Department of Environmental and Life Sciences

Advanced Enviromental Technology

Ecological Engineering

Bioscience and Biotechnology

Molecular Chemistry

Applied Sensing Technology Laboratory

Staff	• Professor **Saburo TANAKA** (E-mail : tanakas@ens.tut.ac.jp)
Laboratory URL	http://ens.tut.ac.jp/squid/
Key words	Magnetics, Superconductor, SQUID, Magnetic sensor, Contaminant detector

Saburo Tanaka received his B.E. and M.E. from Toyohashi University of Technology in 1981, and 1983, respectively. He received his Doctoral Degree in engineering from Osaka University in 1991. Since 1987 he has been involved in the research of high-temperature superconductors at Sumitomo Electric Itami Research Lab. He was engaged in the development of multichannel high-Tc SQUID systems at the Superconducting Sensor Laboratory from 1991 to 1995. He was a visiting research associate at the Department of Physics, University of California at Berkeley from 1996 to 1997. Currently, he is a professor at faculty of Environmental and Life Sciences.

One of my main interests is in the applications of Superconducting Quantum Interference Devices (SQUIDs). The applications include the contaminant detection system in food and a Li-ion battery, and the magnetic nanoparticle imaging.

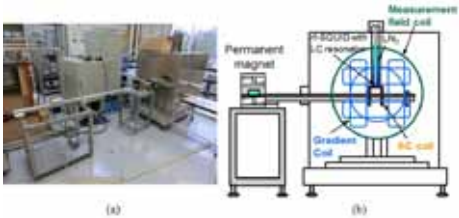
Theme 1 ▶ Ultra-sensitive Metallic contaminant detector for Li ion battery. And Food

The detection technique is based on recording the remnant magnetic field of a contaminant using SQUID sensors. SQUID is a high-sensitivity magnetic sensor based on the superconductivity phenomenon. The sensitivity for food inspection is 0.3 mm in diameter and for Li ion battery is 35 micron in diameter.

Metallic contaminant detection system using HTS-SQUID. Inset shows the appearance of the electromagnetic shield with SQUID electronics when the front door is open.

Theme 2 ▶ Ultra-Low Field NMR/MRI using SQUID

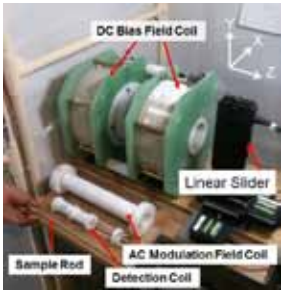
We have developed an ultra-low field (ULF) magnetic resonance imaging (MRI) system using a high-temperature superconducting quantum interference device (HTS-SQUID) for food inspection.



Ultra-low field magnetic resonance imaging system using HTS-SQUID.
(a) Appearance of the system. (b) Schematic diagram of the system.

Theme 3 ▶ Magnetic nano-particle imaging using SQUID.

We have developed a method to improve the detection sensitivity for the magnetization M of MNP (Magnetic Nano-Particle) and the imaging technique based on the detection of a second harmonic of the response. The advantage of the use of the second harmonic response is that the response can be taken for small AC magnetic field.



Magnetic Nanoparticle imaging Scanner using HTS-SQUID.

Applied Light Sensing Laboratory

Staff	• Associate Professor **Seiichiro ARIYOSHI** （E-mail：ariyoshi@ens.tut.ac.jp）
Laboratory URL	http://ens.tut.ac.jp/squid/
Key words	Terahertz Technology, Superconducting Devices

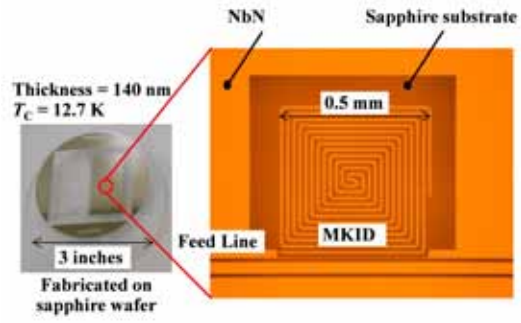
Terahertz-waves (0.1-10 THz, 3 mm-30 um), located in the gap between radio-waves and light-waves, are called as the frontier of light. Terahertz-waves show both properties of transparency in various materials that are visually opaque and invasive nature compared to X-ray and gamma-ray. This ability has opened a wide range of possibilities in various application fields such as security, medicine, biology, astronomy, material science and so on.
This laboratory is pushing ahead with the development on highly sensitive terahertz-wave detectors using superconductor, two-dimensional terahertz spectroscopy and their new applications.

Theme 1 ▶ Development of Superconducting Terahertz-wave Sensors

Two-dimensional terahertz spectroscopy offers potential opportunities in material science research into soft materials for example, and industrial application development. This laboratory have progressed the development of a Microwave Kinetic Inductance Detector (MKID, Fig.1) array operating at 3 K with a cryogen-free He-4 refrigerator, and exhibiting both superior detection sensitivity of greater than one digit or more compared to conventional semiconductor bolometers, and greater speed response. Such an array aims to realize the application of a 2D-Fourier transform terahertz spectrometer.

Theme 2 ▶ Terahertz Spectroscopy of General-purpose Plastics

Polymer properties such as hardness, fragility, workability, and thermal stability are determined not only by the chemical composition but also the higher-order structure related to the crystallinity, molecular chain length, and chain packing in the solid state. In conventional diagnostic methods employed for general-purpose plastics, destructive techniques to measure tensile and bending strengths and subjective observation of the degree of deterioration such as a change in color or transparency are commonly applied. New analysis techniques are currently being developed to allow nondestructive and objective inspection of plastics.



Left: Fabricated spiral-MKIDs on a sapphire substrate. Right: Microscopy image of a spiral-MKID. The NbN film thickness is 140 nm and its Tc is 12.7 K.

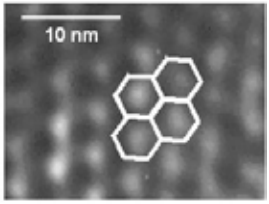
Functionalized Interface Science Laboratory

Staff	• Professor **Akihiko MATSUMOTO** (E-mail：aki@ens.tut.ac.jp) • Assistant Professor **Hiromitsu ITO** (E-mail：hiro_ito@ens.tut.ac.jp)
Laboratory URL	http://www.tut.ac.jp/english/schools/faculty/ens/227.html
Key words	adsorption, adsorption microcalorimetry, energy of adsorption, fullerene, gas adsorption, mesoporous silica, nanoporous carbon, nanoporous material, zeolite, PCPs/MOFs

Our laboratory has been interested in adsorption of gases on micro/mesoporous materials. The research topics focus on development and characterization of pore structure of adsorbents and interaction between gas molecules and solid surfaces by aid of physicochemical techniques, such as adsorption microcalorimetry, adsorption measurement, and spectroscopic methods. Our researches also include development of novel porous materials by controlling surface chemical features and pore structures which are suitable for adsorption removal of target gas molecules. Based on these research results, we are undertaking application studies on adsorption removal of air pollutants and adsorption storage of hydrogen and methane.

Theme 1 ▶ Surface functionalization of porous materials and developing novel nanoporous materials

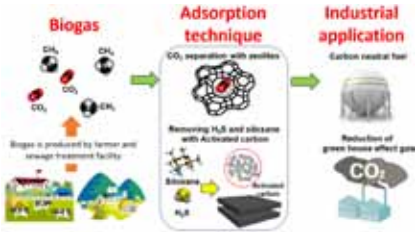
Adsorbed state of molecules on porous materials strongly depends on the chemical composition of the surface, the pore structure, and the chemical characteristics of adsorbate molecules. We study gas adsorption mechanisms and adsorption characteristics of molecules on porous materials such as zeolites, MOFs/PCPs, ordered mesoporous silica, and nanoporous carbon by the aid of various adsorption techniques such as adsorption isotherm measurements, adsorption microcalorimetry, and spectroscopic method (UV/VIS, FT-IR and Raman).



TEM image of hexagonal pore structure in ordered mesoporous silica

Theme 2 ▶ Selective separation of CO_2 and CH_4 purification from biogas by gas adsorption technique

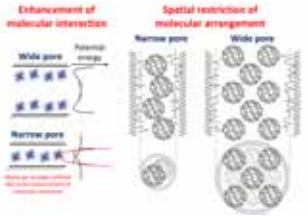
The biogas, which consisted by CH_4, CO_2 and misc. is one of carbon neutral energy sources produced by anaerobic fermentation of sewage sludge.
Our research focuses on purification of biogas by pressure swing adsorption (PSA). Especially we are interested in the separation of CO_2, H_2S, and siloxane gas by zeolites, MOFs/PCPs and surface modified activated carbons.



Biogas separation for the sustainable society by gas adsorption

Theme 3 ▶ Controlling molecular and atomic arrangements by using nanosapace in porous materials

When molecules and atoms are confined in nanospace or micropore in molecular dimension (ex; length < a few nm), features of the confined molecules such as crystal structure and electric properties are often dramatically changed from the bulk state due to enhancement of intermolecular interaction in the nanospace. These phenomena depend on both the size of the nanospace and the combination of the container and confined molecules. We challenge to create novel molecular arrangement in the nanospace of nanoporous materials.



Controlling molecular and atomic arrangements.

