BIOTECHNOLOGY

Knockout Mice for Inflammatory Disease Research

Valuable for drug discovery, especially for validation of the target mechanisms of various inflammatory diseases

Professor Yasuo Mori – School of Global Environmental Studies
Dr. Shinichirou Yamamoto – Graduate School of Pharmaceutical Sciences

Prof Yasuo Mori and Dr. Shinichiro Yamamoto have developed the TRPM2 knockout mice. TRPM2 is a member of the transient receptor potential protein (TRP) family and its gene encodes a plasma-membrane calcium ion channel. Recent research have suggested that TRPM2 plays important roles in inflammatory responses, and that it is/may be related to rheumatoid arthritis, asthma, Alzheimer's, or other diseases caused by inflammation. TRPM2 knockout mice serve as a valuable animal model for drug discovery, in screening, developing and clarifying mechanisms of various inflammatory diseases. TRPM2 knockout mice are available as research materials.
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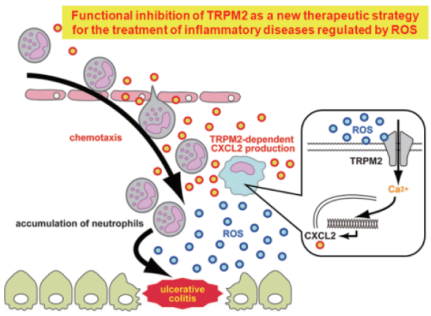

An ENU-induced Mutant Archive for Gene Targeting in Rats

A method for generating rat models of human diseases

Professor Tadao Serikawa – Institute of Laboratory Animals
Dr. Tomoji Mashimo – Institute of Laboratory Animals

Chemical mutagenesis is a powerful tool to produce genetically modified mutations in many species, especially where no functional embryonic stem cell lines exist. The ENU (N-ethyl N-nitrosourea) mutagenesis, followed by a screening method to detect single nucleotide substitutions within the targeted gene, is one of the most promising technologies in rats. Prof Tadao Serikawa and Dr. Tomoji Mashimo have developed a novel, efficient approach that combines two methods: a high-throughput, low-cost screening assay which makes use of the Mu-transposition reaction (MuT-POWER); and intracytoplasmic sperm injection (ICSI) for the recovery of the rare heterozygous genotypes from their newly generated frozen sperm repository, the Kyoto University Rat Mutant Archive (KURMA). So far several rat models of gene-targeted human diseases, such as cancer, obesity, hyperlipidemia, and neurological diseases, have been developed from the KURMA and used for drug development and translational research.
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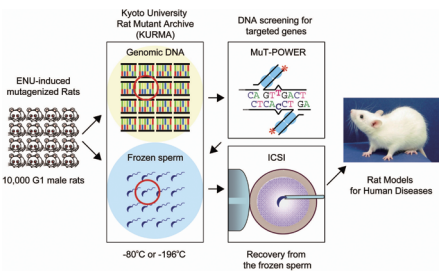

Prognostic Factor in Sarcoma, and Metastasis Inhibitor

Use of AFAP1L1 as a gene involved in the distant metastasis of a tumor or its long-term prognosis

Professor Junya Toguchida – Institute for Frontier Medical Sciences *and* CiRA

Prof Junya Toguchida and his research team found that the gene encoding a protein of previously unknown function, AFAP1L, specifically expresses in sarcomas and colon cancer cells and that the intracellular accumulation of AFAP1L varies according to the grade of malignancy of tumor cells. The present discovery thus provides a method for determining the risk of distant metastasis in a tumor by (1) measuring the expression level of AFAP1L1 in tumor tissue, and (2) examining the correlation between the expression level and incidences of distant metastasis. Also provided is a metastasis inhibitor comprised of a polynucleotide complementary to mRNA encoding AFAP1L1.

