

SANKEN, Osaka University

# Annual Report 2022

Year ended March 31, 2022

SANKEN



The Institute of Scientific and Industrial Research (ISIR: SANKEN) was established at Osaka University in 1939 in response to strong demand from the Kansai business community for a research institute focused on “basics and applications of natural sciences necessary for industry”. From the very beginning, we have been aiming at developing new interdisciplinary research areas, and in response to the needs of society and times, we have been reshaping our organization and broadening our research fields. In 2009, we have expanded to the current four research divisions: Information and Quantum Sciences, Advanced Materials and Beam Science, Biological and Molecular Sciences, and Nanoscience and Nanotechnology.

In 2010, we started Japan’s first Network-type Joint Research Center for Materials and Devices, consisting of five research institutes, in collaboration with IMRAM (Tohoku University), RIES (Hokkaido University), CLS (Tokyo Institute of Technology), and IMCE (Kyushu University). We are also carrying out a joint research project that has renewed from 2022 as “Crossover Alliance for Creating the Future with Human, Knowledge and Materials (Five-star Alliance)” involving five research institutes; hence, forming a strong scientific network all over the country and increasing research abilities.

During this period, the social situation and industrial structure of Japan and the rest of the world have been constantly changing. However, even today, 80 years after foundation of the SANKEN, its philosophy has not changed, and we are vigorously promoting our goals - finding the next direction of science and technology and leading advanced scientific and social implementation of world-leading technologies.

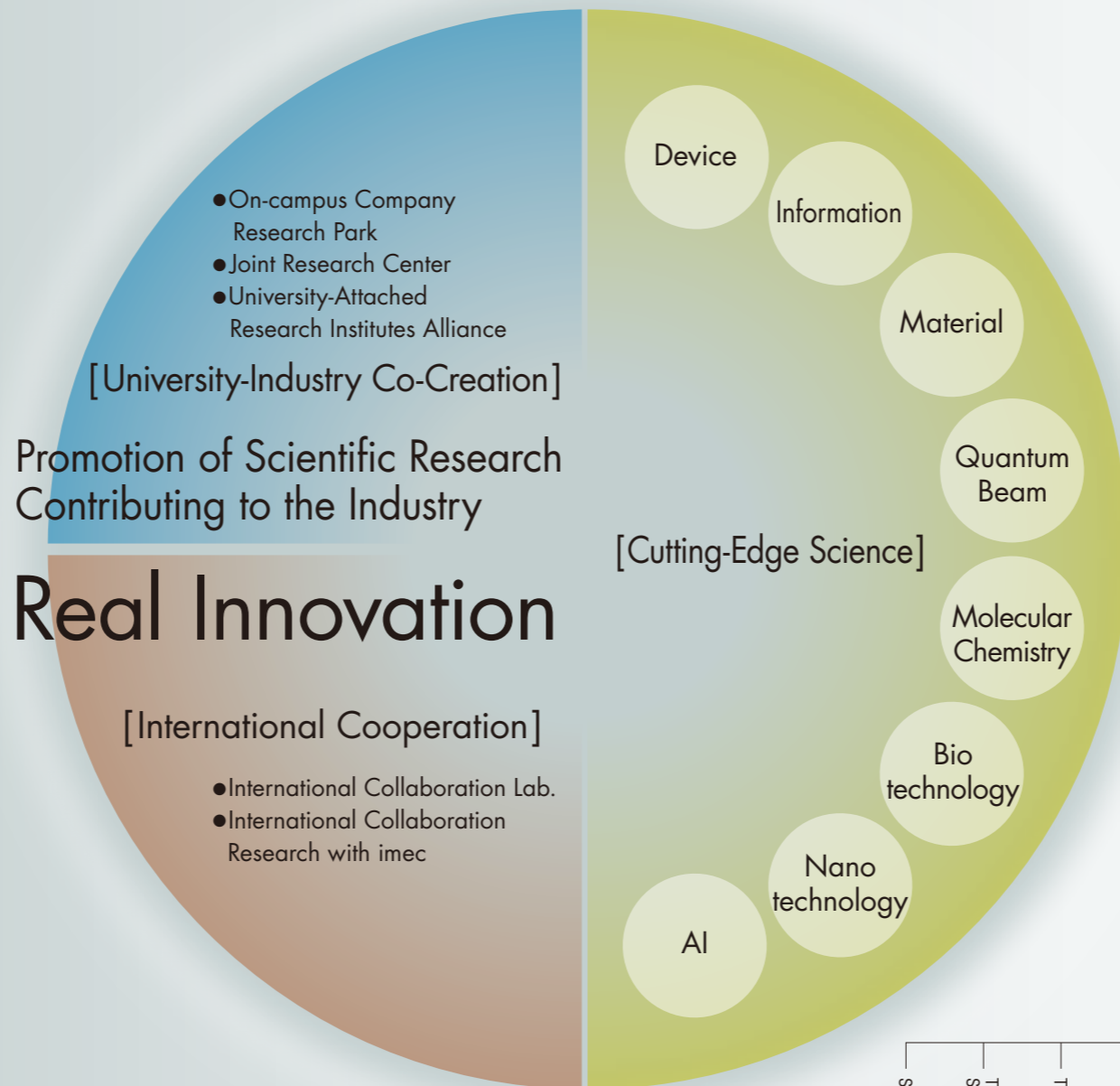
For example, the SANKEN, which has been leading nanotechnology research organization since the 1980s, has established its Nanoscience Nanotechnology Center at the early stages of development of nanoscience and has led the world since. In the field of information and AI, where social implementation is currently progressing greatly, we have established cutting-edge research laboratories in the 1970s, that are still functioning and have been contributing greatly to the development of the academic area. Based on extensive history and features of the SANKEN, the Artificial Intelligence Research Center (AIRC) was launched in April 2019 to combine interdisciplinary fields of quantum, materials, beam, biology, molecule, and nanotechnology sciences with information science. Through the activity in AIRC, we aim to bring next-generation industrial innovations to society by building the basis of AI-driven science and its implementation.

For the future, without forgetting SANKEN’s mission - accumulating the knowledge generated from daily research across diverse scientific fields, sublimating it as a technology, and surely transferring it into society for solving social problems and sustainable development for all over the world, we will strive to provide the highest level of research and education. As one of our actions, we changed our official English name of the Institute to “SANKEN” in June 2021, and to develop into a more globally recognized and familiar research institute.

To that end, we will strongly promote collaboration and co-creation with a variety of academic communities, universities, research institutes and companies with different viewpoints. We sincerely ask for your continued support and encouragement.

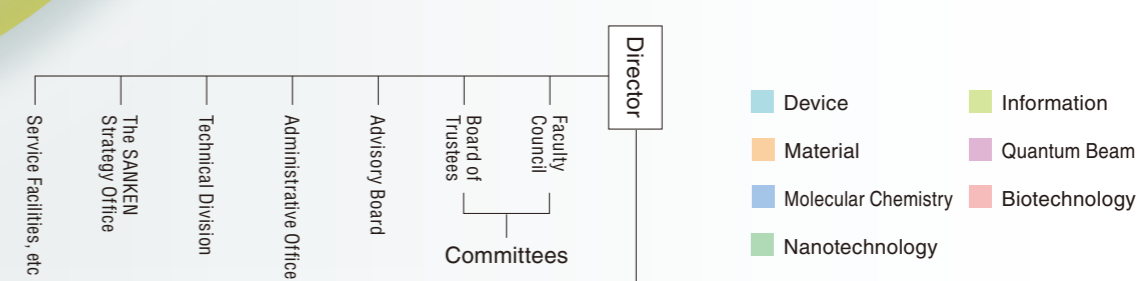


Director  
*Tohru Sekino*  
Tohru Sekino



## Organization

Division of Information and Quantum Sciences Department of Architecture for Intelligence Department of Knowledge Science Department of Reasoning for Intelligence Department of Intelligent Media Department of Advanced Electron Devices Department of Interface Quantum Science Department of Quantum System Electronics	Division of Advanced Materials and Beam Science Department of Quantum Beam Physics Department of Excited Solid-State Dynamics Department of Energy and Environmental Materials Department of Advanced Hard Materials Department of Semiconductor Materials and Processes Department of Functionalized Natural Materials	Biological and Molecular Sciences Department of Complex Molecular Chemistry Department of Regulatory Bioorganic Chemistry Department of Synthetic Organic Chemistry Department of Material Excitation Chemistry	Division of Biological and Molecular Sciences Department of Biomolecular Science and Engineering Department of Biomolecular Science and Regulation Department of Biomolecular Science and Reaction	Nanoscience and Nanotechnology Center Department of Nanotechnology for Environmental and Energy Applications Department of Bio-Nanotechnology Department of Soft Nanomaterials Department of Theoretical Nanotechnology Department of Nanofabrication for Nanosystems and Functions Department of Advanced Nanofabrication Department of Functional Nanomaterials and Nanodevices	Artificial Intelligence Research Center Department of AI Introduction to Information and Quantum Sciences Department of Translational Datability Nanotechnology Open Facilities	Division of Next Industry Generation Department of Intellectual Property Research Department of New Industry Generation Systems Big Data Factory Department of AI Introduction to Nanoscience and Nanotechnology Department of AI Introduction to Biological and Molecular Sciences Department of AI Introduction to Advanced Materials and Beam Science Department of AI Introduction to Information and Quantum Sciences	Division of Special Projects Laboratories of Second Project (Department of Three-Dimensional Nanostructure Science) Laboratories of First Project Department of Intellectual Property Research Department of New Industry Generation Systems	Joint Research Division-Alliance Laboratories Division of Yoshino Chemical Industry Polymer Gel Joint Research Laboratory of flexible and power three dimensional system integration	Comprehensive Analysis Center Research Laboratory for Quantum Beam Science Center for Collaborative Research Education and Training International Collaborative Research Center
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- Device
- Information
- Material
- Quantum Beam
- Molecular Chemistry
- Biotechnology
- Nanotechnology