Electrostatics and Plasma Engineering Laboratory

Staff	• Associate Professor **Kazunori TAKASHIMA** (E-mail：takashima@ens.tut.ac.jp) • Assistant Professor **Hirofumi KURITA** (E-mail：kurita@ens.tut.ac.jp) • Research Associate **Hachiro YASUDA** (E-mail：yasuda@ens.tut.ac.jp)
Laboratory URL	http://ens.tut.ac.jp/electrostatics/
Key words	Electrostatics, Plasma catalysis, Plasma medicine, Electrostatic precipitator, Single DNA manipulation, Water droplet based electroporation, Plasma sterilization / virus inactivation

Our research interests include air and water pollution control using plasma catalysis, electrostatic precipitation, fundamental of interaction between plasma and biological objects, application of plasma to medical treatment and life sciences, development of single bio molecule manipulation technique and its application to analysis of interaction between bio molecules.

Theme 1 ▶ Plasma catalysis for pollution control and material

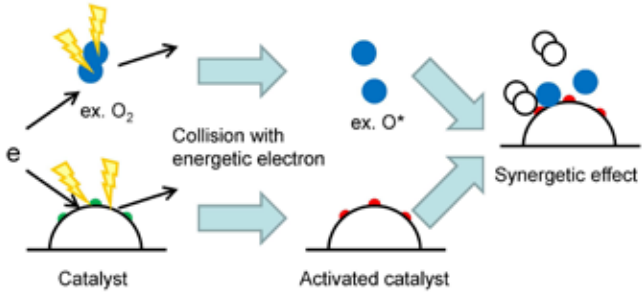
Discharge plasma has been studied as a tool to induce various chemical reactions at moderate conditions taking advantage that various active species are generated in gas and liquid phases by non-thermal plasma. To improve energy efficiency and reaction selectivity, we are working on plasma catalysis in many fields such as diesel NOx emission control, room air cleaning, liquid and gas fuel reforming, ammonia generation at moderate conditions, water treatment etc.

Theme 2 ▶ Non-thermal plasma and electrostatics in life sciences

Phenomenologically, irradiation of plasma is effective for sterilization, inactivation of virus and apoptosis induction, which are potential application in medical treatment but their mechanisms are yet to be studied. We are studying the mechanisms from multi-level analysis of the response of bio molecules, cells, tissues and individuals to plasma irradiation. Electroporation-based gene introduction using electrostatic manipulation of a water droplet in oil is also studied, which is very effective for small volume process.

Theme 3 ▶ Analysis of interaction between bio molecules based on single molecule observation and manipulation

Electrostatic force is exerted on very small objects because forces of gravity and inertia are negligible. Electrostatic manipulation and fluorescent labeling enable us to position and observe a single molecule DNA in liquid under the microscope. For example, DNA molecules can be stretched electrostatically like a thread. Such single molecule in-situ observation is advantageous for the analysis of interaction between bio molecules because not only statistic results but also reaction of individual molecule can be visualized in real time. We are working on the analysis of interaction between bio molecules such as DNA and proteins using newly developed single molecule observation methods.



Plasma catalysis

Advanced Enviromental Technology

Chemical Kinetics and Energy Engineering Laboratory

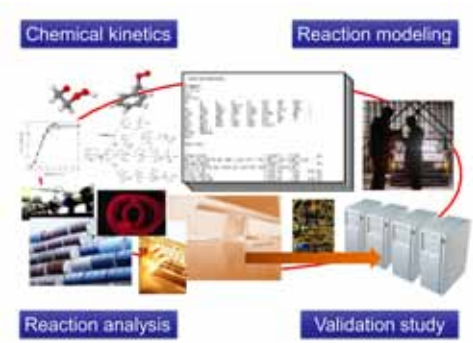
Staff	• Associate Professor **Tastuo OGUCHI** (E-mail : oguchi@tut.jp)
Laboratory URL	http://ens.tut.ac.jp/keel/
Key words	Combustion Chemistry, Chemical Kinetics, Reaction modeling, Combustion synthesis

Although the global climate change due to the carbon dioxide emission from our modern life is serious problem, combustion technology is still very important in our life. We have to improve thermal efficiency and reduce unburned fuel on the internal combustion engines for motor vehicles. These days many people aware that the combustion chemistry is very important to understand the several phenomena in engines. Therefore, the information of detail chemical kinetic mechanism is highly recommended to develop new combustion system.
Now we try to reveal the complicated mechanism for the formation of polycyclic aromatic hydrocarbons (PAHs) from the combustion systems, auto-ignition mechanism for the reference fuels, behavior of the small amount of intermediates in the reactor, and elementally reactions by using our self-constructed experimental apparatuses. Also, the theoretical calculation is a strong tool. We use the quantum chemical calculations to obtain chemical and thermal properties of molecules as well as reaction paths. These results are used to estimate the reaction rate coefficients of the elementally reactions. Finally, reaction models are constructed and are compared with the experimental studies for verification.

Theme 1 ▶ Chemical kinetic analysis and modeling of combustion in engines.

Theme 2 ▶ Reaction mechanism of the formation of particulate matters from combustion.

Theme 3 ▶ Theoretical investigation of elementary reactions in combustion chemistry.



Schematic image of the research process for combustion chemistry.


Recreation: a trip to somewhere with lab's members annually.

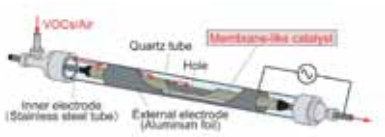
Functional Catalytic System Engineering Laboratory

Staff	• Associate Professor **Takanori MIZUSHIMA** (E-mail : mizushima@ens.tut.ac.jp) • Assistant Professor **Hirohisa SATOH** (E-mail : hsato@ens.tut.ac.jp) • Research Associate **Hironobu OHKITA** (E-mail : ohkita@ens.tut.ac.jp)
Key words	Solid catalyst, Plasma catalytic reaction, Steam reforming of ethanol, Synthesis of 1,3-butadiene, Crystal structure, Phase transition

Solid catalysts are essential substances for chemical industries and environmental protections. The main subject of our research group is to develop heterogeneous catalysts and catalytic reaction systems for environmentally-friendly synthesis of chemical materials and detoxifying of environmental pollutants. We also investigate crystal growth and structure of single crystals of rare earth manganites as new types of inorganic materials.

Theme 1 ▶ Plasma catalytic reaction system for oxidative decomposition of volatile organic compounds

Although non-thermal plasma (NTP) reactions are effective for decomposing volatile organic compounds (VOCs) in air, their energy efficiencies are relatively low because of very low concentration of VOCs. We have designed a tubular membrane-like catalyst for the NTP reactor by dielectric barrier discharge to improve the energy efficiency. In this approach, VOC molecules in air are condensed by selective adsorption onto the catalyst during the plasma-off period and then oxidatively decomposed by short-term NTP discharge. This has the potential to remarkably reduce electric consumption without significantly decreasing the reaction rate.



Membrane-like catalyst-equipped plasma reactor

Theme 2 ▶ Hydrogen production via low-temperature steam reforming of biomass ethanol

Hydrogen demand is expected to increase precipitously for fuel cells in the near future. Currently, hydrogen is mainly produced by steam reforming of fossil fuels such as natural gas and petroleum, but there are environmental concerns such as emission of CO_2 as a greenhouse gas, resource depletion, etc. Recently, biomass ethanol has attracted significant attention as an alternative resource for hydrogen production, because it is a renewable and environmentally- friendly fuel. Steam reforming of ethanol ($C_2H_5OH + 3H_2O \rightarrow 2CO_2 + 6H_2$) is the most promising method for converting biomass ethanol to hydrogen. We now investigate the catalytic performance of CeO_2-supported multi-metallic catalysts.

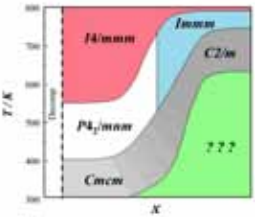
H_2 production from biomass ethanol

Theme 3 ▶ Synthesis of 1,3-butadiene via oxidative dehydrogenation of n-butane

1,3-butadiene as an important chemical raw material of synthetic rubbers is produced by catalytic cracking of naphtha. Because its demand is expected to increase with motorization in developing countries, other synthetic approach is required. We now develop modified bismuth-molybdenum oxide catalysts for 1,3-butadiene synthesis via oxidative dehydrogenation of n-butane.

Theme 4 ▶ Crystal growth and structure analysis of single crystal of rare earth manganites

Single crystal of $BaLn_2Mn_2O_7$ (Ln = rare earth) with layered perovskite structure can be grown by floating zone method. We have investigated the thermal property of the yielded single crystal using DSC and found the thermal anomalies which indicates the existences of several phases and transition paths. Single-crystal X-ray diffraction analysis for each phase heated under the specified condition revealed that the change to another path is caused by increment in oxygen nonstoichiometry.



Phase diagram of BaEu2Mn2O7+x

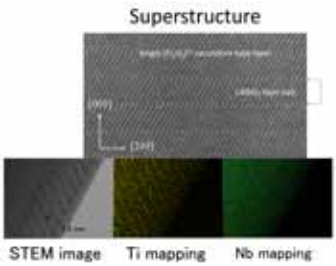
Inorganic Materials Lab.

Staff	• Professor **Hiromi NAKANO** (E-mail：hiromi@crfc.tut.ac.jp)
Laboratory URL	http://www.crfc.tut.ac.jp/nakano/index.html
Key words	Phosphor, Crystal structure, TEM, XRD, Photoluminescence

We synthesize new inorganic materials and determine the relationship between property and crystal structure from macro- to atomic- scale.