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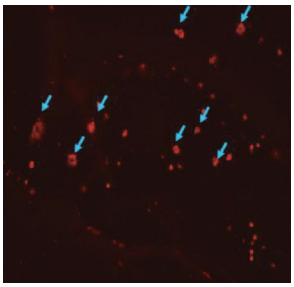
Development of Probe for In Vivo Molecular Imaging of β-amyloid and Tau Proteins in Alzheimer's Brain

Novel modality of molecular imaging for diagnosis and therapy of Alzheimer's disease

Professor Hideo Saji – Graduate School of Pharmaceutical Sciences
Associate Professor Masahiro Ono – Graduate School of Pharmaceutical Sciences

Prof. Hideo Saji and Associate Prof. Masahiro Ono at the Graduate School of Pharmaceutical Sciences have developed several molecular probes for -amyloid (A) and tau proteins, including positron emission tomography (PET) and single photon emission computed tomography (SPECT) tracers labeled with a radioisotope. In addition to PET/SPECT probes, they have currently focused on the development of near infrared fluorescent (NIRF) probes for optical imaging of A and tau proteins. To develop fluorescent probes for optical imaging of A plaques, they first synthesized several derivatives based on boron dipyrromethane (BODIPY), one of the common fluorophores, and evaluated their utility as A imaging probes. When in vitro plaque labeling was carried out using brain sections from a mouse model of Alzheimer's (Tg2576), some of them clearly stained -amyloid plaques in the brain sections. In addition, the BODIPY derivative showed in vivo A plaque labeling in Tg2576 mice.



[right] Ex vivo fluorescent image in the brain after injection of a BODIPY derivative.

Although optical imaging techniques are not quantitative, especially with significant signal attenuation in tissue, NIRF imaging has the potential to provide a rapid, inexpensive, and nonradioactive drug screening system for Alzheimer's. Currently, the research team is also attempting to develop optical imaging probes targeting tau proteins.

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Method of Stabilizing Calcium Phosphate Fine Particles

Hydroxyapatite microcapsule for drug delivery system (DDS)

Professor Takeshi Yao – Graduate School of Energy Science

Prof Takeshi Yao has developed the technology which relates to a method for stabilizing calcium phosphate fine particles formed from Simulated Body Fluid (SBF) whose ionic concentrations are similar to those of human blood plasma. These fine particles have high activity for forming hydroxyapatite (HAp) from body fluid and are named Apatite Nuclei. The Apatite Nuclei are precipitated from SBF by raising pH or temperature and then the growth is halted by lowering the inorganic concentration surrounding them. The Apatite Nuclei can be preserved for long periods, while maintaining its high activity for forming HAp. Microspheres of metals, ceramics and polymers are easily encapsulated with HAp by using the Apatite Nuclei. The resultant microcapsules are biocompatible, show sustained release and are expected to be applied to one of ideal carriers for DDS.
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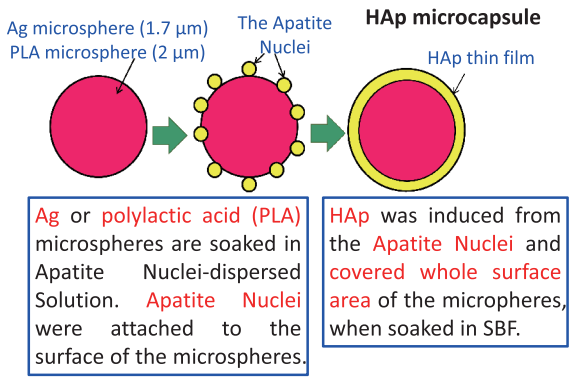

New Method for Producing Alkaloid

Method for mass production of alkaloid

Professor Fumihiko Sato [left] – Graduate School of Biostudies
Dr. Hiromochi Minami [right] – Ishikawa Prefectural University

Prof Fumihiko Sato and Dr. Hiromochi Minami have provided a novel method for producing reticuline and related alkaloids in microbes. Reticuline is the key intermediate for producing the isoquinoline alkaloids. Such isoquinoline alkaloids include morphine, codeine, papaverine, berberine among others. These alkaloids are used in medicine. In this technology, reticuline and the related alkaloids, scoulerine and magnoflorine, are produced with the combination of *Micrococcus luteus* and plant enzymes.
int.icc.kyoto-u.ac.jp/?p=1238