## History

- 1939 ISIR: SANKEN was established in Sakai City with 3 research departments.
- 1968 SANKEN has been relocated to Suita City.
- 1977 Material Analysis Center was established.
- 1995 Restructured to an Institute composed of 6 divisions with 24 departments for the purpose of promoting sciences on materials, information and biology.
- 2002 Nanoscience and Nanotechnology Center was founded. The new Center focused its research on nanomaterials and devices, beam science for nanotechnology and industrial nanotechnology.  
We were awarded the 21 Century COE Program MEXT (the Ministry of Education, Culture, Sports, Science and Technology).
- 2007 4 institutes' Alliance (4 institutes' network) was started.  
ISIR-REIS (Hokkaido Univ.) alliance laboratory was set up.
- 2008 Division of Special Projects was launched.
- 2009 SANKEN was reorganized to 3 divisions and Nanoscience and Nanotechnology Center. Material Analysis Center was reorganized to Comprehensive Analysis Center. SANKEN Incubation Building was constructed and Company Research Park was started.
- 2010 The Network Joint Research Center for Materials and Devices and 5 institutes' Alliance (5 institutes' network) were started. SANKEN was the headquarters of this nation-wide 5 institutes network.
- 2011 We concluded a research-collaboration agreement with Interuniversitair Micro-Electronica Centrum vzw (imec), one of the world's largest nanotechnology research institute and "imec office" was opened at SANKEN.
- 2013 Osaka University has been selected as one of the core universities of the MEXT program, COI STREAM, and ISIR will play a central role of the Osaka Univ.
- 2016 Dynamic Alliance for Open Innovation Bridging Human, Environment and Materials including ISIR (Osaka Univ.), RIES (Hokkaido Univ.), IMRAM (Tohoku Univ.), CRL (TIT) and IMCE (Kyusyu Univ.) was established. SANKEN is the headquarters of this nation-wide 5 institutes network.
- 2017 We established "ISIR imec center" in imec of Belgium to promote the global cooperation network.
- 2019 Artificial Intelligence Research Center was established.
- 2021 In June 1st 2021, the official English abbreviated name of our institute was changed from "ISIR" to "SANKEN".

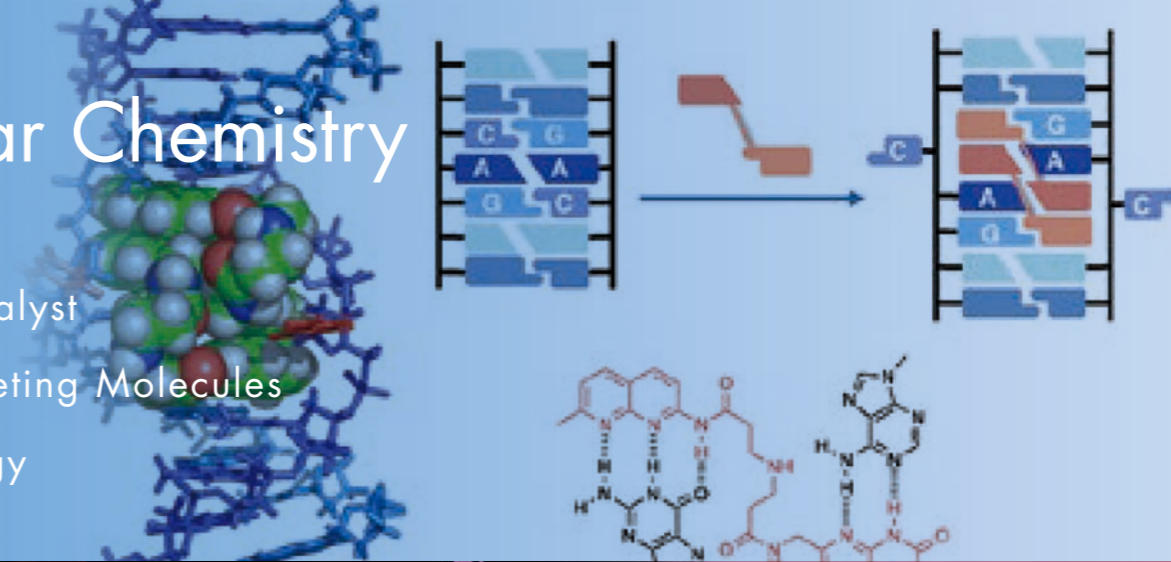


# Device

- Quantum Technology
- Next-generation IoT Sensors
- Flexible Intelligent System
- flexible spintronics sensors

# Molecular Chemistry

- Photochemistry
- Asymmetric Catalyst
- DNA/RNA-targeting Molecules
- Chemical Biology



# Information

- Computer Vision
- Machine Learning
- Spoken Dialogue Systems
- Artificial Intelligence
- Data Mining



# Biotechnology

- Bio-inspired Materials
- Multidrug Resistant Bacteria
- Luminescent Protein
- Smell Digitization

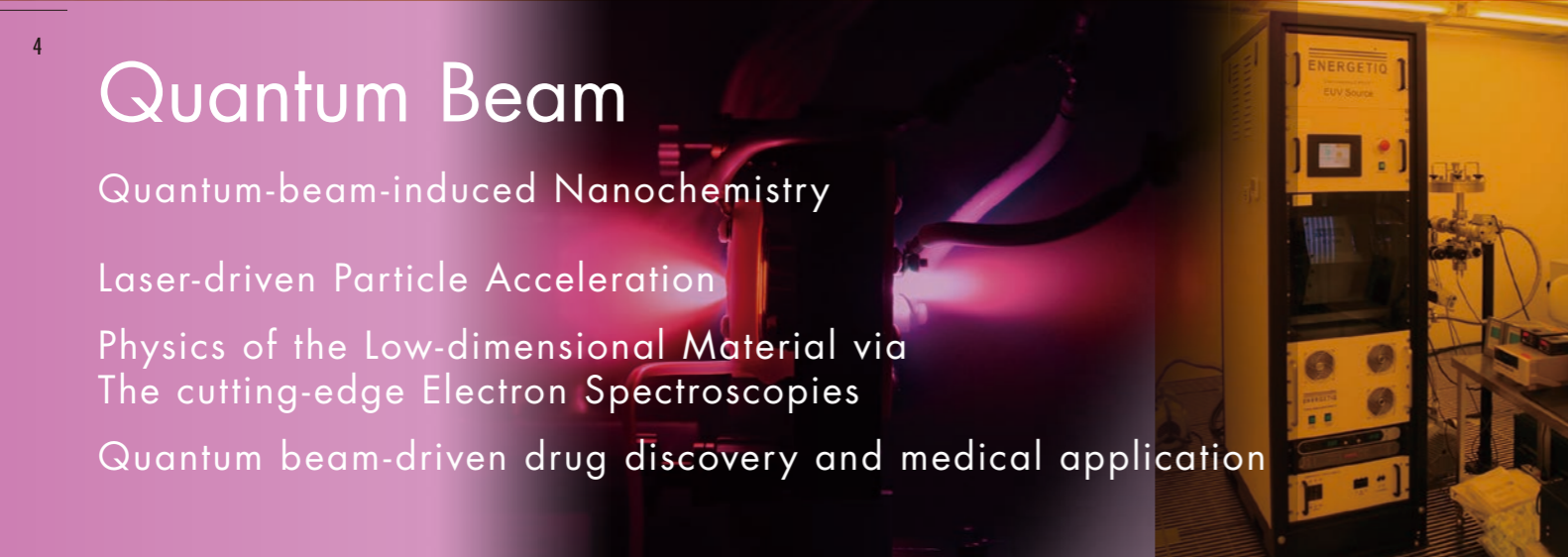
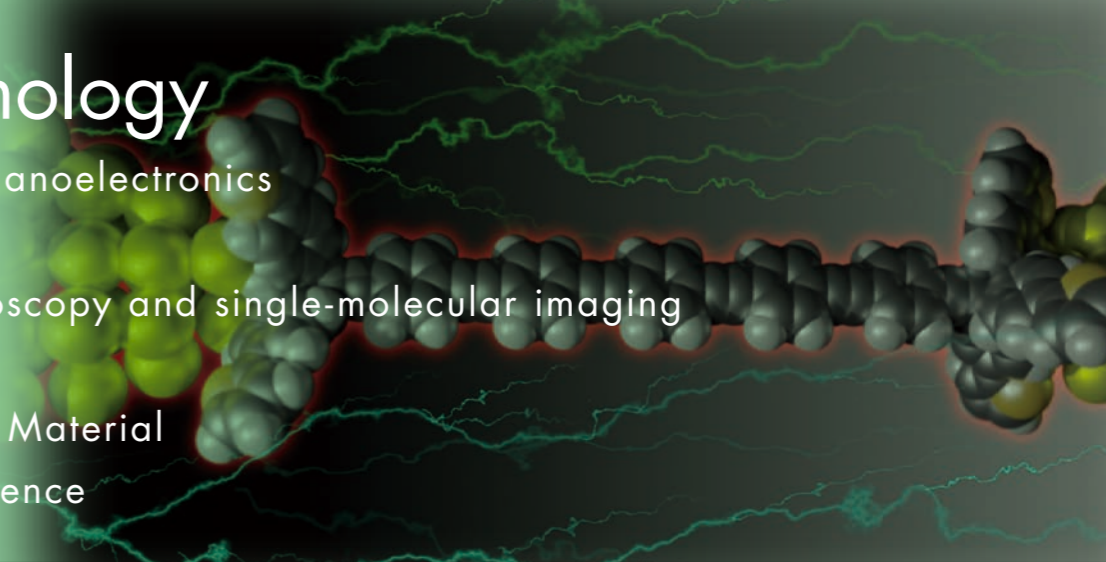


# Material

- Cellulose Nanofiber
- Silicon
- Multi-Functional Materials
- Advanced Batteries

# Nanotechnology

- Functional Oxide Nanoelectronics
- Quantum Beam
- Single-atom spectroscopy and single-molecular imaging
- Materials Design
- Organic Functional Material
- Single-molecule Science



# Quantum Beam

- Quantum-beam-induced Nanochemistry
- Laser-driven Particle Acceleration
- Physics of the Low-dimensional Material via The cutting-edge Electron Spectroscopies
- Quantum beam-driven drug discovery and medical application

We are aiming to contribute to society by promoting state-of-the-art research and solving environmental, energy medical, safety and security issues.