Theme 1 ▶ "Synthesis of new oxide phosphors and clarification of mechanism for relationship between property and crystal structure"

1. Synthesis of new phosphors by solid-phase reaction and liquid-phase-reaction
2. Design and synthesis for new phosphor by controlling of composition and crystal structure
3. Application of red phosphor Li-Ta-Ti-O:Eu excited by 400 nm
4. Relationship between crystal structure and photoluminescence



TEM images of unique structure of LNT ceramic

Theme 2 ▶ "Anisotropic structure and property in oriented bulk ceramics"

In this work, as a first step toward application of the unique qualities of an electro-ceramic with an anisotropy structure, we prepared an oriented LNT balk ceramic by slip casting in a strong magnetic field of 12 T. The direction of the magnetic field was parallel to the casting direction. The obtained specimen was analyzed by X-ray diffraction, scanning electron microscope, and transmission electron microscope. Consequently, the c-axis of the LNT powders was aligned parallel to the magnetic field and a high orientation degree was achieved in a strong magnetic field of 12 T. This investigation is being pursued in collaboration with NIMS (Dr. Suzuki).


Meeting in Lab.

Theme 3 ▶ Microstructure and mechanical property of metallic materials controlled by metallographic-structure and -phases

We are investigating metallic films with a nano-lamellar structure or porous metals. TEM observations and simulations by molecular dynamics and first-principles analysis are used to study the mechanism of metallic materials' physical properties.
This investigation is being pursued in collaboration with Kyoto University (Prof. Mabuchi Lab.) and AIST JPN (Dr. Chino).

Atmosphere and Thermal Environment System Laboratory

Staff	• Lecturer **Takayuki TOKAIRIN** （E-mail：tokairin@ens.tut.ac.jp）
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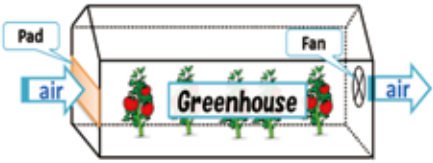
Key words	plant factory, micro meteorology, computational fluid dynamics, environmental control

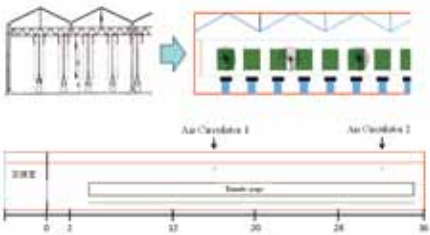
This laboratory mainly researches atmospheric and thermal environment inside a plant factory (greenhouse) using various sensors and computational fluid dynamics model (CFD model) to clarify the appropriate environment for plant growth. Details are described below.

Theme 1 ▶ Evaluation of environment for various types of plant factory (green house) using a computational fluid dynamic model.

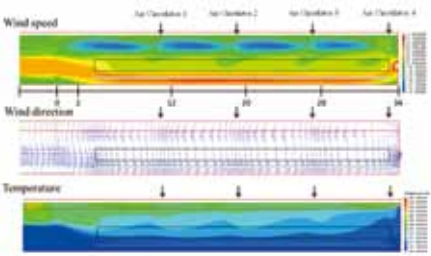
Atmospheric and thermal environment inside a plant factory (greenhouse) have been evaluated mostly based on empirical method, therefore it is difficult to know the detailed distribution of air temperature, humidity, airflow and CO2 concentration and their control. The objective of this study is to evaluate and predict the detailed distribution of environmental components mentioned above in a plant factory for contribution to the environmental control to maximize crop yield. In future, photosynthesis model will be considered for modeled crop in CFD to clarify the effect of CO2 application on crop yield.



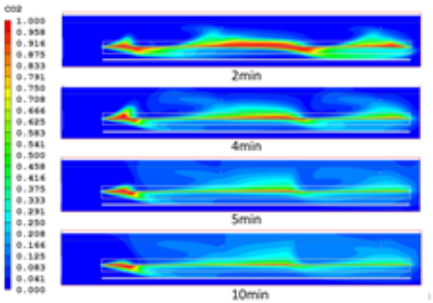
Plant factory equipped with a pad and fan evaporative cooling system



Modeled plant factory.



Calculated wind and temperature fields using a computational fluid dynamics model.



Calculated CO_2 distributions due to CO_2 application in a modeled crop.

Ecological Engineering

Laboratory for Production and Utilization of Biomass

Staff	• Professor	**Hiroyuki DAIMON**	(E-mail：daimon@cir.ignite.tut.ac.jp)
	• Project Associate Professor	**Yoichi ATSUTA**	(E-mail：atsuta@water.ens.tut.ac.jp)
	• Project Associate Professor	**Hirotugu KAMAHARA**	(E-mail：kamahara@cir.ignite.tut.ac.jp)
Laboratory URL	http:// water.ens.tut.ac.jp/index.html		
Key words	Subcritical water; Rare metals; Hydrothermal reaction; Liquid feed; Amino acids; Organic recycling resource; Lipid biomarkers profile; Anaerobic digestion; Wastewater treatment; Microbial community		

We have been developing waste recycling and biomass utilization technologies to establish sound material-cycle society with high ecological homeostasis. Research projects are focused on development process and methodology by utilizing the high-temperature and high-pressure water and supercritical carbon dioxide technologies. These researches include intensive investigation of the whole process from production to disposal and from inorganic to organic matters. Our group is also involved in the development of "biomass town project" in several cities.

Theme 1 ▶ Construction of Research Center for Production and Utilization of Biomass

In general the utilization of biomass is an ongoing challenge shared by every region. This challenge, however, is a complex task that involves various sectors, including the local authorities, industries, agriculture, as well as the movements towards CO_2 emission. Based on the project "Development of Biomass, CO_2, Heat Utilization System" (2011-2016), our group proposes a new biomass utilization system that combines biomass utilization (energy and nutrients recovery) with biomass production. This new system is in response to the call of innovation in terms of social needs as well, as it can be the catalyst to create new opportunities, as well as enhance the present regional development. Our group aims to build up a research and development base that invites cooperation between different sectors to approach the biomass issues, by applying present or new concepts that well-suit to each case' conditions and needs.

Development from the Viewpoint of the Research Center for Production and Utilization of Biomass

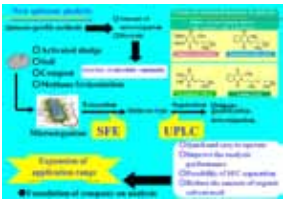
Theme 2 ▶ Environmental Assessment for Production and Utilization of Biomass

Biomass has been a basic resource supporting human life since ancient times. Recent technological innovations now allow us to convert various type of biomass into energy or industrial products. On the other hand, the expansion of biomass use, including for food consumption is having an impact on land use change and water pollution. We are looking for ways to mitigate its environmental impact by analyzing the material and energy balance.

High-Temperature and High-Pressure Water Application

Theme 3 ▶ Development and Application of a Novel Method for Analysis of Microbial Community Structure

Supercritical fluid extraction using carbon dioxide as solvent is a green technology and offers numerous advantages for analytical purpose, mainly rapidity and low organic solvent usage. We have been developing a new application of supercritical carbon dioxide extraction on the determination of microbial community structure for environmental assessment. Four lipid biomarkers including respiratory quinones (RQ), phospholipid fatty acids (PLFA), phospholipid ether lipids (PLEL), and polyhydroxyalkanoates (PHA) have been investigated. The studies showed potential application of supercritical carbon dioxide extraction as a routine method for the comprehensive analysis of microbial community structures in environmental assessment using the lipid biomarkers profile.



New Quinone Analysis

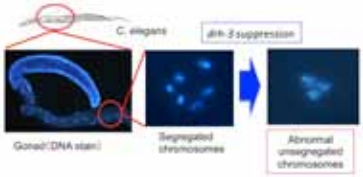
Molecular Genetics Laboratory

Staff	• Professor **Toshihiko EKI** (E-mail：eki@ens.tut.ac.jp) • Assistant Professor **Yuu HIROSE** (E-mail：hirose@ens.tut.ac.jp)
Laboratory URL	http:// ens.tut.ac.jp/molgenetics/
Key words	*C. elegans*, soil nematode, yeast, RNAi, genome editing, cyanobacteria, Dicer-related helicase, DNA barcoding, next generation sequencer

A number of chemicals or wastes are continuously produced by our social activities and are accumulated in the environment. These substances may be potentially and unexpectedly changed into genotoxic agents, causing DNA damage to lead to dysfunctions of genetic information. Since it has been well known that excess DNA damage increase the risk of various cancers via genetic mutations, studies of "genome environment" are important for environmental and medical sciences. Therefore, first, we are studying molecular mechanism of maintenance of genome integrity via a novel Dicer-related helicase DRH-3 in nematode *C. elegans* and also developing novel yeast-based genotoxicity tests using reporter assay. Secondly, we are developing yeast-based chemical sensing method as well as genome editing technologies with CRISPR/Cas9. Thirdly, we analyze taxonomic structure of soil nematodes by DNA barcoding to assess soil environments. Finally, we are also interested in the light color sensing system of cyanobacteria. We explored new photosensing systems for application of optogenetics using the next generation sequencer.

Theme 1 ▶ Study of two *C. elegans* Dicer-related helicases DRH-1 and DRH-3

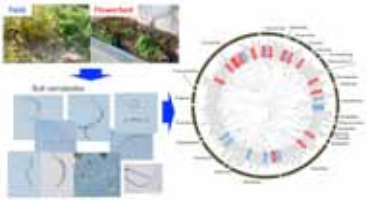
We identified a novel *C. elegans* gene *drh-3* that functions in both maintenance of chromosome integrity and RNA interference (RNAi). Since the relationship between RNAi and chromosome regulations has been largely unknown, we have focused on functional analyses of DRH-3 protein as well as the related DRH-1 that acts in antiviral function by biochemical approach.