The microbial platform is further developed for the effective synthesis of stereo-specific reticuline and related alkaloids from glucose or glycerol as a culture substrate .
dx.doi.org/10.1038/ncomms1327

Suppressive Effect of Siphonaxanthin on the Differentiation of Preadipocytes to Adipocyte

Antiobesity effects of siphoxanthin from green algae

Professor Takashi Hirata – Graduate School of Agriculture
Associate Professor Tatsuya Sugahara – Graduate School of Agriculture

Prof Takashi Hirata and Associate Prof Tatsuya Sugahara evaluated the suppressive effects of naturally occurring carotenoids on the differentiation of 3T3-L1 preadipocytes to adipocytes. Treatment with siphonaxanthin significantly reduced lipid accumulation in 3T3-L1 cells during differenciation to adipocytes. This suppressive effect was stronger than that of fucoxanthin which is also known to show anti-obesity effects. Their findings provide that the green algal carotenoid, siphonaxanthin, is an active component for antiobesity.
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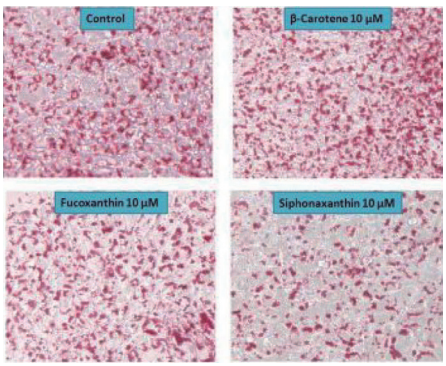

CHEMISTRY

Cross-Coupling Catalyst System for Synthesis of Aromatic Compounds

Novel Iron-based Cross-coupling catalysts

Professor Masaharu Nakamura – Institute for Chemical Research
Assistant Professor Takuji Hatakeyama – Institute for Chemical Research

Recent advances in cross-coupling methodologies have made an enormous contribution to the synthesis of organic electronic materials as well as medicinal/agrochemical compounds. Prof Masaharu Nakamura and Assistant Prof Takuji Hatakeyama have developed several iron-based catalyst systems that are highly effective for the cross-coupling reactions. By using their methods, a variety of alkyl halides are cross-coupled with arylmetal reagents in high to excellent yields, mostly exceeding 90%. The newly developed catalyst systems are easy to handle, ecologically friendly, cost-effective and less toxic compared to the conventional catalysts. Therefore, the methods developed in the Nakamura group can be used as powerful alternatives to the Nobel Prize-winning Suzuki-Miyaura and Negishi coupling reactions, which are regularly applied for the syntheses of functional aromatic compounds by using the rare-metal catalysts, such as palladium and nickel.
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fig1


fig2

Synthesis of Cycloparaphenylenes from a Square-Shaped Tetranuclear Platinum Complexes

General synthesis of hoop-shaped π-conjugated molecules

Professor Shigeru Yamago – Institute for Chemical Research

Prof Shigeru Yamago has developed a new synthetic method for cycloparaphenylenes, which are the simplest structural unit of armchair carbon nanotubes. The method allows the synthesis of several cycloparaphenylenes including [8]cycloparaphenylene, which is the smallest cycloparaphenylene derivative synthesized to date, by way of square shaped tetranuclear biaryl-platinum complexes. Cycloparaphenylenes shows different fluorescence depending on the ring size and provides new fundamental skeletons of organic opt-electronic materials. Also, this technology can be applied for the synthesis of various cycloparaphenylene derivatives.