## Company Research Park

We operate a space "Company Research Park."

This space promotes open innovation by companies in cooperation with our research activities. The users can receive state-of-the-art technical counseling for practical application research and can form and utilize networks as an open innovation base.



## Alliances among Research Institutes and Network Joint Research Center

Promotion and support of diverse joint research through collaboration among the five university research institutes

### Crossover Alliance to Create the Future with People, Intelligence and Materials (Five-star Alliance)



Five-Star

Five university research institutes across Japan Archipelago (Research Institute of Electronic Science at Hokkaido University; Institute of Multidisciplinary Research for Advanced Materials at Tohoku University; the Laboratory for Chemistry and Life Sciences, Institute of Innovative Research at Tokyo

Institute of Technology; Institute of Scientific and Industrial Research at Osaka University; Institute for Materials Chemistry and Engineering at Kyushu University) cooperate with each other to organically cross-over rich research resources including human resources, knowledge, technology, and facilities, and promote research aimed at solving social issues and the development of young researchers. Through CORE<sup>2</sup>-A laboratory joint research, the Young Scientists Feasibility Study Program, and Alliance Group activities, we are developing an active brain circulation across the five research institutes.



[alliance.tagen.tohoku.ac.jp/english/](http://alliance.tagen.tohoku.ac.jp/english/)



NJRC

### Network Joint Research Center for Materials and Devices (NJRC)

The Network Joint Research Center for Materials and Devices (NJRC) has been established in FY2011 as a first network of such centers in Japan (a project approved by the Ministry of Education, Culture, Sports, Science and Technology). The five research institutes that make up the center work together to invite researchers from a wide range of research institutions for joint research thorough open recruitment. Taking advantage of the characteristics of the network of centers, we promote joint research with universities, public research institutes, and private companies in Japan and overseas, and strengthen research capabilities and develop human resources in the fields of materials and devices and their related fields. The Institute of Scientific and Industrial Research (SANKEN) has become the headquarter of the center starting from FY2022, and plays an increasingly central role in the global materials and devices research community.



[five-star.sanken.osaka-u.ac.jp/en/](http://five-star.sanken.osaka-u.ac.jp/en/)

## Education

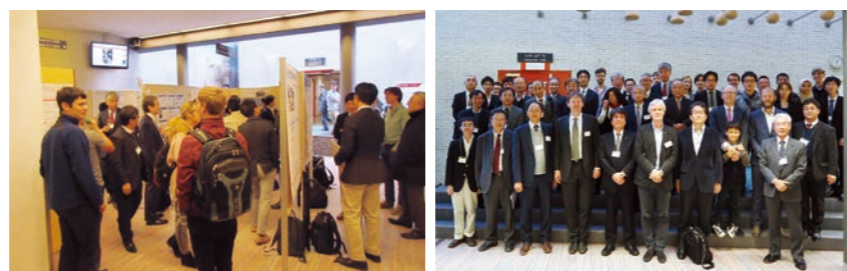
Members of SANKEN participate in graduate education in cooperation with the Graduate School of Science, Engineering, Engineering Science, Pharmaceutical Sciences, Information Science and Technology and Frontier Biosciences. In addition, we provide the lectures in Interdisciplinary Educational Subjects and contribute partly to the advanced human resource development by participating in R<sup>3</sup> Institute for Newly-Emerging Science Design, Osaka University.



## International Cooperation

Academic Exchange Agreements of ISIR with Universities and Research Institutions Abroad (April, 2022)

- Inter-University Exchange Agreements: 14
- Faculty-level Exchange Agreements Based on Inter-University Exchange Agreements: 6
- Faculty level Exchange Agreements: 14
- ISIR Overseas Center: 1



## Facilities

### Research Laboratory for Quantum Beam Science



Developments and applications of ultimate short-pulsed electron beam, high-brightness electron beam, light source base on FEL and positron beam have been promoted together with an intense Co-60 gamma-ray source in this facility.

#### Machine List

- 1 L-band electron linac
  - 2 Co-60 gamma-ray irradiation facility
  - 3 150 MeV S-band electron linac
  - 4 RF-Gun equipped S-band electron linac
  - 5 Time-resolved electron microscope
- THz light source based on FEL of L-band linac



[www.sanken.osaka-u.ac.jp/labs/rl/English/](http://www.sanken.osaka-u.ac.jp/labs/rl/English/)

### Comprehensive Analysis Center



As a common facility for comprehensively performing composition and structural analysis of various materials, Comprehensive Analysis Center has equipment of composition analysis system, spectroscopic analysis system, electron microscope system, state analysis system.

#### Machine List

- 1 Element analyzer
  - 2 Transmission electron microscope
  - 3 Nuclear magnetic resonance
  - 4 X-ray diffractometer
  - 5 Mass spectrometer
- Scanning electron microscope



[www.sanken.osaka-u.ac.jp/labs/cac/](http://www.sanken.osaka-u.ac.jp/labs/cac/)

### Nanotechnology Open Facilities



Nanotechnology Open Facilities totally contributes to creations of novel nano-materials and nano-devices for companies / universities / institutes researchers in nanotechnology research fields with the latest equipment and technical support.

#### Machine List

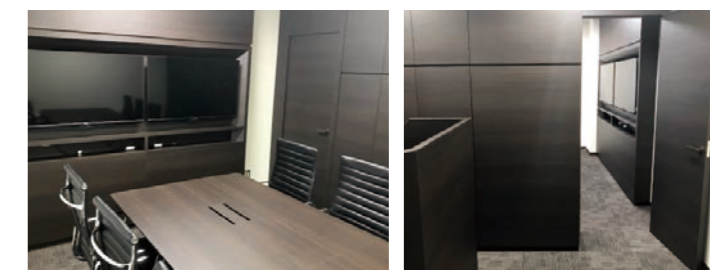
- 1 125keV EB Lithography
- 2 Helium Ion Microscope
- 3 Deep Reactive Ion Etching
- 4 Pulsed Laser Deposition
- 5 Scanning Electron Microscope
- 6 Scanning Probe Microscope



[nanoplatform.osaka-u.ac.jp](http://nanoplatform.osaka-u.ac.jp)

## Artificial Intelligence Research Center

The Artificial Intelligence Research Center was established for realizing laboratory-led "bottom-up type AI introduction" at SANKEN, which has a wide range of research fields in the under-one-roof. Specifically, the AI center (1) trains young researchers in each research field to be suitable for AI introduction, (2) establishes an AI introduction protocol appropriate for each research field, (3) establishes "AI introduction liaison office" for returning the fruits to each department of Osaka university, and aiming for implementation in industry and transmission to the world, (4) conducts researches to lead the solutions obtained by AI to scientific principles without ending them as a black box.



[www.sanken.osaka-u.ac.jp/labs/aic/](http://www.sanken.osaka-u.ac.jp/labs/aic/)

# Featured Researcher: 01

## Touring industrial laboratories and meeting with research groups

SANKEN has engaged in cutting-edge scientific research and development of contemporary academic-industrial collaborations for nearly 80 years, as a leading multidisciplinary laboratory of science and technology in Japan.

At present, the Institute has a focus on three research fields, information/quantum science, material/beam science, and biology/molecular science, and has an industrial nanotechnology center. The Institute has expanded its research interests in response to recent developments in scientific technology, and has obtained world-leading research findings in collaboration with various groups. The research scientists who have produced these great achievements are introduced here, with a description of the latest topics.

# Development of a high-performance electron microscope and observation of nanolevel phenomena

Professor, **Kazutomo Suenaga**  
Department of Nanocharacterization for Nanostructures and Functions

K. Suenaga

### Largest project in Europe

In the 90 years since its invention, electron microscopy (EM) has advanced to the point that it can show individual atoms and components, and examine electronic states reflecting atomic behavior. Resolution, an indicator of visual performance in EM, has been gradually improved and EM is now expected to make a major contribution to development of nanotech materials that produce physical phenomena in the nanometer (one billionth of a meter) world. Professor Suenaga began to develop EM with the world's highest resolution with researchers in Europe, as the largest project of the European Research Council (ERC). He described his motivation, "In addition to visualization of nanomaterial structures, I wanted to investigate nanolevel physical phenomena including superconducting systems and measurement of charge transfer in electrodes of lithium-ion batteries".

Unlike optical microscopy with visible light, EM uses an accelerated electron beam (electron flux) with an extremely short wavelength to irradiate a sample. The intensity of the electrons passing through the sample forms an image, like a transfer picture, that can discriminate atomic levels based on wavelength. Furthermore, a spectrometer in EM measures energy loss from electrons during transmission, representing the electron status of the sample. The energy resolution in this project will reach the highest level of accuracy using the leading technology worldwide.

### Atomic vibrational energy captured

Prof. Suenaga published results of one of his studies in *Nature*, a British scientific journal, in 2019, when he was a senior researcher at the National Institute of Advanced Industrial Science and Technology (Tsukuba, Ibaraki Prefecture). In this study, he used graphene, a nanomaterial with bonded carbon atoms on planar surfaces with the thickness of one atom, and measured the energy and momentum after electron beam irradiation induced atomic vibration (lattice vibration), and induced waves spread throughout the sample. Data were extracted for basic atomic properties, including thermal conductivity. The measurable range (spatial resolution) was 10 nanometers, which is about one-hundredth of the

conventional resolution. Consequently, this device can directly and accurately determine differences between the center and end of semiconductor materials, which is needed for development of nanotechnology. Conventional devices can only determine the average (bulk) for the whole material.