DRH-3 is essential for chromosome segregation in *C. elegans*

Theme 2 ▶ Development of biosensing assay systems using genetically altered yeasts

It is important to detect genome toxicities of chemicals and waste products. We have developed the biosensing assays by recombinant reporter yeasts for detecting genotoxicity and/or oxidative toxicity. We also tried to develop recombinant yeasts that can detect a broad range of chemicals and editing technology of yeast genome using CRISPR/Cas9.



DNA barcode analysis of soil nematodes

Theme 3 ▶ DNA sequence analyses of soil nematodes and cyanobacteria

De novo sequencing of cyanobacteria is in progress to study genome structures and transcription profiles using the next generation sequencer. We are also performing DNA barcode analyses to clarify taxonomic structure of soil nematodes for assessment of soil environment.

Cyanobacteria and next generation sequencers

Theme 4 ▶ Characterization and application of cyanobacterial photoswitch

Cyanobacteria harbor photoswitch systems that sense various light colors. We utilize green and red light sensing CcaS/R system for regulating the gene expression in other organisms, contributing the development of sophisticated optogenetic tools.

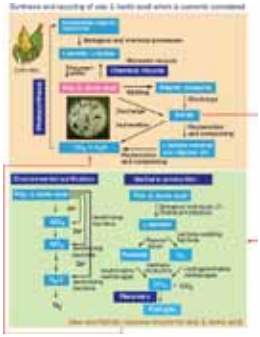
Hydrosphere Environmental Biotechnology Laboratory

Staff	• Lecturer **Takeshi YAMADA** (E-mail：tyamada@ens.tut.ac.jp)
Laboratory URL	http://ens.tut.ac.jp/microbes/
Key words	Poly(L-lactic acid), wastewater treatment, nitrogen removal, anaerobic digestion, methane, bulking, microbial measurement, microbial index

This laboratory conducts research on the following themes in the pursuit of a stable and efficient biological wastewater treatment system.

Theme 1 ▶ Microbiological technologies for environmental purification and methane production using poly(L-lactic acid)

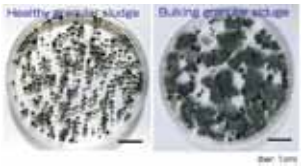
Poly(L-lactic acid) (PLLA) is superior to other biodegradable plastics owing to its mechanical, chemical, and physical properties. Various types of PLLA products such as packing and agricultural materials have expanded into further generic use. However, the disposal and re-use of this material is a serious problem because of the large amount of PLLA waste generated. Although "clean" PLLA wastes can be chemically recycled to lactic acid by thermal decomposition and hydrolysis, disposal of PLLA wastes that are unsuitable for such recycling has been handled by methods such as landfill deposition, incineration, and composting. Although no increase in global carbon emission has been reported owing to these methods, a more effective and earth-friendly PLLA waste management system should be established. We have been attempting to develop technologies that produce methane from PLLA waste in anaerobic digestion reactors. Additionally, we have been trying to develop a technology that would facilitate the functioning of PLLA as an electron donor and as a carrier for microorganisms in denitrification reactors.



Suggestion of a new resource recycling system for PLLA.

Theme 2 ▶ Elucidation and possible control strategies of the unknown phenomenon of "anaerobic bulking" observed during anaerobic wastewater treatment

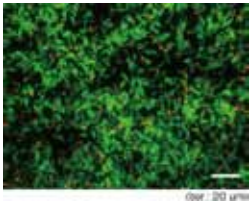
Anaerobic wastewater treatment processes have become part of the core treatment process for middle-strength and high-strength organic wastewater. However, several problems, unforeseen even by the manufacturer, have often occurred during the operation and startup of the reactor. Particularly serious problems include the sudden rise and consequent overflow of anaerobic sludge (anaerobic sludge bulking), which decreases the wastewater treatment efficiency and, subsequently, necessitates stoppage of the functioning of reactors. However, the mechanisms and microbes responsible for anaerobic sludge bulking remain unknown. We have been investigating the ecology, physiology, and genetics of causative microbes, and aim to develop technologies to prevent anaerobic sludge bulking and detect the causative microbes.



Healthy granular sludge and bulking sludge formed in anaerobic wastewater treatment reactor.

Theme 3 ▶ Development of rapid, simple, and on-site measurement techniques for microbes in wastewater treatment

Wastewater treatment reactors are controlled on the basis of water quality indices such as pH and loading rate, while microbes in the reactor are treated as a "black box." Once effluent quality of the reactor deteriorates, the ensuing problems require laborious intervention. As a solution, we suggest the indexing of microbes that play an important role in the reactor and building mutually complementary management systems consisting of water quality and microbes. We have been developing rapid, simple, and on-site measurement technologies for microbes involved in wastewater treatment to contribute in the strengthening of wastewater treatment control methods.
light sensing CcaS/R system for regulating the gene expression in other organisms, contributing the development of sophisticated optogenetic tools.



A double-stained image by the 5-cyano-2,3-ditoryl tetrazolium chloride method and fluorescence in situ hybridization method using bacterial specific DNA probe.

Laboratory of Genetic Engineering

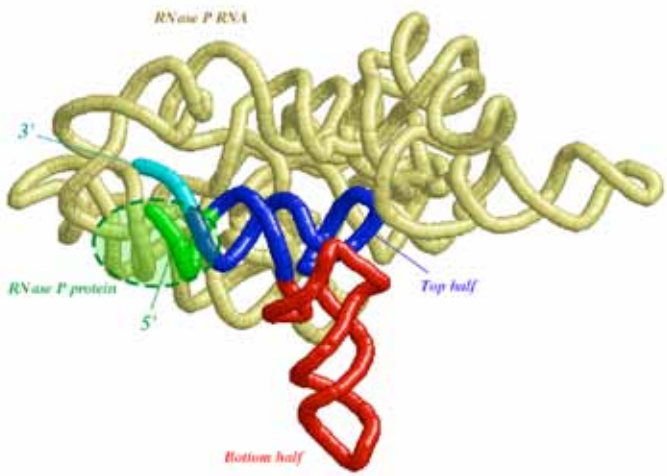
Staff	• Associate Professor **Terumichi TANAKA** (E-mail：terumichi-tanaka@tut.jp)
Key words	protein engineering, recombinant DNA, tRNA, ribonuclease P, vector, β-lacatamase, evolution,

All lives on the Earth, including human species, use common biological system, and which are performed by nano-sized molecules genes and enzymes. In my laboratory, we analyze and reveal hidden mechanism of genes and enzymes, and we also apply recombinant DNA technique to design and obtain new functional enzymes.

Theme 1 ▶ Analysis on the mechanism of ribonuclease P.
This enzyme ubiquitous and essential enzyme and is made up of RNA and protein subunits. This enzyme catalyzes the 5'-maturating reaction of tRNA precursor. We have focused on the substrate recognition mechanism of this enzyme how this enzyme accepts the substrate to form the high energy Michaelis complex, and to release the catalyzed product from the enzyme.

Theme 2 ▶ Analysis and designing of new drug resistant gene.
Drug resistant genes are to be found everywhere and they sometimes prohibit curing from the disease caused by bacteria. We have focused on the substrate recognition mechanism of beta-lactamase, which hydrolyzes penicillin-related drugs, to obtain detailed information of the enzyme to design new effective drugs.

Theme 3 ▶ Development of biological species detection kit.
We have developed gene detection tool of various biological species including food animal and vegetables using the multiplex-PCR technique and PCR-RFLP technique.



Computer generated structure of E.coli ribonuclease P and tRNA. The RNA subunit of the enzyme (orange), the putative position of the protein subunit of the enzyme (green), the top-half part of tRNA (blue), the bottom-half part of tRNA (red), and the 3'-terminus of tRNA (cyan), are shown.

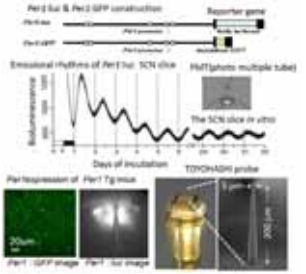
Regulatory Biofunction Lab.

Staff	• Associate Professor **Rika NUMANO** (E-mail：numano@eiiris.tut.ac.jp)
Laboratory URL	http://www.tut.ac.jp/english/schools/faculty/ens/677.html
Key words	Circadian rhythms, *Period1*, Transgenic mice, TOYOHASHI probe, pacemaker neuron,, LiGluR, azobenzene, MAG, a water-in-oil droplet electroporation, Transfection

We would like manipulate neural activity and physiological reaction by our original electrical probe, photo-switched nanomachines and transfection method both *in vitro* and *in vivo*. For example, the pacemaker neuron activity of circadian rhythms in the SCN can be manipulated by stimulating the SCN target circuit, which investigates the mechanism to control rhythms of the whole body, and shows how to maintain and administer the health life with normal rhythms.