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Alcohol as Initiator for Living Radical Polymerization – Based on Reversible Chain Transfer Catalyzed Polymerization (RTCP)

Easily obtain end-functional polymers, block copolymers, star and comb-shaped branched polymers, and graft polymers on surfaces

Associate Professor Atsushi Goto – Institute for Chemical Research
Professor Yoshinobu Tsujii – Institute for Chemical Research

Associate Prof Atsushi Goto and Prof Yoshinobu Tsujii have developed a novel class of living radical polymerization using organic catalysts, termed RTCP. The catalysts are attractive for their low cost, low toxicity, and ease of handling. In this work, Goto and Tsujii develop a novel initiating system for RTCP using alcohols as the initiators (initiating dormant species) (this work concerns the initiator but not the catalyst). In LRP (living radical polymerization), a number of works have used alcohols as the initiating moieties by attaching LRP dormant species to them via esterification or other methods. In most cases, the product was purified and isolated, and then subjected to polymerization. This is a two-step process consisting of the attachment and the polymerization as separate steps. A striking advantage of the invention is that many non-conjugated alcohols can be used. Without prior chemical modification (attachment of LRP dormant species), we may obtain from molecules and substrates with hydroxyl group(s), end-functional polymers, block copolymers, star and comb-shaped branched polymers, and graft polymers on surfaces in a single step.

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Triaryl (1-pyrenyl) bismuthonium Salts: Efficient Photoinitiators for Cationic Polymerization of Oxiranes and a Vinyl Ether

Photoinitiators for cationic polymerization with low-toxicity

Professor Hiroshi Imahori – Graduate School of Engineering
Associate Professor Yoshihiro Matano – Graduate School of Engineering

Photoirradiation of triaryl(1-pyrenyl)bismuthonium salts in acetonitrile afforded triarylbismuthanes and pyrene, accompanied by the generation of protic acids. Prof Hiroshi Imahori and Associate Prof Yoshihiro Matano have found that triaryl(1-pyrenyl)bismuthonium hexafluoroantimonates behave as efficient photoinitiators for the cationic polymerization of oxiranes and vinyl ethers, affording the corresponding polymers in good yields within a minute.

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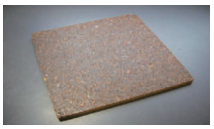
MATERIALS



Wood-based Materials without Harmful Chemical Substances

Potential applications in construction materials: particleboards, medium-density fiberboards and plywood

Associate Professor Kenji Umemura – Research Institute for Sustainable Humanoshere (RISH)

Associate Prof Kenji Umemura has developed recyclable wood-based materials from bark and waste wood etc. without using petroleum-based chemical adhesives. The product can be used for making house-hold items such as furniture and for other purposes. The procedure to produce thiese products is simple and uses only non-toxic natural materials. First, bark powder or wood chips etc. are mixed with citric acid and sucrose. Second, the mixture is heat-pressured under controlled conditions. The materials become hardened in about 10 minutes. Various wood-based materials such as moldings, particleboards, fiberboards, and plywood can be fabricated. They are suitable for various uses in: construction materials, houses, furniture, etc.
int.saci.kyoto-u.ac.jp/?p=1151

Metal Nanostructures Formed by Electrodeposition within Hydrophobic Microporous Silicon

Metal nanostructures

Professor Yukio Ogata – Institute of Advanced Energy
Assistant Professor Kazuhiro Fukami – Institute of Advanced Energy

Assistant Prof Kazuhiro Fukami and Prof Yukio Ogata have recently developed a method to prepare metal nanostructures, such as nanoparticles and nanofibers, by electrodeposition in chemically-modified porous silicon electrodes. Porous silicon, several nanometers in diameter, have very large surface areas and high porosity. Therefore it has garnered attention for its utilization as a template for metal electrodeposition. However, the oxidation of silicon, which induces the uncontrollable displacement deposition process always takes place in aqueous deposition baths. The researchers modified the porous silicon by using organic molecules. In addition, they found that the organic molecules modified on the porous silicon wall must be hydrophobic, otherwise metal electrodeposition would not proceed within the template. For instance, they succeeded in the formation of dispersed platinum nanoparticles supported within a porous silicon matrix.
int.icc.kyoto-u.ac.jp/?p=1820

Ductile Porous SiC Ceramics with Fiber Reinforcement

Novel silicon carbide composites with high temperature oxygen-resitance

Associate Professor Tatsuya Hinoki – Institute of Advanced Energy

Silicon carbide ceramics are very attractive engineering ceramics, particularly for high temperature use and nuclear applications due to its tolerance to high temperatures, oxygen resistance, chemical stability, low activation, radiation resistance and so on. However the application of silicon carbide ceramics is limited due to its brittle features, leading to the development of Novel silicon carbide composites by the Hinoki research group. The material consists of silicon carbide fibers and a porous silicon carbide matrix as shown in the following figure. The composites show pseudo-ductile behavior and complex fracture behavior due to frictional stress at the debonded fiber/matrix interface.