### Success from a backwards idea

"Results that can be predicted by anyone will be obtained by someone. Therefore, I selected different directions and sought a subject that was unpredictable for anyone" Prof. Suenaga looked back at his career. When he was a graduate student at the University of Tokyo, he became aware of fullerene, an allotrope of carbon with a molecular structure that consists of dozens of carbon atoms. This structure was unknown and EM at the time could not show the arrangement of the carbon atoms. Therefore, he started a study of fullerene because he wanted to see the actual arrangement in detail. After he graduated, Prof. Suenaga worked as a postdoctoral fellow at a university in France to obtain understanding of European technology of electron beam analyses, which differed from technology in Japan focusing on larger EM. He successfully observed the structure of nanotech materials including carbon nanotubes, which are cylindrical molecules with bonded carbon atoms, and the long-sought fullerene structure. He achieved breakthrough results with a "backwards" idea "to decrease the electron accelerating voltage to a tenth" using technology developed in Germany to correct electron lens aberrations (lags). The view at the time was that "light carbon atoms are dispersed by electron beams accelerated at high voltage to increase resolution, resulting in conditions that do not permit measurements". EM using a low accelerating voltage is now a mainstream approach to observe light atoms, including carbon and lithium.

"Studies using EM are expensive and only a few laboratories regularly present papers. We have developed the only high-performance EM in the world. I intend to allow anyone to use this EM." Prof. Suenaga also tries to foster younger researchers. "I was surprised at how students in Europe were good at switching from work to play. They spent their day on the beach if they had time, even immediately before a presentation." Prof. Suenaga enjoys walking in between work.

# Featured Researcher: 02

## Achievement of safety of a lithium-ion battery using water



**Professor Yuki Yamada**  
Department of Energy and Environmental Materials

山田 裕貴

### To prevent fire accidents

A lithium-ion battery is commonly used as a power supply for portable devices, including smart phones and laptop computers. This is because this kind of battery provides voltages that are more than 2 volts higher than common dry cells (1.5 volts) and has longer charge and discharge cycles, which permits information to be sent and received anywhere. However, fire accidents may sometimes be caused by abnormal heating because flammable organic solvents are used to enhance the performance of lithium-ion batteries. Prof. Yamada successfully developed a novel approach using water, which had been considered to be unsuitable, with a comparable performance to organic solvent. This work has created a new path to safe and low-cost batteries, and will promote development of large-scale batteries for electric vehicles and other applications.

Prof. Yamada said, "I believe in the necessity for incombustible water to achieve ultimate safety for this battery".

### To suppress water electrolysis

A lithium-ion battery transfers positively charged lithium ions between positive and negative electrodes. In discharge



mode, lithium ions move from the negative to the positive electrode; consequently, electrons (which are negatively charged) in the negative electrode transfer to a different circuit and produce an electric current. Lithium ions then return to the negative electrode when the battery is recharged by an external voltage supply. The lithium ion path is filled with electrolyte solution. Organic solvents are used to promote electrical stability under conditions of more than 3 volts. If some water is present, the water is electrolyzed at 1.2 volts or higher, oxygen and hydrogen are produced, and lithium ion transfer is suppressed, which results in reduced performance.

Focusing on this problem, Prof. Yamada has studied electrolyte solutions in which water is not electrolyzed. It is feasible to use salts with lithium ions and anions containing fluorine and sulfur in a water base; however, the mixture becomes solid and does not serve as an electrolyte solution. Prof. Yamada found that two kinds of lithium salts mixed in water at a high concentration and a specific ratio led to a "hydrate-melt" status that conducted lithium ions at normal temperatures in liquid form. Under these conditions, water molecules do not aggregate, but separate from each other and bind with lithium ions; consequently, the water molecules are not electrolyzed. In studies of this electrolyte, Prof. Yamada obtained voltages of more than 3 volts and demonstrated that charge and discharge can be repeated more than 200 times.

He described his plan, "I would like to improve this electrolyte solution to achieve practical use. Use of water not only maintains safety, but also reduces environmental effects of waste during the battery manufacturing process. Consequently, the manufacturing costs will be reduced because there is no need for extensive drying equipment. Furthermore, in the chemical industry, a new production process may be developed that utilizes this electrolyte to apply high voltage to a reactant and induce chemical reactions that have been only possible in organic solvents."

### To challenge common beliefs

In fact, Prof. Yamada is a rare researcher of electrolyte solutions in the field of lithium ion batteries. Electrodes are widely studied and a Japanese scientist was awarded Nobel Prize; however, electrolyte solutions have not experienced remarkable progress that is directly linked to battery performance.

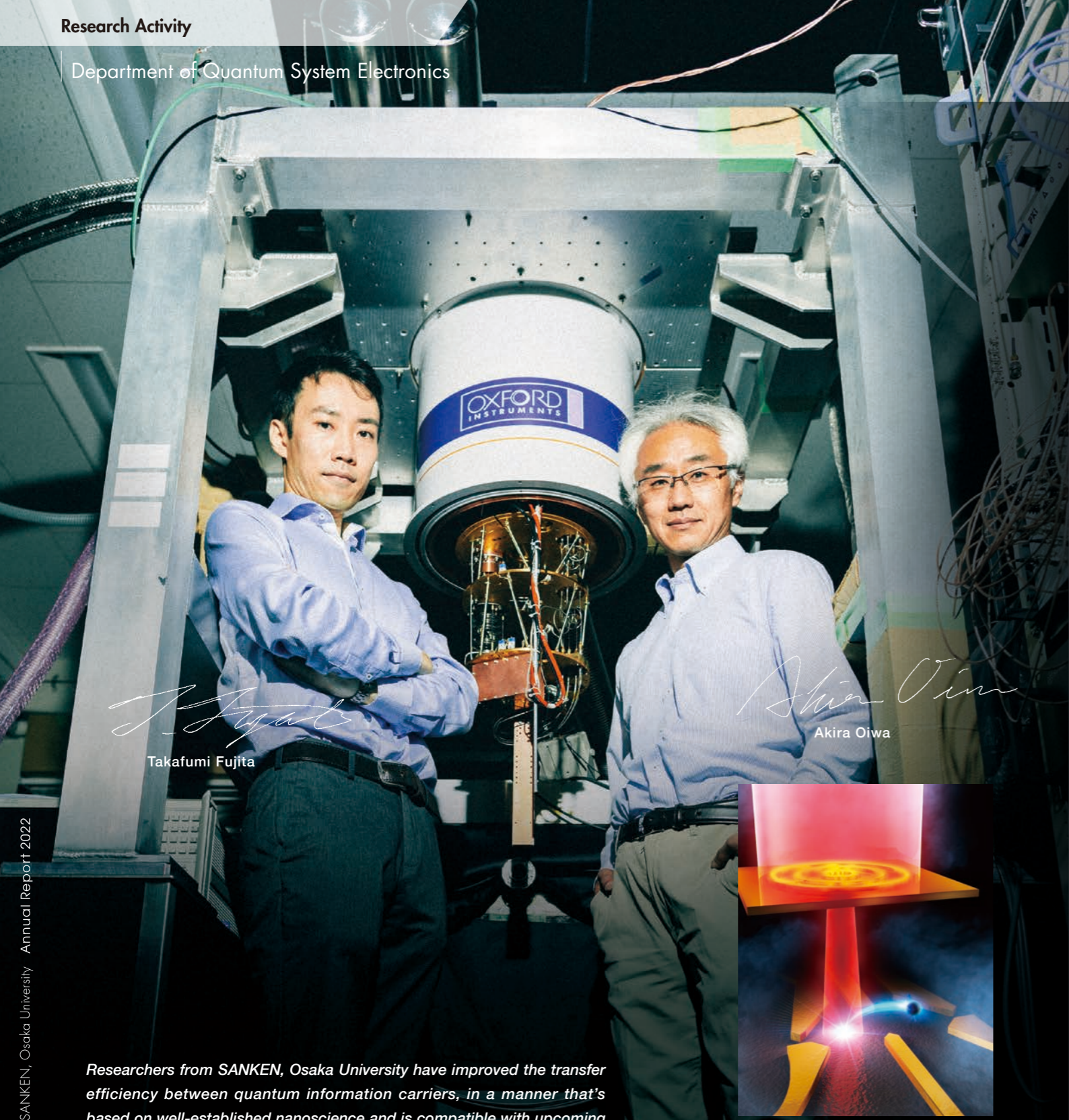
"I aim to contribute to energy and environmental problems through chemical studies." Prof. Yamada entered Kyoto University and began to study lithium ion batteries at the interface between electrodes and electrolyte solutions in graduate school. He found a phenomenon in which behaviors of lithium ions are dramatically altered by changing the electrolyte composition. He continued this study of electrolyte solutions as an Assistant Professor, Lecturer and Associate Professor at the University of Tokyo, and then came to Osaka University last April. Prof. Yamada said, "My credo is to challenge common beliefs. I found an important issue in electrolyte solutions that nobody had previously hit upon". He also aims to develop a new academic field focusing on electrolyte solutions.

Prof. Yamada spends his days on research. To relax from his research activities, he enjoys burgundy at home, a trip to sample some local sake with his wife, and rest and enjoyment playing with his children.



Written by Yoshinori Sakaguchi, former editorialist and former reporter for Sankai Shimbun, and current Adjunct Professor at Nara Institute of Science and Technology. Covers general science fields, mainly medical science, as a science journalist.

The article, "Detection of photogenerated single electrons in a lateral quantum dot with a surface plasmon antenna," was published in *Applied Physics Express* at DOI: <https://doi.org/10.35848/1882-0786/ac336d>



*Takafumi Fujita*

Takafumi Fujita

*Akira Oiwa*

Akira Oiwa

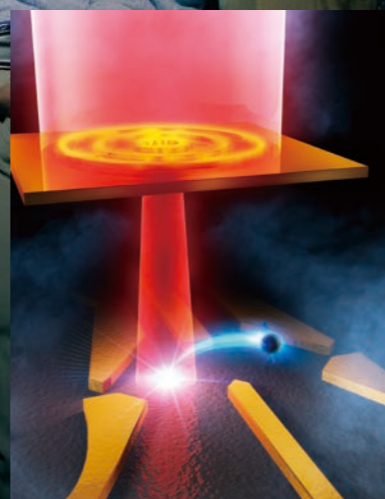


Fig.1 Conceptual illustration of efficient illumination of photons to semiconductor lateral quantum dots, by using a surface plasmon antenna and excitation of electrons in the quantum dots. Original content, credit: copyright © 2021 Oiwa lab. All Rights Reserved

Researchers from SANKEN, Osaka University have improved the transfer efficiency between quantum information carriers, in a manner that's based on well-established nanoscience and is compatible with upcoming advanced communication technologies

Osaka, Japan – Information storage and transfer in the manner of simple ones and zeros—as in today's classical computer technologies—is insufficient for quantum technologies under development. Now, researchers from SANKEN in Japan have fabricated a nanoantenna that will help bring quantum information networks closer to practical use.