Theme 1 ▶ Analysis of pacemaker neurons in mammalian circadian rhythms using Per1 Tg mice and TOYOHASHI probe

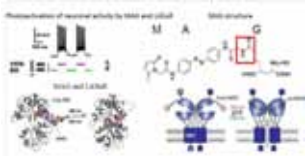
The biochemical, physiological and behavioral processes are under the control of internal clocks with the period of approximately 24 hr, circadian rhythms. The expression of mouse *Period1* (m*Per1*) gene oscillates autonomously in the suprachiasmatic nucleus (SCN). *Per1* is an indispensable member of the central clock system to maintain the autonomous oscillator. I constructed *Per1:luc* Tg mice and rats in which firefly luciferase was rhythmically expressed under the control of the mouse *Per1* promoter in order to monitor mammalian circadian rhythms by *Per1* rhythmic expression.
I performed functional analysis of circadian pacemaker neurons in the SCN by TOYOHASHI original electrophysiological probe with nano-size electrode other than *Per1* expressional rhythms.



Rhythmic emission from the cultured SCN slices of *Per1:luc* Tg mouse persisted for up to some months in vitro. Per1 expression could be observed in one cell level by the SCN slice of *Per1*:GFP Tg. Electric activity of the SCN pace maker neurons could be detected in one cell level by TOYOHASHI probe with nano-several micro meter diameter probe.

Theme 2 ▶ Manipulation of neural activity under optical control by bionanomachine.

I recognize intact biostructure ionotropic glutamate receptors (iGluR6) as machinery, which is normally expressed in synaptic neural processes in mammalian brain. To control any neural activity remotely and reversibly, photoswitchable nanomachine LiGluR were developed based on iGluR6 and operated using photoiosomerizable new chemicals, MAG. Two iGluR6 mutants could be photo-switched using a series of maleimde-azobenzene-glutamate (MAG) compounds, which dangled 2R,4R-allyi glutamate (G) from a linker containing the photoisomerizable azobenzene (A) that was attached to the introduced cysteines via maleimide (M). Three kinds of MAGs were examined at cysteine positions around the "mouth" of the ligand binding domain "clamshell" from geometry. LiGluR: opening in UV light and closing in visible light by all MAGs. In neural cells with LigluR, action potentials were optimally evoked and extinguished by UV and visible light, respectively. These photo-switched nanomachines could manipulate neural activity under optical control both *in vitro* and *in vivo*.



LiGluR is based on the reversible photoisomerization of maleimide-azobenzene-glutamate (MAG) between its *trans* configuration under 500 nm light and its *cis* configuration under 380 nm light. MAG is covalently attached by the maleimide moiety to a cysteine introduced into the ligand-binding domain (LBD) of the receptor. MAG binding under 380 nm light activates the receptor and opens its cation-selective channel, resulting in membrane depolarization.

Theme 3 ▶ Novel Parallelized Electroporation by Electrostatic Manipulation of a Water-in-oil Droplet as a Microreactor

Electroporation is the most widely used transfection method for delivery of cell-impermeable molecules into cells. We developed a novel gene transfection method, water-in-oil (W/O) droplet electroporation, using dielectric oil and an aqueous droplet containing mammalian cells and transgene DNA. When a liquid droplet suspended between a pair of electrodes in dielectric oil is exposed to a DC electric field, the droplet moves between the pair of electrodes periodically and droplet deformation occurs under the intense DC electric field. This method has several advantages over conventional transfection techniques, including co-transfection of multiple transgene DNAs into even as few as 1000 cells, transfection into differentiated neural cells, and the capable establishment of stable cell lines. This technique will lead to the development of cell transfection methods for novel regenerative medicine and gene therapy.

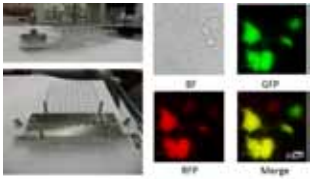


Image of the parallel W/O droplet electroporation electrode for the 8-well string of disposable 96-well plates and HEK293cells transfected fluorescent protein plasmid by W/O droplet electroporation. BF: Bright field image, GFP: Green Fluorescent Protein image RFP: Red Fluorescent Protein image, Merge: Merge image of GFP and RFP

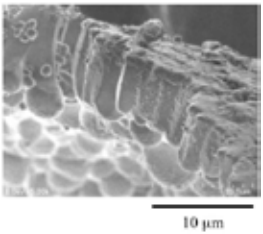
Biomolecular Engineering Laboratory

Staff	• Associate Professor **Eri YOSHIDA** (E-mail : eyoshida@ens.tut.ac.jp)
Laboratory URL	http://www.tutms.tut.ac.jp/~eyoshida/
Key words	Artificial biomembrane models, Molecular self-assembly, Giant vesicles, Morphology control, Polymer surfactant, Amphiphilic block copolymer, Photo-controlled/living radical polymerization, Superhydrophobic surface, Supercritical carbon dioxide, Intelligent supramolecules

Our research group focuses on engineering new materials with high performance and functions by biomimetic approaches using synthetic polymers. We study the mechanisms of structure formation and function expression of biomolecules and tissues from a chemical aspect, and use nanotechnology to fabricate functional biomaterials. We also design intelligent supramolecules using polymers with the structure strictly controlled by the nitroxide-mediated controlled/living radical polymerization technique recently established in our lab.

Theme 1 ▶ Artificial Biomembrane Models Using Polymer Giant Vesicles

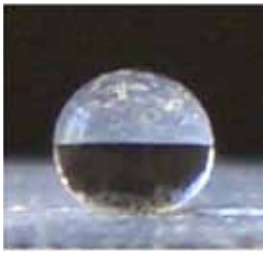
The polymer giant vesicles we created using amphiphilic diblock copolymers are regarded as possible artificial models of biomembranes for cells and organelles, such as erythrocytes, mitochondria, and chloroplasts based on the similarities in their size, structure, and behavior. The models involve an artificial cholesterol model formed with amphiphilic random copolymers. We investigate biological phenomena within the biomembrane from the viewpoint of chemistry based on the slow movement of the copolymers composing the vesicles and engineer the functions originating from the biomembrane on the vesicle membranes. These biomembrane models enable us to presume the shape and morphology of the vesicles through the hydrophobic free energy calculation found in our lab. We also focus on designing the diblock copolymers to control their critical packing shapes in the vesicles. The control of critical packing shapes of the copolymers allows us to fabricate artificial tissues of villus-like structure and to provide the vesicle membrane with the biomembrane phenomena and functions, such as morphological transformation, budding separation in endocytosis, and pore formation in membrane transport.



The FE-SEM image of the villus-like structure prepared by an amphiphilic diblock copolymer

Theme 2 ▶ Fabrication of Superhydrophobic Surface

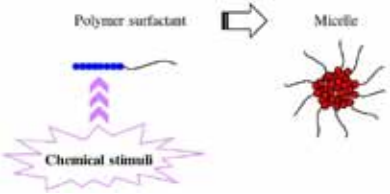
Our group explores new approaches to the superhydrophobic surface with self-cleansing ability by imitating the lotus leaf structure. The simple methods we have recently developed include coating with nanospheres prepared by dispersion polymerization of perfluoroalkyl methacrylate. The surface coated with the nanospheres has superamphiphobicity with the contact angles of 173° for water and 160° for diiodomethane. The synergistic effect of the spherical structure and the high concentration of fluorine on the top of the surface produces the superamphiphobicity. We also have fabricated superhydrophobic surface using micellar-like nanospheres prepared in supercritical carbon dioxide. The nanospheres are formed by self-assembly of CO_2-amphiphilic random copolymers and have the CO_2-philic shell of fluoroalkyl chains and the CO_2-phobic cores. This highly safe method wherein no unreacted monomer and organic solvent remain inside the nanospheres is useful for creating wiperless vehicles.



The image of a water droplet on the surface coated with the nanospheres.

Theme 3 ▶ Design of Intelligent Supramolecules Using Controlled/Living Radical Polymerization

We design and develop a new type of intelligent supramolecules with the responsivity to chemical stimuli, such as electron transfer in oxidation and reduction, photolysis, photo-rearrangement in addition to physical stimuli of temperature, pH, and salt concentration. The supramolecular aggregates, like micelles, serve as nano-sized oxidizing and reducing agents, dyes, and adhesion-latent materials. For obtaining such intelligent supramolecules, we employ polymer surfactants with the structure precisely controlled by the nitroxide-mediated controlled/living radical polymerization.



The schematic image of designing intelligent supramolecules.

Life Science Laboratory

Staff	• Lecturer **So UMEKAGE** (E-mail : umekeage@ens.tut.ac.jp)
Laboratory URL	http://ens.tut.ac.jp/LifeScience/main/
Key words	RNA, RNA pharmaceuticals, RNA engineering, RNA biology, Origin of Life, RNA world

In this laboratory, the development of RNA pharmaceuticals by RNA engineering, the development of a production method of RNA pharmaceuticals using microorganisms and the experimental verification of RNA world hypothesis are performed.

Theme 1 ▶ Design of RNA pharmaceuticals

RNA pharmaceuticals as a new class of drug for gene therapy has attracted considerable attention. However, general RNAs have the disadvantage that they are easily degraded by RNA degradation enzymes; therefore, the development of the technique for stabilization of RNA is required. Our research group has succeeded in the development of the stabilization techniques by circularization and aggregation. In this theme, new creation of RNA pharmaceuticals is attempted using these RNA stabilization techniques.

