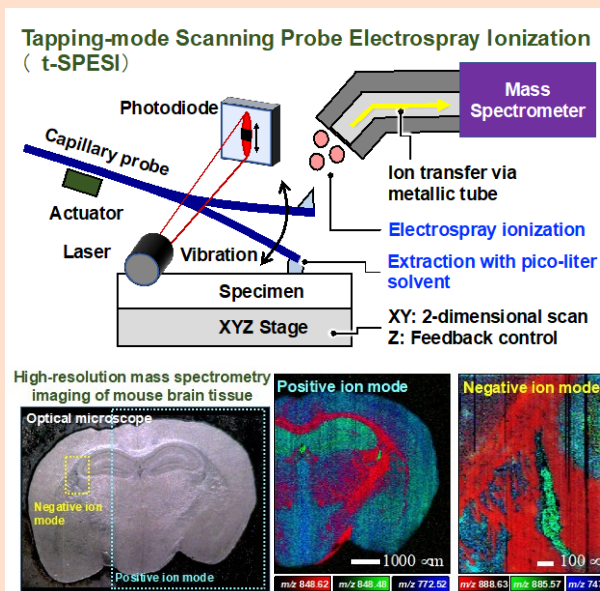
Research Themes

1. Development of precise control technology for picoliter solvents
2. Mass spectrometry imaging of biological tissues through interdisciplinary research

The mass spectrometry imaging has the advantage of visualizing the distribution of chemical components in biological tissues, and is expected to be applied in the future to the investigation and diagnosis of scientifically based diseases.

Tapping-mode scanning probe electrospray ionization (t-SPESI) can perform multiple component extraction and soft ionization in milliseconds at high speed by supplying charged pico-liquid to the sample via a capillary probe that vibrates in the vertical direction.

This project aims to realize an innovative ultra-fine mass spectrometry imaging method using precise fluid control of micro-volume liquids based on t-SPESI, which has been developed by the project leader. We will also conduct interdisciplinary joint research to obtain multidimensional chemical distribution information on changes in various components in diseased tissues and cells, and to gain knowledge that will lead to the identification and understanding of diseases.



Project on establishing a research platform for environment friendly polymeric materials

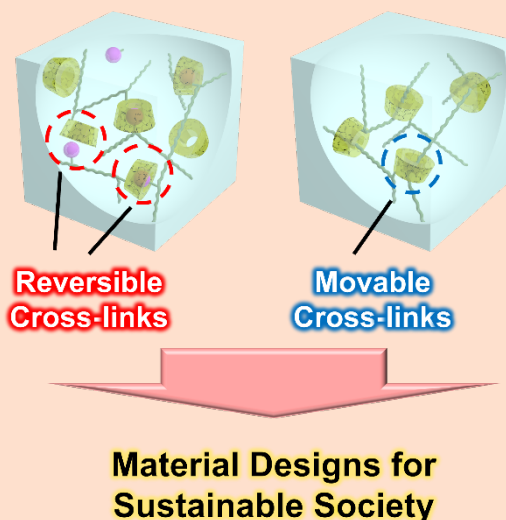
Research Themes

1. Establishment of various designs for various functional materials
2. Enhancement of functions by composite materials

To achieve a sustainable society, both “Zero-discard” and “Zero-usage of petroleum resources” are required. We have focused on a mechanical toughness which improves durability and a self-healing property which recovers mechanical properties and original shapes after fracture to deal with the two “Zero-” concepts.

This project group have utilized reversible cross-links in which the cross-links dissociate and re-associate responding a deformation of materials, achieving the self-healing property. Movable cross-links where the cross-links consisting of penetrating polymer chains and macrocyclic molecules release the stress by moving the macro cyclic molecules during the deformation, improving mechanical toughness. Compared with the conventional materials consisting of fixed covalent cross-links, the polymeric materials consisting of reversible or movable cross-links have shown good durability contributing to “Zero-discard”.

“Zero-usage of petroleum resource” have been achieved by fabricating plant-based cellulose composite materials. In addition, the composite materials also showed good mechanical toughness and self-healing properties.



Molecular mechanism of gross chromosomal rearrangement (GCR)

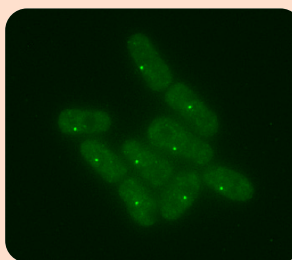
Research Themes

1. Identification of the genes involved in GCR
2. Elucidating the molecular mechanism of GCR

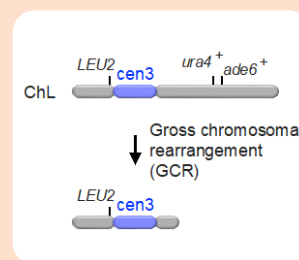
An extremely large number of repetitive sequences are present in a eukaryote genome. Intriguingly, repetitive sequences occupy around half of the human genome. Gross chromosomal rearrangement (GCR) such as translocation occasionally occurs using the repetitive sequences as “DNA glue”. GCR can cause genetic diseases including cancer and cell death. Understanding how spontaneous GCR occurs will facilitate developing the way to prevent and cure the diseases. From the evolutionary point of view, on the other hand, GCR may be one of the driving forces because chromosomes are frequently rearranged during evolution. Therefore, GCR appears to be the integral phenomenon of living organisms.

Using fission yeast as a model organism, we are trying to identify the genes that suppress or promote GCR and elucidate the molecular mechanism of GCR.

Fission yeast is very useful to perform genetic analyses. However, as it is a haploid, GCR usually results in cell death. Using an extra-chromosome ChL, derived from chromosome 3, we have established the means to determine the spontaneous GCR quantitatively and define the detailed structure of GCR products. Taking the advantage of this system, we can clarify the effects of various factors on GCR.



A fluorescent image of fission yeast shows centromeres containing DNA repeats.



GCR on the ChL chromosome results in a loss of *ura4* and *ade6* marker genes.

Glycochemical biology Research Group

Research Themes

1. Carbohydrate synthesis
2. Chemical biology using synthetic glycan for elucidation and regulation of glycan functions

Glycans cover the cell surface (Glycocalyx) and regulates various biological phenomena, including infections, cell adhesion, immune responses, and signal transduction. Since glycans have diverse and heterogeneous structures, the molecular basis of their functions has remained to be elucidated.

The purpose of our project is elucidation and regulation of the cell surface glycan function using synthetic biology. The first step of our research is chemical syntheses of the glycans to provide sufficient amounts of target glycans. We are investigating the methods for the efficient and practical synthesis of complex glycans. The synthesized glycans are introduced onto membrane proteins on living cell surface by biocompatible reactions, enabling the structure-based functional analyses of glycans. We also investigate the cell surface glycan editing to control their functions. In the future, these innovative technologies will be applied for the development of glycomedicines.

Many diseases are caused by disturbances in homeostasis, and glycans play an important role in maintaining the homeostasis. We believe that elucidation and regulation of the glycan functions will enable to restore the homeostatic disturbances in various diseases, including cancer, immunological disorders, and neurological disorders. This unprecedented approach is expected to lead innovative drug development. Our research is also expected to make a significant contribution to cellular medicines, such as iPS cells and CAR-T immunotherapy. Although cells are covered with glycans, glycans have been almost neglected in the cellular medicines. We believe that glycan function control can dramatically improve cellular medicines. Overall, this research project aimed to elucidate the glycan functions at the molecular level and promote their utilization for novel glycomedicines.