In a study recently published in *Applied Physics Express*, researchers from SANKEN, Osaka University and collaborating partners have substantially enhanced photon-to-electron conversion through a metal nanostructure, which is an important step forward in the development of advanced technologies for sharing and processing data.

Classical computer information is based on simple on/off readouts. It's straightforward to use a technology known as a repeater to amplify and retransmit this information over long distances. Quantum information is based on comparatively more complex and secure readouts, such as photon polarization and electron spin. Since the quantum information cannot be amplified, long distance transmission should be performed based on a quantum mechanical way. Semiconductor nanoboxes known as quantum dots are materials that researchers have proposed for storing and transferring quantum information. However, quantum repeater technologies have some limitations—for example, current ways to convert photon-based information to electron-based information are highly inefficient. Overcoming this information conversion and transfer challenge is what the researchers at Osaka University aimed to address.

"The efficiency of converting single photons into single electrons in gallium arsenide quantum dots—common materials in

quantum communication research—is currently too low," explains lead author Rio Fukai. "Accordingly, we designed a nanoantenna—consisting of ultra-small concentric rings of gold—to focus light onto a single quantum dot, resulting in a voltage readout from our device."

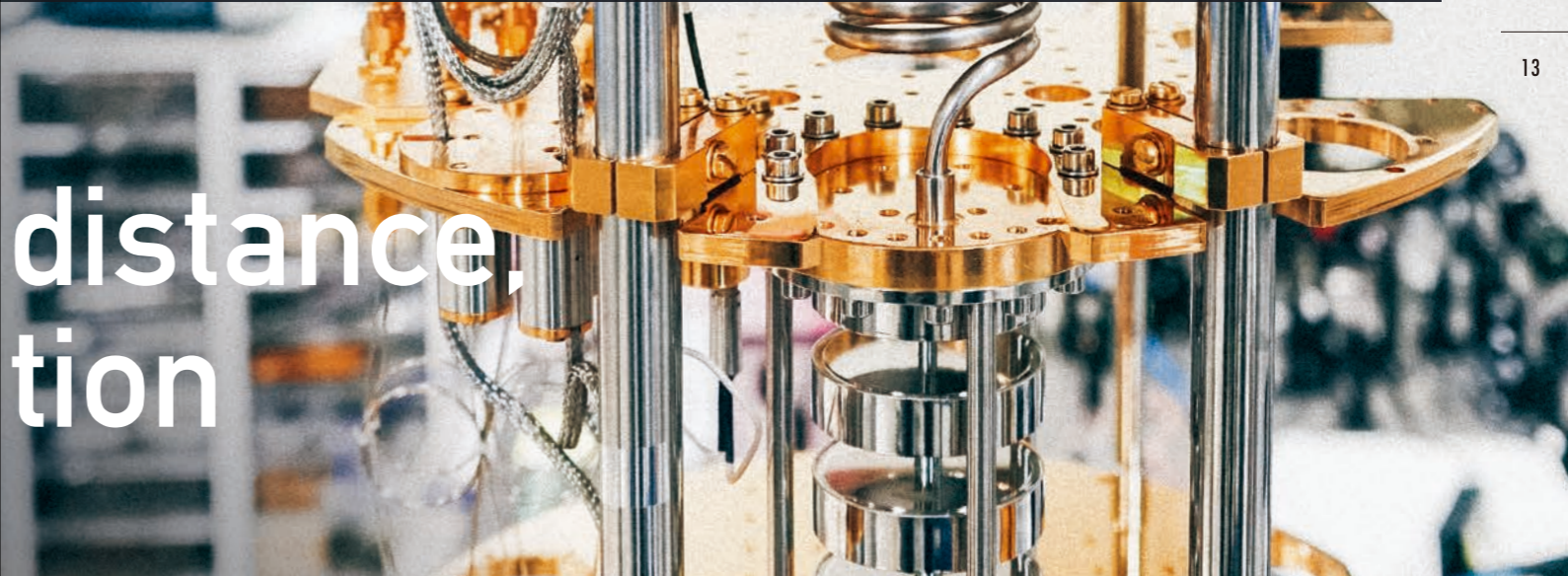
The researchers enhanced photon absorption by a factor of up to 9, compared with not using the nanoantenna. After illuminating a single quantum dot, most of the photogenerated electrons weren't trapped there, and instead accumulated in impurities or other locations in the device. Nevertheless, these excess electrons gave a minimal voltage readout that was readily distinguished from that generated by the quantum dot electrons, and thus didn't disrupt the device's intended readout.

"Theoretical simulations indicate that we can improve the photon absorption by up to a factor of 25," says senior author Akira Oiwa. "Improving the alignment of the light source and more precisely fabricating the nanoantenna are ongoing research directions in our group."

These results have important applications. Researchers now have a means of using well-established nanophotonics to advance the prospects of upcoming quantum communication and information networks. By using abstract physics properties such as entanglement and superposition, quantum technology could provide unprecedented information security and data processing in the coming decades.



# A nanoantenna for long-distance, ultra-secure communication



# Sequencing multiple RNA base modifications simultaneously: a new era of RNA biology

*Researchers from SANKEN, Osaka University have been able to simultaneously detect two types of microRNA modification while sequencing single RNA molecules*

Osaka, Japan – After a gene is transcribed into RNA, modifications can occur to the subunits or “bases” that make up the RNA molecule, which can affect its structure and function. The study of these changes is known as “epitranscriptomics.” These base modifications can occur to most types of RNA molecule, including microRNAs.

Now, a research group at Osaka University, led by Professor Masateru Taniguchi and Professor Hideshi Ishii, have sequenced a microRNA that is a marker for “refractory” gastrointestinal cancer, which does not respond to treatment. They were able to directly detect two types of chemical base modifications simultaneously using a single-molecule quantum sequencer.

MicroRNAs are small non-coding RNA molecules that play a regulatory role by interfering with and suppressing the expression of a gene. Base modifications to microRNAs can affect how they are processed and the efficiency by which they can suppress their targets, altering their function. These modifications are therefore important for understanding the functions of RNAs but have previously proved hard to detect.

谷口正輝  
Masateru Taniguchi



State-of art ultra-fine electron beam lithography system

Washio group developed noise reduction techniques in tunneling currents and pattern recognition techniques of the microRNA sequence based on machine learning. These techniques were essential for the quantum sequencer.

鷲尾隆

Takashi Washio

The Osaka University team isolated microRNAs from colorectal cancer cells and sequenced single RNA molecules. The quantum sequencer uses electricity to distinguish bases based on their unique electrical conductance values, which measure the ability of the molecules to conduct an electrical current. Because chemical modifications alter the electrical conductance of the bases, this method could potentially be used to identify any kind of nucleotide modification. Here, the researchers focused on two common modifications, m6A and 5mC, involving the addition of a methyl group to an adenosine (A) nucleotide and a cytidine (C) nucleotide, respectively.

Using the single-molecule quantum sequencer, the team observed modification ratios that were comparable to those calculated using other methods that are only able to detect a single kind of modification at a time. Not only that, but the results they observed suggest that the two types of modification were able to influence each other. The presence of m6A modification seemed to facilitate 5mC modification. “The rate of 5mC methylation is generally affected by the activities of methylation and demethylation enzymes, and so our results imply that the activities of these enzymes can be promoted or deactivated by m6A modifications,” explains Takahito Ohshiro, lead author of the paper.

This work provides a robust new tool for sequencing various types of RNA base modifications. “Our method can be used for comprehensive analysis and detection of methylation sites in the epitranscriptome,” says corresponding author Masateru Taniguchi, “which will allow increased understanding of these methylation events and their mechanisms, changing the landscape of RNA biology and ushering in a new era.”



Figure: Operating principle of single-molecule quantum sequencing to determine base sequences and identify chemically modified base molecules. ©Takahito Ohshiro et al.

The article, “Single-molecule RNA sequencing for simultaneous detection of m6A and 5mC” was published in *Scientific Reports* at DOI: <https://doi.org/10.1038/s41598-021-98805-z>





# Patching up your health

Researchers at SANKEN, Osaka University and JOANNEUM RESEARCH develop ultrathin self-powered e-health patches that can monitor a user's pulse and blood pressure, which may lead to new flexible motion-based energy harvesting devices

Osaka, Japan – Scientists at SANKEN, Osaka University, in cooperation with JOANNEUM RESEARCH (Weiz, Austria), introduced wireless health monitoring patches that use embedded piezoelectric nanogenerators to power themselves with harvested biomechanical energy. This work may lead to new autonomous health sensors as well as battery-less wearable electronic devices.

As wearable technology and smart sensors become increasingly popular, the problem of providing power to all of these devices become more relevant. While the energy requirements of each component may be modest, the need for wires or even batteries become burdensome and inconvenient. That is why new energy harvesting methods are needed. Also, the ability for integrated health monitors to use ambient motion to both power and activate sensors will help accelerate their adoption in doctor's offices.