Theme 2 ▶ Development of RNA pharmaceuticals production method using engineered bacteria

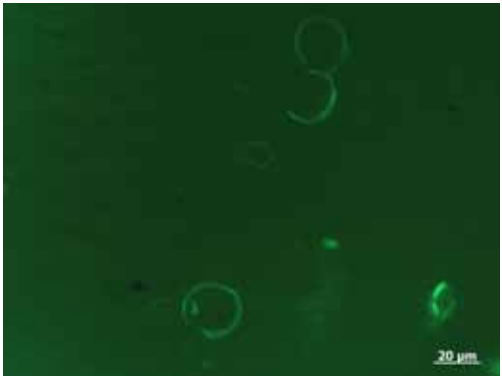
Since RNA pharmaceuticals are produced by the organic synthesis, there is a problem that their production costs are high. In order to solve this problem, the genetically engineered bacteria specialized for the economical production of RNA pharmaceuticals are developed.

Theme 3 ▶ Reproduction of RNA world in test tubes

It is considered and widely accepted that on the prebiotic early earth, the RNA world consisting of self-replicating RNA was structured. However, there are almost no data supporting this idea. In this theme, in order to verify the RNA world experimentally, the environment of primitive earth is reproduced in test tubes, and whether the Darwinian evolution of RNA is possible in this environment is verified. Furthermore, it is attempted to structure a primitive cell model that encapsulates the RNA world in lipid membrane vesicles.

Theme 4 ▶ Identification of circular RNA involved in memory formation

Recently, a circular RNA as new non-coding RNA was discovered. Circular RNA often expresses in brain and spinal cord, and its involvement in the generation and differentiation of brain and the memory formation is pointed out. In this theme, the circular RNA involved in memory formation is identified among the circular RNA generated during neurogenesis.



RNA membrane as a model of primordial membrane

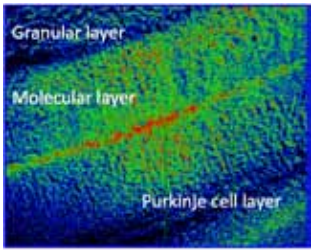
Physiological Bioscience Laboratory

Staff	• Lecturer **Sachiko YOSHIDA** (E-mail : syoshida@ens.tut.ac.jp)
Laboratory URL	http://www.rodent.ens.tut.ac.jp
Key words	Cerebellar development, spatio-temporal visualization of neurotransmitter, developmental neurotoxicity, epigenetics, acoustic impedance microscopy, non-invasive cancer research

We study neuronal development and organ research using animal models and cultured cells through the development of new visualizing device. Our devices could have visualized both the distribution of cancers cells in organs non-invasively, and the neurotransmitter release in living brain slices and neurospheres spatio-temporally. New research system gives us new views and new ideas about lives. We collaborate many engineers and develop something new for biological research.
First theme is visualization of neurotransmitter release in developing cerebellar cortex, and second theme is non-invasive cancer cell research. Newest third theme, which is autism and neuropsychological deficit induced chemicals or environmental conditions, is related epigenetics and evolution of our brain system.

Theme 1 ▶ Visualization of neurotransmitter release in developing cerebellar cortex.

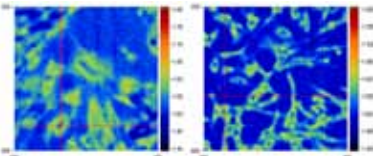
Neurotransmitters are known to play important roles as modulators in the survival and development of cerebellar neurons. We have developed an enzyme-linked real-time assay system of released glutamate, GABA and ATP, and observed their release spatio-temporally. Dynamical change through the development shows the progress of neuronal circuits.



GABA release in developing cerebellar cortex

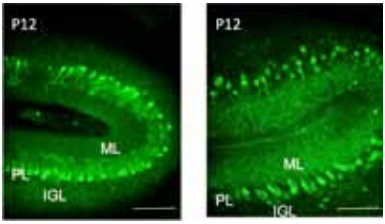
Theme 2 ▶ Non-invasive living cell observation using ultrasonic microscopy

Ultrasonic visualizing system is useful for non-invasive observation of organs, however, its spatial resolution was too poor to visualize cell-level structure and alteration. We have developed the acoustic impedance microscopy for observation of intracellular dynamic structure. This system becomes possible to identify cancer cells in living organs.


Cancer cell observation using acoustic impedance microscopy. Left: normal glial cells, right: cancer cells.

Theme 3 ▶ Autism and neuropsychological deficit induced Chemicals or environmental conditions

Some drugs or chemicals, and environmental stress conditions are known to induce autism of offsprings. We have developed the in vivo detection system for slow-onset neuropsychological deficit using animal models. In autistic animal models, neuronal cells were developed earlier and made irregular distribution. This system is applicable for detection of the chemicals to avoid, and development of recovery treatment from the deficit.



Cerebellar alteration in autistic animal model. Left: control rat cerebellar cortex, right: cerebellar cortex in autistic model animal. Both animals were postnatal day 12. PL: Purkinje cell layer, ML: molecular layer, IGL: internal granular layer.

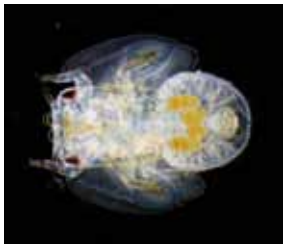
Applied Symbiosis Laboratory

Staff	• Associate Professor **Atsushi NAKABACHI** (E-mail：nakabachi@eiiris.tut.ac.jp)
Laboratory URL	http://www.tut.ac.jp/english/schools/faculty/eiiris/701.html
Key words	insects, bacteria, intracellular symbiosis, aphids, psyllids, bacteriocytes, genomics, secondary metabolites, agricultural pests

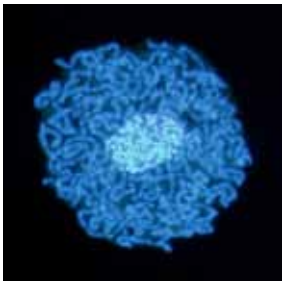
Our research interests focus on the molecular basis for the symbiosis between multicellular organisms and microbes, which has not only been playing key roles in the evolutionary history of life, but is also important for agricultural and medical biotechnologies.

Theme 1 ▶ Studies on intracellular symbioses of pest insects

Many insect lineages including agricultural/medical pests have mutually indispensable associations with bacterial symbionts that are localized in specialized cells called bacteriocytes. We are trying to elucidate the molecular mechanisms for developing and maintaining this type of intimate symbioses.



A nymph of the Asian citrus psyllid, *Diaphorina citri*. The yellow and U-shaped structure is the symbiotic organ that harbors organelle-like intracellular bacteria.



A bacteriocyte of the hackberry petiole gall psyllid, *Pachypsylla venusta*. The cytoplasm is packed with tubular cells of the obligate symbiont, *Candidatus* Carsonella ruddii, surrounding a central nucleus.

Selected publications

•Nakabachi A. (2015) Horizontal gene transfers in insects. *Curr Opin Insect Sci* 7: 24–29.
•Nakabachi A, Ishida K, Hongoh Y, Ohkuma M, Miyagishima SY. (2014) Aphid gene of bacterial origin encodes a protein transported to an obligate endosymbiont. *Curr Biol* 24(14): R640-R641.
•Sloan DB, Nakabachi A, Richards S, Qu J, Murali SC, Gibbs RA, Moran NA. (2014) Parallel histories of horizontal gene transfer facilitated extreme reduction of endosymbiont genomes in sap-feeding insects. *Mol Biol Evol* 31(4): 857-871.
•The International Aphid Genomics Consortium. (2010) Genome sequence of the pea aphid *Acyrthosiphon pisum*. *PLoS Biol* 8(2): e1000313.
•Nikoh N, McCutcheon JP, Kudo T, Miyagishima S, Moran NA, Nakabachi A. (2010) Bacterial genes in the aphid genome: Absence of functional gene transfer from Buchnera to its host. *PLoS Genet* 6(2): e1000827.
•Nakabachi A, Yamashita A, Toh H, Ishikawa H, Dunbar HE, Moran NA, Hattori M. (2006) The 160-kilobase genome of the bacterial endosymbiont *Carsonella*. *Science* 314 (5797): 267.
•Nakabachi A, Shigenobu S, Sakazume N, Shiraki T, Hayashizaki Y, Carninci P, Ishikawa H, Kudo T, Fukatsu T. (2005) Transcriptome analysis of the aphid bacteriocyte, the symbiotic host cell that harbors an endocellular mutualistic bacterium, *Buchnera*. *Proc Natl Acad Sci USA* 102(15): 5477-82.

Theme 2 ▶ Studies on symbiotic bacteria as genetic resources

Making use of omics technologies, we are also pursuing the possibility of utilizing symbiotic bacteria as genetic resources.

Selected publications

•Nakabachi A, Ueoka R, Oshima K, Teta R, Mangoni A, Gurgui M, Oldham NJ, van Echten-Deckert G, Okamura K, Yamamoto K, Inoue H, Ohkuma M, Hongoh Y, Miyagishima SY, Hattori M, Piel J, Fukatsu T. (2013) Defensive bacteriome symbiont with a drastically reduced genome. *Curr Biol* 23(15): 1478-84.
•Moran NA, McCutcheon JP, Nakabachi A. (2008) Genomics and evolution of heritable bacterial symbionts. *Annu Rev Genet* 42: 165-90.

Lab members working at the bench.

Theme 3 ▶ Studies on various agriculture-related symbioses

Agricultural plants have complicated symbiotic relationships with a wide variety of organisms including microbes. We have started some research on this knotty issue.

Selected publications

•Nakabachi A, Nikoh N, Oshima K, Inoue H, Ohkuma M, Hongoh Y, Miyagishima SY, Hattori M, Fukatsu T. (2013) Horizontal gene acquisition of Liberibacter plant pathogens from a bacteriome-confined endosymbiont of their psyllid vector. *PLoS One* 8(12): e82612.