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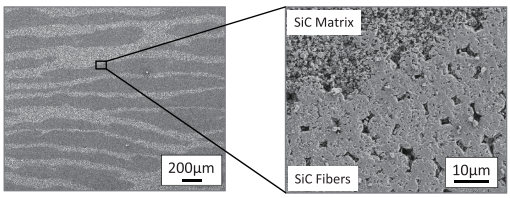

[Right] SEM images of the novel silicon carbide composites with porous matrix

ENERGY & ENVIRONMENT

Photocatalytic Membrane Reactor Based on Integration of Hydrogen Generation and Separation Functions

A new hydrogen separation membrane for fuel cell application

Professor Kazumi Matsushige – Graduate School of Engineering
Dr. Kei Noda – Graduate School of Engineering

Prof Kazumi Matsushige and Dr. Kei Noda have recently developed a new photocatalytic hydrogen separation membrane, where hydrogen generation and separation functions are integrated inside a single membrane. This membrane consists of anodized titanium dioxide (TiO_2) nanotube arrays (TNAs) and a hydrogen permeable metal film. In this membrane, hydrogen can be generated photocatalytically from alcohol or water on the surface of TNAs under ultraviolet illumination and the generated H_2 can be separated from other byproduct gases through the hydrogen permeable metal film. Thus, the generation and separation of hydrogen is simultaneously achieved in a single membrane. This technique is promising for realizing further miniaturization and low temperature operations of hydrogen reformers.

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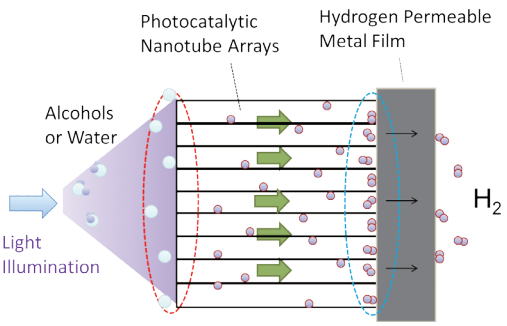

Rational Molecular Design of Organic Dyes for Highly Efficient Dye

Sensitized solar cells using Intramolecular B–N coordination as a key scaffold

Associate Professor Atsushi Wakamiya – Institute for Chemical Research

Associate Prof Atsushi Wakamiya and his research team have disclosed a new molecular design concept of organic dyes for dye-sensitized solar cells (DSSC) in which -electron accepting unit containning an intramolecular boron-nitrogen (B-N) bond is used as a key skeleton (Fig. 1). The introduction of the intramolecular B-N bond enables the tuning of the electronic structure of organic dyes to increase its pi-electron accepting capacity. As a model compound of this molecular design concept, the researchers synthesized boryl-substituted thienylthiazole-containing organic dye. The DSSC using this compound showed a high incident photon-to-current efficiency (IPCE) of over 90% in the 410-550 nm region and with an overall conversion efficiency of 5.99%. The electronic structure of the present systems can be easily tuned by the substituent on the boron atom, suggesting the potential for more red-shifted absorption and higher overall conversion efficiency.

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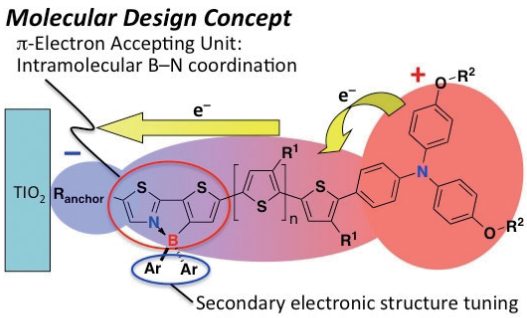

Fig 1. Molecular design concept using π-electron accepting unit containing an intramolecular B–N coordination bond as a key skeleton.