Now, an international team of researchers from Japan and Austria has invented new ultraflexible patches with a ferroelectric polymer that can not only sense a patient's pulse and blood pressure, but also power themselves from normal movements. The key was starting with a substrate just one micron thick. Using a strong electric field, ferroelectric crystalline domains in a copolymer were aligned so that the sample had a large electric dipole

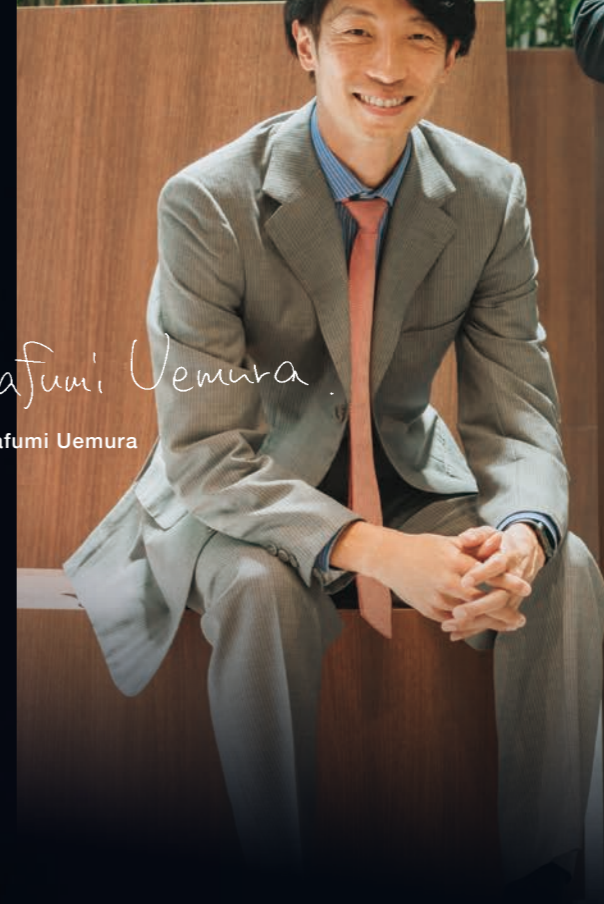
moment. Based on the piezoelectric effect, which is very efficient in converting natural motion into small electric voltages, the device responds rapidly to strain or pressure changes. These voltages can be transduced either into signals for the medical sensors or to directly harvest the energy. "Our e-health patches may be employed as part of screening for lifestyle-related diseases such as heart disorders, signs of stress, and sleep apnea," first-author Andreas Petritz says.

The authors estimate that multilayer patches can harvest up to 200 millijoules per day from biomechanical motions if placed on joints, like knees or elbows. This is enough to monitor cardiovascular parameters several times a day. And the patches are so thin that they are barely perceptible thus making a necessary evil for many patients – daily health monitoring - less unpleasant.

"We expect that our findings will assist in the development of other sheet-type sensor systems that can perform precise biomonitoring when affixed to the skin surface," senior author Tsuyoshi Sekitani says. Additional modules allow other features, such as wireless communication with a smartphone or computer.



Takafumi Uemura  
Takafumi Uemura



Teppei Araki  
Teppei Araki

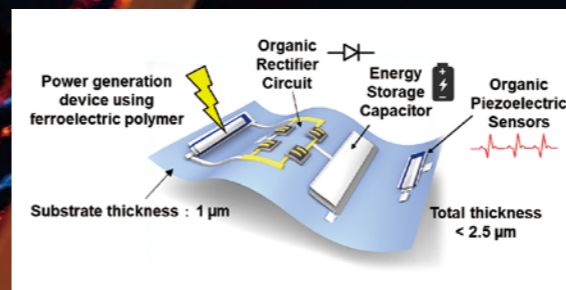


Figure 1. Sheet-type piezoelectric system with self-generation and storage functions (Image of an integrated system) (credit: Osaka University)

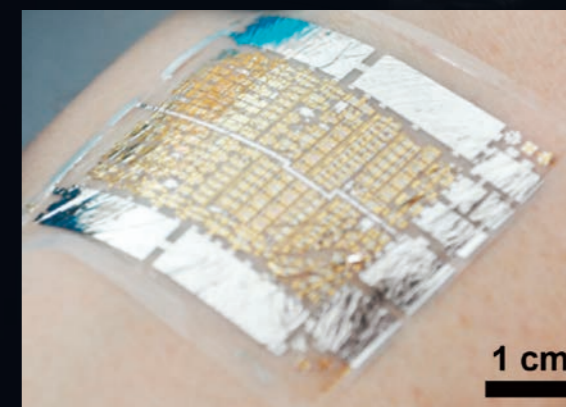


Figure 2. Photograph of the sheet-type piezoelectric system. Accurate biomonitoring is possible without being noticed; the extremely thinness and softness realize that the sheet system closely contacts with the skin. (credit: Osaka University)

The article, "Imperceptible energy harvesting device and biomedical sensor based on ultraflexible ferroelectric transducers and organic diodes," was published in *Nature Communications* at DOI: <https://doi.org/10.1038/s41467-021-22663-6>



# Seeing both the forest and the trees: Trans-scale scope shows big picture of tiny targets

Researchers at SANKEN, Osaka University use a 120-megapixel camera to simultaneously image over a million cells in a single microscope field of view, a feat which may accelerate the study of population dynamics and rare biological phenomena

Osaka, Japan – Scientists from SANKEN and the Transdimensional Life Imaging Division of the Institute for Open and Transdisciplinary Research Initiatives (OTRI) at Osaka University created an optical imaging system that can capture an unprecedented number of cells in a single image. By combining an ultra-high pixel camera and a huge lens, the team was able to easily observe exceedingly rare, “one-in-a-million” situations. This work provides a valuable new tool for the simultaneous observation of centimeter-scale dynamics of multicellular populations with micrometer resolution to see the functions of individual cells.

In biology, scientists are often interested in the outliers of a population, such as cells with a rare function that may appear in fewer than one in a million individuals. These experiments have been hampered by the inherent tradeoff with microscopes between seeing cells at a sufficient spatial resolution while still maintaining a large enough field of view to capture unusual specimens. Scientists often spend several minutes moving slides in search of just the right cells to study.

Now, a team of scientists led by Osaka University has devised a system that can produce an image containing up to a million cells at once. “Conventional biological microscopes can observe at most 1,000 cells, with a field of view limited to a few millimeters. Our setup uses machine vision powered by a high-pixel camera with a macro lens,” first author Taro Ichimura says. The team built the optical imaging system with a 120-megapixel camera and a telecentric macro lens. This provided a much larger field

of view than conventional microscopes, up to about one and half by one centimeter, while still resolving individual cells and the interactions between them that characterize the population. The team termed the imaging technology “trans-scale scope,” which signifies that the technology can be applied to imaging from the micrometer-scale to the centimeter-scale. “As a technological singularity for a powerful cell measurement, our trans-scale scope system AMATERAS is expected to contribute to a wide range of applications, from basic research for understanding the operating mechanism of multicellular systems, to medical applications such as the quality control of artificial cell sheets,” senior author Takeharu Nagai says.

The team tested the AMATERAS by dynamically imaging calcium ions in cultured cells and successfully detected anomalies that occurred in less than 0.01% of specimens. This work may accelerate research in a wide range of fields that deal with large cell populations, such as neuroscience, oncology, and immunology.

永井 健治  
Takeharu Nagai

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AMATERAS

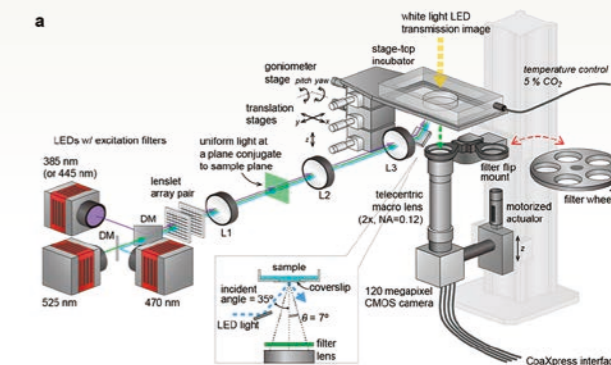


Fig.2: Schematic showing the configuration of the trans-scale scope system AMATERAS1.0. ©2021 T. Ichimura et al., Scientific Reports

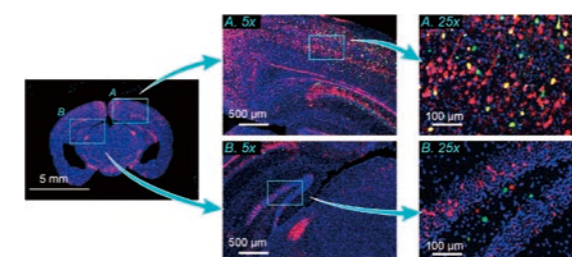


Fig.1: Imaging a mouse brain slice. A multicolor image of a mouse brain slice with two regions indicated by light blue squares, namely, the cerebral cortex (A) and the hippocampus (B). These are displayed in the whole-brain image (left) and digitally magnified 5x (middle). The local regions of light blue squares in the 5x images are further digitally magnified five times (right). Red, green, and blue represent the fluorescence due to a red fluorescent protein expression in excitatory projection neurons, a green fluorescent protein expression in inhibitory interneurons, and Hoechst 33342 attached to nuclear DNA, respectively. ©2021 T. Ichimura et al., Scientific Reports

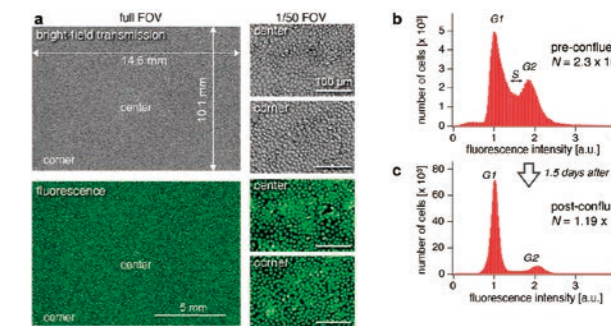


Fig.3: Simultaneous detection and analysis of more than one million cells. ©2021 T. Ichimura et al., Scientific Reports

The article, “Exploring rare cellular activity in more than one million cells by a transscale-scope,” was published in *Scientific Reports* at DOI: <https://doi.org/10.1038/s41598-021-95930-7>



# Research Reports

## 2021.4.2 From dinner to sustainable electronics, the surprising versatility of crabs

Department of Functionalized Natural Materials/  
Hiroataka Koga



## 2021.4.2 Cohesive circuit protection for wearable electronics

Department of Functionalized Natural Materials/  
Takaaki Kasuga, Hiroataka Koga, Masaya Nogi