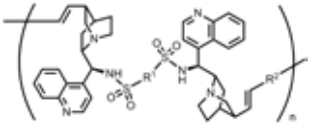
Functional Polymer Chemistry Laboratory

Staff	• Professor **Shinichi ITSUNO** (E-mail : itsuno@ens.tut.ac.jp)
Laboratory URL	http://ens.tut.ac.jp/chiral/
Key words	Asymmetric reaction / polymer-immobilized catalyst / chiral polymer synthesis / chiral organocatalyst / chiral transition metal catalyst / peptide folding / protein folding structure

We carry out research in several areas at the interface of organic chemistry and polymer chemistry and are especially concerned with asymmetric synthesis, reactive polymers, and new chiral polymer synthesis. We mainly focus on the development of new methods of asymmetric synthesis with the aid of polymer immobilized chiral catalysts. We are also considering statistical theory of protein (peptide) folding, which will provide a novel approach to design of new asymmetric catalyst system.

Theme 1 ▶ Chiral polymers as organocatalysts in asymmetric synthesis

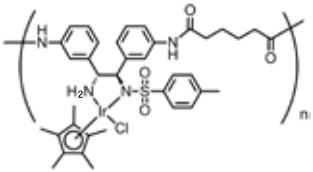
Various efficient asymmetric catalysts have been designed based on cinchona alkaloids, an important class of which are their sulfonamide derivatives. We have developed several syntheses of polymeric cinchona-based catalysts including quaternary ammonium salts, sulfonamides, and squaramide derivatives. These chiral polymers showed excellent catalytic activities with high level of stereoselectivities in various kinds of asymmetric reactions.



Cinchona sulfonamide polymer

Theme 2 ▶ Chiral polymer – transition metal complexes in asymmetric synthesis

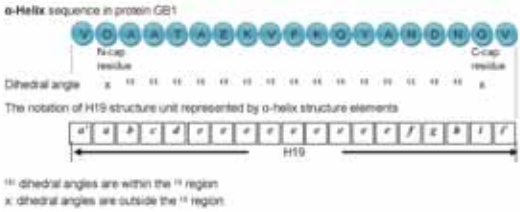
A chiral main-chain polyamide consisting of (*R*,*R*)-1,2-diphenylethylenediamine monotoluenesulfonamide (TsDPEN) repeating unit was prepared. Treatment of the main-chain polymer chiral ligand and transition metal complexes such as $[IrCl_2Cp^*]_2$, $[RhCl_2Cp^*]_2$, and $[RuCl_2(p\text{-cymene})]_2$ afforded the polymer chiral metal complexes. Asymmetric transfer hydrogenation of cyclic sulfonamide was efficiently catalyzed by the chiral TsDPEN polymer - metal complex to give the optically active cyclic sulfonylamine in quantitative conversion and high enantioselectivities.



Chiral polymer - transition metal complex

Theme 3 ▶ Protein folding structures based on probability theory

Decoding, rather than predicting, the initiation mechanism of protein folding from amino acid sequences is a stringent requirement for protein folding researchers. We proposed 44 kinds of folding elements, which covered all the amino acids in the protein chains, and defined all folding structure units. Folding structure formation based on probability theory is the general solution for the initiation mechanism of Anfinsen's tenet of protein folding.



Peptide folding

Melecular Chemistry

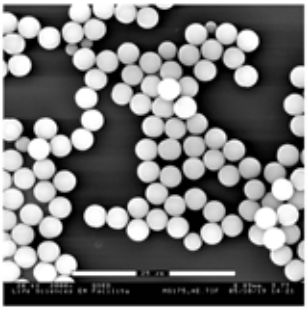
Applied Polymer Chemistry Labratory

Staff	• Associate Professor **Naoki HARAGUCHI** (E-mail：haraguchi@ens.tut.ac.jp)
Laboratory URL	http:// ens.tut.ac.jp/chiral/
Key words	Polymer microsphere, Polymeric catalyst, Functional polymer, Asymmetric reaction, Chiral Organocatalyst, One-pot reaction, Environmentally benign reaction

Our research group is focused on the molecular design and precise synthesis of functional polymers such as polymer microsphere, polymer-supported chiral catalyst and architectural polymer, and the development of their practical use. These functional polymers are applied as asymmetric catalysts for the synthesis of pharmaceuticals, agrochemicals and functional materials. We have further investigated the relationship between polymeric structure and its performance in detail. Through these studies, we are challenging the development of high performance polymeric catalyst and construction of new organic synthesis system.

Theme 1 ▶ Synthesis of functional polymer microsphere

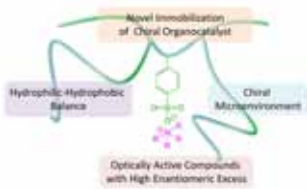
Polymer microspheres have been applied to paints, coatings, diagnostic drugs, cosmetics, precision machines, etc. Precise synthesis of well-defined monodispersed functional polymer microspheres, core-shell polymer microspheres, and hollow polymer microspheres has been developed by precipitation polymerization. Polymer microspheres functionalized with chiral catalyst have been used for a general asymmetric reaction, one-pot asymmetric reaction and an automated flow system for chiral compound synthesis.



Well-defined monodispersed functional polymer microspheres by precipitation polymerization

Theme 2 ▶ Polymer-supported chiral catalyst for asymmetric reaction

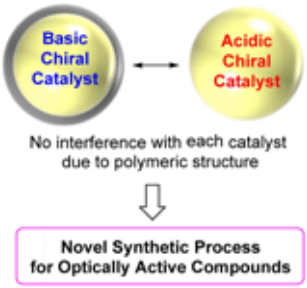
Polymer-supported chiral organocatalysts and polymer-supported chiral organometallic catalysts have been developed for the efficient synthesis of chiral product using asymmetric reaction. Immobilization of chiral catalyst onto polymer facilitates the separation of chiral product from reaction mixture. In addition, the recovered polymeric chiral catalyst can be reused. Recently, main-chain polymer of chiral organocatalyst, novel immobilization of chiral organocatalyst onto polymer by ionic bonding, and amphiphilic polymer-supported chiral catalyst for asymmetric reaction in water have been developed. These polymeric catalysts show high catalytic activity in a variety of asymmetric reaction.



Polymer-supported chiral organocatalyst

Theme 3 ▶ Development of novel organic synthesis process using polymeric catalyst

Polymeric catalyst can provide specific microenvironment that it is difficult to realize in a reaction using the corresponding molecular catalyst. We have focused on one-pot reaction by using combination of multiple catalysts (i.e. acid and base catalysts) which are difficult to use simultaneously. Automated synthesis using polymeric catalyst has also been investigated.



Novel synthetic process by using combination of multiple catalysts

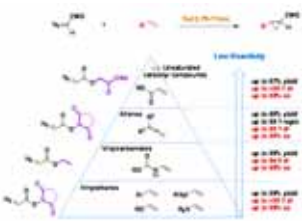
Synthetic Organic Chemistry Laboratory

Staff	• Professor **Seiji IWASA** (E.mail：iwasa@ens.tut.ac.jp) • Project Assistant Professor **Soda CHANTHAMATH** (E.mail：cs008@edu.imc.tut.ac.jp)
Laboratory URL	http://www.siorgchem.ens.tut.ac.jp/index.html
Key words	asymmetric catalyst, ruthenium, carbene, diazo compound, cyclopropanation, antibody, molecular sensor, computational chemical analysis

Our research group is engaged on several areas of organic molecular research such as development of new methodologies for catalytic asymmetric synthesis, highly sensitive immunoassay for pesticide residue and natural products chemistry.
And

Theme 1 ▶ Development of Enantioselective Catalysts for Carbene Transfer and Various Bond Forming Reactions

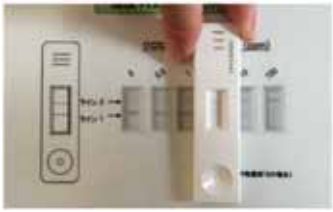
Newly designed chiral ligands, a series of chiral bis (oxazolinyl) pyridine and phenyl oxazoline (Pheox) derivatives and their transition metal complexes can be used for synthesis of optically active organic molecules. Especially, Ru(II)-Pheox catalyst and its microporous polymer are found to be a powerful chiral catalyst for carbene transfer reactions to synthesize optically active cyclopropane derivatives. We are also pursuing application of the newly developed methods for the synthesis of biologically relevant molecules.



Ru(II)-Pheox catalyzed cyclopropanations

Theme 2 ▶ Development of A Monoclonal Antibody-based Immunoassay

We have developed an enzyme-linked immunosorbent assay (ELISA) system based on a monoclonal antibody (MoA) to detect small molecules such as pesticide residue in environment, combining with synthetic organic chemistry, molecular biology and antibody technology. The working range was 0.3ng/mL level. Recently, we developed novel immunochromatographic assay kits for analyzing pesticide residue in agricultural products.



Novel immunochromatographic assay kits

Theme 3 ▶ Natural Products Chemistry

Our research interests are extraction, isolation and purification of natural products from various plants cooperation with southern Asian countries and also total synthesis of natural products such as DCG-IV, Dysibetaine CPa, Strychnine.