Sensoring Hydrogen Gas Concentration at Room Temperature Using Electrolyte Made of Proton Conductive Manganese Dioxide

Hydrogen fuel type automobile in near future needs simple H_2 sensor for the fuel meter

Associate Professor Hideki Koyanaka – iCeMS
Assistant Professor Yoshikatsu Ueda – RISH

Hydrogen gas promises to be a major clean fuel in the near future. Thus, sensors that can measure the concentrations of hydrogen gas covering a wide dynamic range (e.g. 1-99.9%) are in demand for its production, storage, and utilization. However, it is difficult to directly measure hydrogen gas concentrations greater than 10% using conventional sensors. Associate Prof Hideki Koyanaka and Assistant Prof Yoshikatsu Ueda have introduced a simple sensor using an electrolyte made of proton conductive manganese dioxide that enables in-situ measurements of hydrogen gas concentrations within a wide range of 0.1-99.9% at room temperature.

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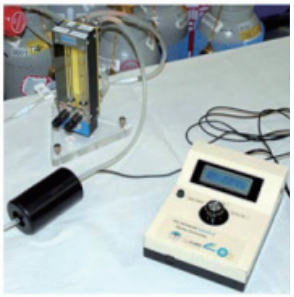

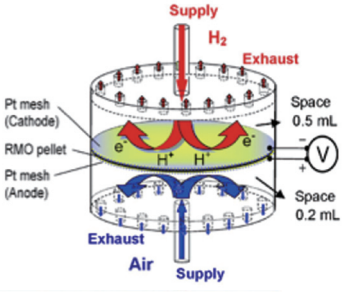

OTHERS

A Topology Optimization Method Based on the Level Set Method Incorporating a Fictitious Interface Energy

Professor Shinji Nishiwaki – Graduate School of Engineering
Assistant Professor Kazuhiro Izui – Graduate School of Engineering

Prof Shinji Nishiwaki and his research team have proposed a new topology optimization method, which can adjust the geometrical complexity of optimal configurations, using the level set method and incorporating a fictitious interface energy derived from the phase field method. First, a topology optimization problem is formulated based on the level set method, and the method of regularizing the optimization problem by introducing fictitious interface energy is explained. Next, the reaction–diffusion equation that updates the level set function is derived and an optimization algorithm is then constructed, which uses the finite element method to solve the equilibrium equations and the reaction–diffusion equation when updating the level set function. Finally, several optimum design examples are shown to confirm the validity and utility of the proposed topology optimization method.

Comput. Methods Appl. Mech. Engrg. 199 (2010) 2876–2891

Analysis-and-Manipulation Approach to Pitch and Duration of Musical Instrument Sounds Without Distorting Timbral Characteristics

Professor Hitoshi G. Okuno – Graduate School of Informatics

The aim of the technology is to manipulate the pitch and duration of a musical instrument sound with minimal distortion to timbral features. It also provides a method to superimpose two musical instrument sounds. The user can choose and mix any instrument timbre like a sound palette, and then replace some parts of the musical performance with it. The technology consists of three steps: (1) “Analysis”: Separation of signals from a musical instrument by using an integrated instrument sound model of harmonic and non-harmonic structures while extracting timbral features. It also obtains the residue. (2) “Manipulation”: Manipulation of pitch, duration, and non-harmonic structure to create a new sound from signals of any musical instrument and (3) “Synthesis”: Synthesizing harmonic and non-harmonic signals for the new sound and adding them to the residue to get a new performance.
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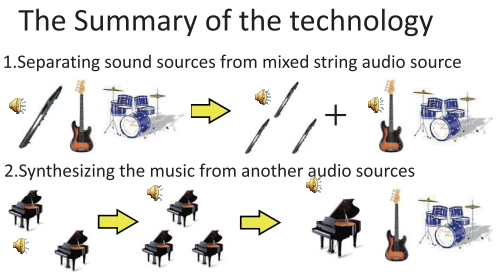

For further information of available technologies：
www.kyoto-u.ac.jp/en/research