## 2021.4.13 When FRETing over cancer biomarkers won't work, focus on blinking instead

Department of Material Excitation Chemistry/  
Mamoru Fujitsuka, Kiyohiko Kawai



## 2021.4.23 Patching up your health

Department of Advanced Electron Devices/Takafumi Uemura, Teppei Araki, Tsuyoshi Sekitani



## 2021.5.14 Above the noise

Department of Bio-Nanotechnology/Makusu Tsutsui  
Department of Reasoning for Intelligence/Tomoji Kawai, Takashi Washio



## 2021.5.24 Keeping it rolling

Department of Architecture for Intelligence/Ken-ichi Fukui



## 2021.6.17 Passing the COVID test in just five minutes

Department of Bio-Nanotechnology/Masateru Taniguchi



## 2021.8.19 Seeing both the forest and the trees: Trans-scale scope shows big picture of tiny targets

Department of Biomolecular Science and Engineering/Takeharu Nagai



## 2021.8.20 Accessing high-spins in an artificial atom

Department of Quantum System Electronics/Haruki Kiyama, Akira Oiwa



## 2021.8.24 In situ extraction and detection of DNA is an im-pore-tant development

Department of Bio-Nanotechnology/Makusu Tsutsui  
Department of Reasoning for Intelligence/Takashi Washio, Tomoji Kawai



## 2021.9.21 Tuning flexible circuits with light

Department of Advanced Electron Devices/Takafumi Uemura, Tsuyoshi Sekitani



## 2021.9.24 Kirigami cools electronics

Department of Functionalized Natural Materials/  
Kojiro Uetani, Masaya Nogi



## 2021.9.29 Sequencing multiple RNA base modifications simultaneously: a new era of RNA biology

Department of Bio-Nanotechnology/Masateru Taniguchi  
Department of Reasoning for Intelligence/Takashi Washio



## 2021.10.18 Cutting through the noise: AI enables high-fidelity quantum computing

Department of Quantum System Electronics/  
Takafumi Fujita, Akira Oiwa



## 2021.11.18 A nanoantenna for long-distance, ultra-secure communication

Department of Quantum System Electronics/  
Takafumi Fujita, Haruki Kiyama, Akira Oiwa



## 2021.11.18 A CARE-ing route to advanced nanoelectronics

Department of Three-Dimensional Nanostructure Science/Ai Osaka, Azusa N Hattori



## 2021.12.3 Stable and moveable; is hexagonal boron nitride the universal foundation?

Department of Three-Dimensional Nanostructure Science/Ai Osaka, Azusa N Hattori  
Department of Functional Nanomaterials and Nanodevices/Hidekazu Tanaka



## 2022.2.14 Nanopores feel the heat

Department of Bio-Nanotechnology/Makusu Tsutsui  
Department of Reasoning for Intelligence/Tomoji Kawai



## 2022.3.16 Drug-resistant bacteria flaunt their curves

Department of Biomolecular Science and Regulation/Mitsuko Hayashi-Nishino, Kunihiro Nishino  
Department of Intelligent Media/Kota Aoki



# Awards

## The Commendation for Science and Technology by the Minister of Education, Culture, Sports, Science and Technology (The Young Scientists' Award)

Department of Interface Quantum Science  
Associate Professor, Tomohiro Koyama



### Research on electrical control of magnetic domain wall dynamics in ferromagnetic nano-structure

I am very pleased to receive this prestigious award. I would like to express my deep gratitude to everyone who has supported my study so far. This study concerns an electrical manipulation of magnetic domain wall dynamics in ferromagnetic thin films. Our group has revealed the mechanism of domain wall motion induced by electrical current. Moreover, the modulation of domain wall speed, which has been believed to be universal in the same environment, has been demonstrated using an electric field effect. The results of our study pave the way for realizing next-generation memory devices based on the domain wall motion, which is expected to have superior characteristics such as non-volatile, high speed, and low power consumption.



## Osaka Science Prize

Department of Interface Quantum Science  
Professor, Daichi Chiba



### Pioneering research on acquired control of magnetism

I am honored to receive such a prestigious award. I would like to express my sincere gratitude to all the members of my laboratory, to SANKEN, and to all the professors who have taken care of us. In our laboratory, we are conducting research to draw out the unknown potential of materials and to develop devices and sensors that operate based on new principles. We would like to continue to promote interesting research from various perspectives.



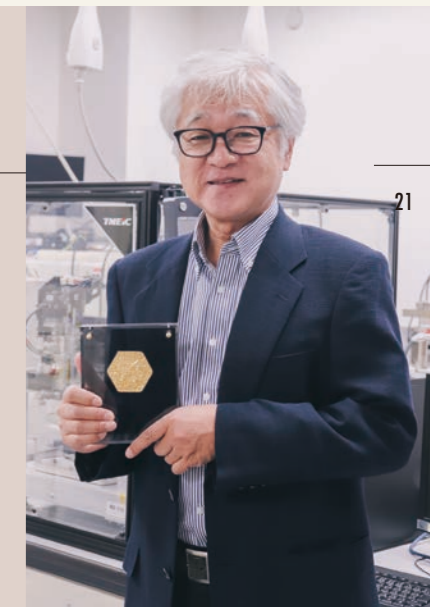
## The Commendation for Science and Technology by the Minister of Education, Culture, Sports, Science and Technology (Research Category)

Flexible 3D System Integration Laboratory  
Specially Appointed Professor, Katsuaki Suganuma



### Establishment of basic science on lead-free interconnections

It is my great pleasure to receive the honorable award this time. This award was for interconnection science and technology in electronics packaging such as lead-free soldering, printed electronics, power packaging, and organic/ceramic substrates. I would like to express my special thanks to my students, to research staffs, and to collaboration partners from companies. Their work has a great contribution to my research work. Since electronics packaging has been evolving into 3D semiconductor packaging era recently, I am very much happy to make one more step in interconnection science in electronics.



# Introduction of Flexible 3D System Integration Laboratory



Members: K. Suganuma, C. Chen, Z. Zhang, M.-C. Hseih, A. Suetake, H. Yoshida, K. Takahashi, Y. Liu, S. Zhao, S. Moribe

Post 5G and beyond 5G technologies will open a new world in near future. Not only mobile communications, but also autonomous driving, distant doctor diagnostic, instant security/ natural hazard surveillance, Industry 4.0 manufacturing, and many other new social systems and services will be realized soon or later. Flexible 3D System Integration Laboratory (F3D) has been established in 2020 to explore open innovation of advanced packaging technology for new era. The current main topics are the electric power conversion with wide band gap semiconductors such as SiC and GaN and the post 5G communication systems, which require excellent high functions as well as high reliability. We have developed numbers of essential interconnection materials from lead-free soldering, soft interconnections to heat-resistant sinter joining. For example, Ag sinter joining has been first established before 2010 and has been world widely expanding for power semiconductor assembly. The basic mechanism, why one can sinter affordable Ag flakes at so low temperature below 200°C, was understood by the nano-structure observation with thermodynamic simulation.

F3D has excellent academic partners outside, sharing deep knowledge and analytical skills for developing new materials. F3D and the partners initiate national project both for technology developments and for international standardization if required under the strong support of industries with METI/NEDO and MEXT.

F3D is organizing many open seminars as well as consortium close meetings. You can find the information at our website (<https://www.f3d.sanken.osaka-u.ac.jp/>). Laboratory facilities are open for industrial members. If you have any questions, please reach us at F3D (F3D@sanken.osaka-u.ac.jp).

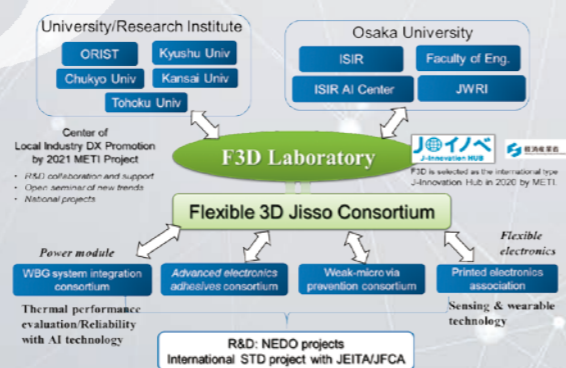


Fig.1 F3D's collaboration and industrial consortium activity.

Figure. 1 shows our activity and collaboration structures. F3D has four active consortiums, WBG system integration, Advanced electronics adhesives, Weak-micro via prevention, and Printed electronics. Not only inside Osaka University,



# 10<sup>th</sup> imec Handai International Symposium December 6 – December 13, 2021

The 10th memorable symposium composed of a real time online and web hybrid configuration was held during December 6 to December 13, where prof. Tohru Sekino, director SANKEN, prof. Jo De Boeck, executive vice president & CSO, imec joined. After giving keynote speech of profs. Tohru Sekino and Chris Van Hoof, imec fellow, there were 20 oral presentations on imec HP for 1 week with research activities of next generation computing, information processing, flexible, wearable electronics, nano, and bio electronics. On the final day, December 6th, a live on line Q & A session was held. Total participants were 93, including 39 from imec and 49 from Osaka University. The feature of this year was that there were 2 presentations and 5 attendees from Tokyo Institute of Technology. I hope that next year, we will be able to develop stronger cooperation by holding a real event.

In Osaka University COI project, we developed latest MOOD8 EEG headset with new software Onyx with signal processing pipeline and DAE chips in place of two chip configuration (FEOL and BEOL) and also new adjustability for all head sizes.