Natural products from Melaleuca tree in VN

Melecular Chemistry

Polymer Materials Engineering Laboratory

Staff	• Professor **Hideto TSUJI** (E-mail : tsuji@ens.tut.ac.jp) • Assistant Professor **Yuki ARAKAWA** (E-mail : yarakawa@ens.tut.ac.jp)
Laboratory URL	http://ens.tut.ac.jp/BDPolym/
Key words	bio-based polymers; sustainable polymers; biodegradable polymers; poly(lactic acid); stereocomplex; liquid crystal, structure-property relationship

We carry out three research projects; (1) Development of bio-based, sustainable, and biodegradable polymers, (2) Stereocomplex formation between enantiomeric polymers, and (3) Synthesis of novel liquid crystalline molecules, and investigation of their phase structures and optical/electrical properties. Our publications have now gathered more than 12,000 citations (SCOPUS).

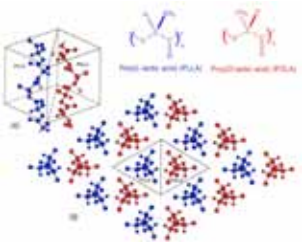
Theme 1 ▶ Development of Bio-based, Sustainable, and Biodegradable Polymers

Bio-based, sustainable, and biodegradable polymers such as poly(lactic acid) (PLA), which is produced from renewable resources like corn starch and other plant-derived resources, have been extensively studied for various applications. We synthesize bio-based, sustainable, and biodegradable polymers with a wide variety of molecular and higher ordered structures via ring-opening-polymerization of aliphatic lactones (including lactide) or polycondensation of aliphatic hydroxycarboxylic acid utilizing various combination of monomer, comonomer and initiator and various treatments and investigate their crystallization behavior, physical properties, and biodegradation behavior, and are aiming to develop high performance or functional bio-based, sustainable, and biodegradable polymers.

Synthesis, recycling, and degradation of poly(lactic acid) (PLA).

Theme 2 ▶ Stereocomplex Formation between Enantiomeric Polymers

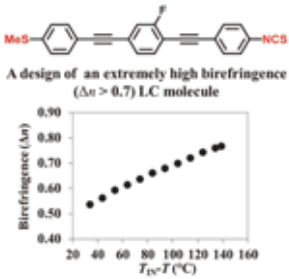
Stereocomplex (SC) formation or crystallization occurs between enantiomeric optically active polymers such as poly(L-lactic acid) and poly(D-lactic acid). Stereocomplexation elevates material mechanical properties and resistance to thermal/hydrolytic degradation. Of SCs, PLA SC is attracting much attention from polymer researchers in terms of their unique crystallization behavior and applicability for reinforcing material properties. We utilize PLA SC as a model SC and investigate the effects of a wide variety of molecular structures on SC crystallization and the effects of SC crystallization on physical properties and morphologies. We are also looking for the new pairs and combinations of enantiomeric polymers which can form SC and have found seven polymer pairs and combinations which can form SC.



Crystal structure of PLA SC.

Theme 3 ▶ Synthesis of novel liquid crystalline molecules, and investigation of their phase structures and optical/electrical properties.

Liquid crystals located between solid crystals and isotropic liquids have a unique property which is able to spontaneously orient along external forces including electromagnetic field and rubbing, and so on. Taking advantage of the alignment property, liquid crystalline (LC) materials are of great interest for various optical and electrical applications as well as scientific concern. In order to use them for various applications, synthesis of new LC molecules as well as evaluation of their optical and electrical properties is significantly important. Our study is aimed at revealing the relationships between molecular structures and optical/electrical properties such as refractive index, birefringence, dielectric constant, fluorescence and charge mobility, etc. Our approaches include design, synthesis, thermal and phase structural analysis, and optical/electrical measurements of novel LC molecules including low-molecular compounds as well as polymers.



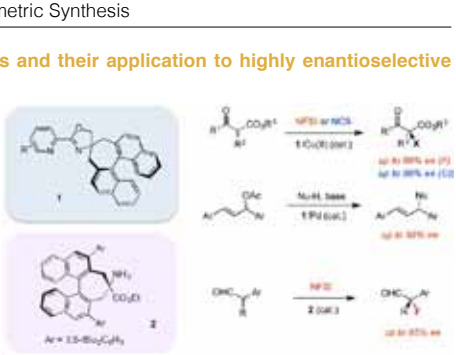
Novel LC molecular and its temperature dependence of Δn at 550 nm.

Organic Chemistry Laboratory

Staff	• Associate Professor **Kazutaka SHIBATOMI** (E-mail：shiba@ens.tut.ac.jp)
Laboratory URL	http://ens.tut.ac.jp/orgchem/
Key words	Organic Chemistry/ Pharmaceutical Chemistry/ Fluorine Chemistry/ Organocatalysis/ Organometallic Chemistry/ Asymmetric Synthesis

Theme 1 ▶ Development of novel chiral catalysts and their application to highly enantioselective reactions

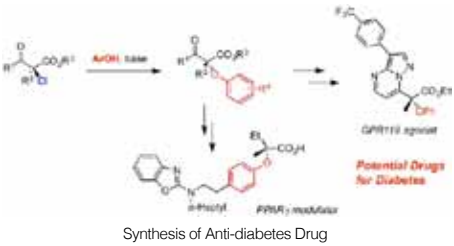
We have been studying the development of novel chiral transition-metal catalysts and organocatalysts. For example, we synthesized a new class of chiral oxazoline ligands 1 with a spiro structure and successfully applied them to various metal-catalyzed asymmetric transformations giving high enantioselectivity, such as Cu(II)-catalyzed enantioselective halogenation and Pd(0)-catalyzed C-C bond forming reactions. Recently, we also developed a new chiral primary amine catalyst 2 having an axial chiral binaphthyl backbone, which catalyzed the asymmetric fluorination of a-branched aldehydes with high enantioselectivity. These reactions could be utilized to the asymmetric synthesis of biologically active compounds.



Asymmetric Reactions with Newly Developed Chiral Catalysts

Theme 2 ▶ Asymmetric synthesis of chiral halogenated compounds and their derivatization via the stereospecific carbon-halogen bond cleavage

We achieved highly enantioselective halogenation reactions with the above-mentioned chiral catalysts, which have had difficulty in achieving high enantioselectivity so far. We also achieved the derivatization of the resulting halogenated compounds via stereospecific carbon-halogen bond cleavage. In particular, the S_N2 substitution of α-chloro-β-keto esters proceeded smoothly despite the fact that the reaction occurred at a tertiary carbon center. Using this method, we demonstrated the synthesis of a potential treatment for type 2 diabetes.



Synthesis of Anti-diabetes Drug

Melecular Chemistry

Interface physical chemistry Laboratory

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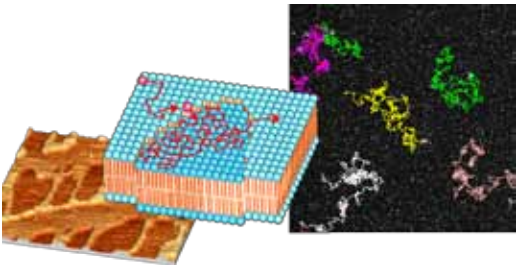
Laboratory URL	http://ens.tut.ac.jp/interface/
Key words	Lipid bilayer, cell membrane, surface chemistry, atomic force microscopy, fluorescence microscopy, single molecule observation

Lipid bilayers are fundamental structures of cell membranes, and provide reaction fields to membrane proteins relating to the transportation of signal, materials and energy into and out of cells. Our research targets are fundamental processes in artificial cell membrane systems, (e.g. lipid diffusion, domain formation/dissipation, peptides and protein assemblies) during the activities of membrane proteins and functional peptides. We are also interested in applications of the artificial cell membrane systems to nanomaterials and plasma medicine.

Theme 1 ▶ Structure and dynamics in artificial cell membrane systems

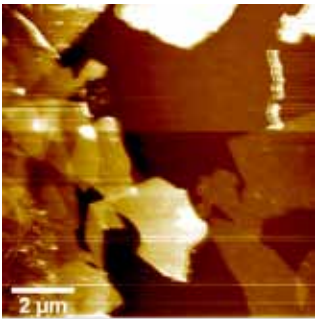
Lateral lipid diffusion and domain formation are important fundamental processes at biological reactions on cell membranes. We investigate lateral diffusion, domain formations and their relation with protein reactions using supported lipid bilayers as artificial cell membrane systems. Atomic force microscope and fluorescence microscope are complementary methods to observe structures in the supported bilayers on nano- to micrometer scales. We use fluorescence microscope-based techniques for the investigation of molecular diffusion, to evaluate diffusion coefficient and its spatiotemporal dependence quantitatively: fluorescence recovery after photobleaching and fluorescence single molecule tracking.



Theme 1: Domain formation and lateral diffusion in a supported lipid bilayer

Theme 2 ▶ Artificial lipid bilayer platform on graphene oxide

Graphene oxide is a single atomic sheet material, derived from graphene, sp2 carbon sheet. Graphene oxide is an amphiphilic 2D material consisting of hydrophobic pristine graphene region and that modified with oxygen functional groups, and shows a unique fluorescence quenching property. We are investigating the interaction between GO and lipid bilayer, and developing lipid bilayer platform on graphene oxide.



Theme 2: AFM topography of lipid bilayer on GO deposited on a SiO2/Si substrate.

Theme 3 ▶ Plasma on plasma membrane

Atmospheric pressure plasma is applied as a novel and valuable tool in the medical and biological fields. We apply artificial lipid bilayer systems to understand the mechanism how the plasma-induced active species (reactive oxygen/nitrogen species) affect and pass through cell membrane. We showed that irradiation of irradiation of atmospheric pressure plasma made nanopores on lipid bilayer membranes.