MOOD8 EEG headset



Jo De Boeck welcome word



Chris Van Hoof keynote speech

## The 25th SANKEN International Symposium

On January 6th and 7th, 2022, The 25th SANKEN International Symposium on “Innovative Science and Technology after the Emergence of COVID-19” was held on-line concurrently with The 20th SANKEN Nanotechnology International Symposium, The 9th Kansai Nanoscience and nanotechnology International Symposium, The 17th Handai Nanoscience and nanotechnology International Symposium, and The 3rd AIRC-SANKEN International Symposium. This symposium focused on innovative science and technology during the pandemic to provide an opportunity for outlining of upcoming developments in various fields. Prof. Sven Groppe (University of Lübeck), Prof. Jens Sobek (University of Zurich), Dr. Domenico Furfari (AIRBUS Operations GmbH),

and Prof. Jai Pal Mittal (National Academy of Sciences) provided plenary lectures, and 6 professors provided invited lectures. In addition, 19 young scientists of university or company presented their studies as young invited talks. In the symposium, 44 poster presentations were also made on-line, and the poster awards were provided to 6 excellent presentations by students or young researchers. All presentations on timely topics and discussion were stimulating and will promote scientific and technological developments.

## SANKEN - The official English name has changed

We are pleased to announce that the Institutes has changed its official English name to “SANKEN” as of 1 June 2021.

Some of you may feel sad or uncomfortable about the change of the official English name (The Institute of Scientific and Industrial Research) and its abbreviation (ISIR), which you have been familiar with for a long time, to a simple six-letter word. However, the “SANKEN” will remain unchanged, and the achievements of The Institute of Scientific and Industrial Research will continue.

As we approach the centenary of the founding of the Institute and the midst of the 21st century, when the shape of society is likely to change dramatically, we will continue to promote activities based on our philosophy of contributing to society through the promotion of advanced research and co-creation, so that “SANKEN” will be widely recognized and familiar throughout the world as “that research institute” in Osaka.

We would like to ask for your continued support and cooperation so that “SANKEN” can further spread its wings around the world.

### Azusa N. Hattori

Department of 3D Nanostructure Science

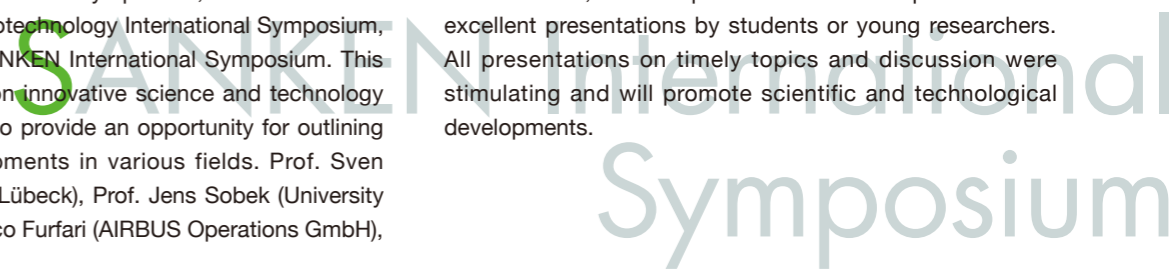
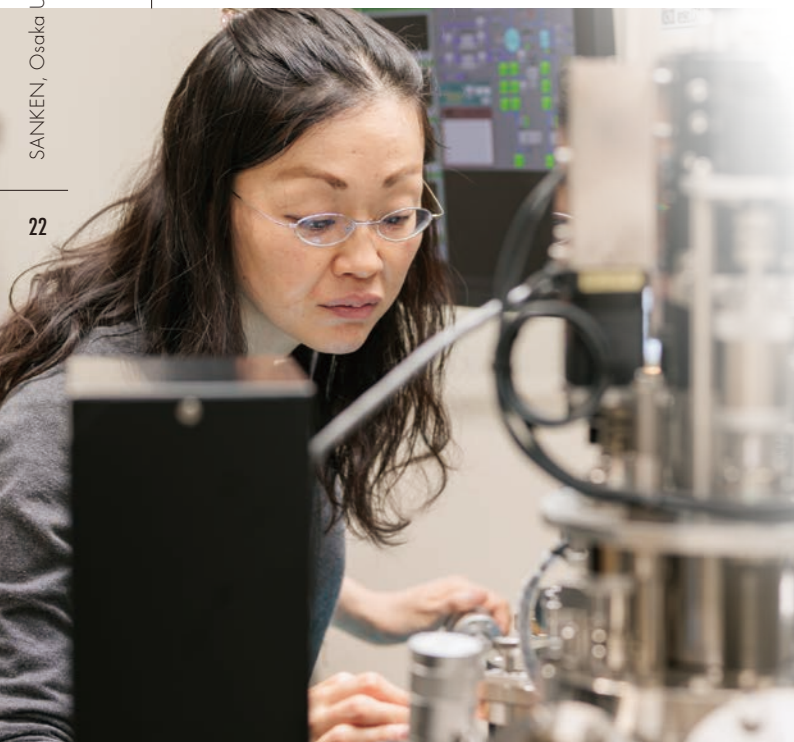
## “Flexo-material science for the strongly correlated electron solids”

### Research Outline

By manipulating the deformation of solids as a new nanotechnology, I can create novel functionalities that are absent in the conventional materials. Focusing on the flexoelectric effect, that is the coupling between polarization and strain gradients, I will elucidate the essential governing factors and establish the methodology to control the electromechanical properties in the strongly correlated electron solids, which open up a new field of material science and lead to the technological innovation.

### Thoughts on Research

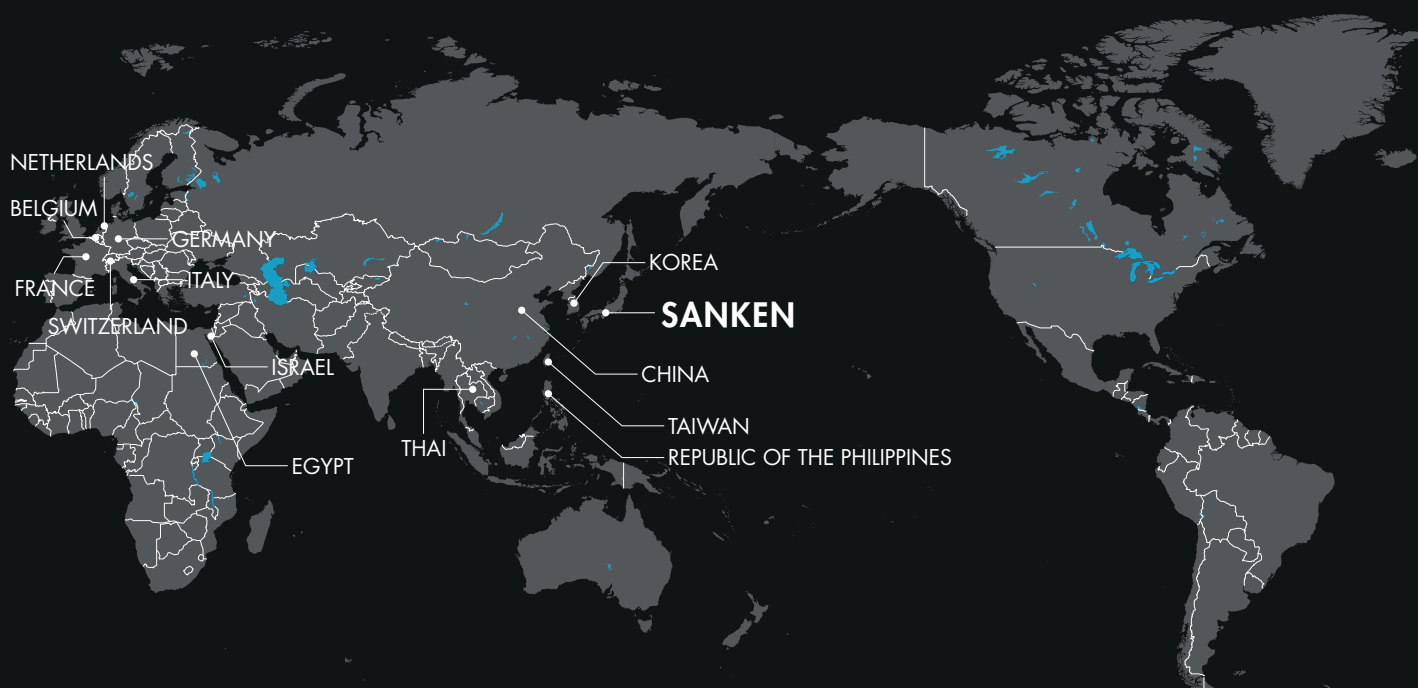
By control and design the inhomogeneous deformation in the nano-space, flexoelectricity in the solids can develop new functionality that can not be realized in the conventional material designed by elemental combinations. Utilizing my original ultra-precision three-dimensional nanostructuring techniques, I will contribute the advanced science and technology in typically material development strategy.



# Academic Exchange Agreements of SANKEN with Universities Abroad

GERMANY	Forschungszentrum Julich RWTH Aachen University University of Augsburg RWTH Aachen University (Institute of Organic Chemistry) Bielefeld University (Faculty of Chemistry) University of Cologne (Faculty of Mathematics and Natural Science)
BELGIUM	Interuniversitair Micro-Electronica Centrum vzw (imec)
NETHERLANDS	Eindhoven University of Technology (Department of Mechanical Engineering)
SWITZERLAND	University of Geneva (Faculty of Science)
FRANCE	The National Center for Scientific Research University of Bordeaux Ecole polytechnique Université Paris-Saclay
ITALY	The University of Genoa
ISRAEL	The Hebrew University of Jerusalem
EGYPT	Assiut University (Faculty of Science)
KOREA	Chonnam National University Pukyong National University (Basic Science Research Institute) Pusan National University (College of Natural Sciences) Chungnam National University (College of Natural Sciences) Hanyang University Sun Moon University (Collage of Engineering) Duksung Innovative Drug Center (DiDC), Duksung Women's University
CHINA	Peking University Peking University (The School of Electronics Engineering and Computer Science) University of Science and Technology Beijing (School of Materials Science and Engineering) Shenzhen University The University of Hong Kong (School of Biological Sciences)
TAIWAN	National Taiwan University National Chiao Tung University (Collage of Science)
THAI	Thammasat University Chulalongkorn University (Department of Computer Engineering, Faculty of Engineering) King Mongkut's University of Technology North Bangkok (Faculty of Applied Science)
REPUBLIC OF THE PHILIPPINES	De La Salle University (College of Computer Studies)

as of April 2022



**SANKEN, Osaka University**

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