GLOBAL PROMINENT RESEARCH

ENGLISH

CHIBA RESEARCH

Highlights of Innovative and Collaborative Research

2021

CHIBA UNIVERSITY

REACHING NEW HORIZONS

Welcome to ***CHIBA RESEARCH 2021***, a publication that showcases the diverse and innovative work being undertaken at the Institute for Global Prominent Research (IGPR), Chiba University.

The institute was established in 2016, with the ambitious goal of becoming a global hub for top-class research in fields as far-researching as neutrino astronomy, the science of plant-based medicine, three-dimensional holography, as well as studies on how to achieve a fair and just society.

The institute is an exciting initiative at Chiba University. It was set up to nurture key research projects being conducted at the university that are deemed to be of special significance. This issue introduces the twenty-two innovative projects currently underway at IGPR. All of these projects were selected by an advisory board that included external experts.

Three of these projects have been singled out as being of top importance – Toshinori Nakayama's work on finding unconventional vaccines that are administered via the mouth, nose or other mucosal system through which most pathogens enter the body (see page 6); Takashige Omatsu's research into spiral-shaped laser beams that exhibit left- and right-handedness and can be used to create helical nanostructures (see page 10); and Shigeru Yoshida's use of ghost-like elementary particles known as neutrinos to explore the high-energy Universe (see page 8).

We hope you enjoy this issue of ***CHIBA RESEARCH*** and we look forward to sharing with you our latest research findings.

Guided by its motto "Always aim higher," CHIBA UNIVERSITY strives to nurture globally minded students who have broad outlooks. The university values academic diversity and actively conducts leading-edge fundamental and applied research.

Chiba University was founded as a national university in Japan in 1949, when Chiba Normal School, established in 1874, merged with Chiba Medical College and several other educational institutions.

Currently composed of 10 faculties and 13 graduate schools, Chiba University is one of Japan's largest national universities, having about 11,000 undergraduate students, 3,500 graduate students and 3,500 faculty members on 4 campuses located near Tokyo. The main campus at Nishi-Chiba occupies an area of almost 400,000 square meters (100 acres) and is conveniently located between Tokyo Station (about 40 minutes by train) and Narita International Airport. The 850-bed University Hospital, a core hospital for the region, is adjacent to the School of Medicine on the Inohana campus.

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Top Research Program

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MUCOSAL IMMUNOLOGY AND THERAPEUTICS

FIGHTING PATHOGENS AT THEIR POINT OF ENTRY

—Vaccines that induce immune responses at mucosal membranes of the intestines, lungs and other organs could help prevent deadly infections.

Research Keywords: Immunology, Mucosal Immunity, Allergy

The mucous membranes that line many of the tracts and structures in the body are the first lines of defense against foreign invaders. Equipped with a powerful and highly specialized immune system, these mucosal sentinels protect the surfaces and, by extension, the body interior, against the threat of gastrointestinal, respiratory and sexually transmitted infections, as well as cancer, allergies and more.

If these immune cells let their guard down, pathogens such as bacteria and viruses can invade. On the other hand, if they are overly vigilant, hyper-reactive conditions like asthma or autoimmune inflammatory bowel disease can take hold. Getting the balance right is the goal of the International Center of Excellence in Mucosal Immunology and Innovative Allergy Therapeutics.

Launched as a joint initiative between Chiba University and the University of California, San Diego, in 2016, the center aims to harness the power of the mucosal immune system to develop the next generation of preventive vaccines against infectious, allergic and inflammatory diseases.

Most vaccines in use today are administered by injection. But since most infectious agents enter the body at mucosal surfaces, vaccinating through the nose, mouth, or some other mucosal route could provide more protection. Since transmission often occurs at these sites, boosting the body's ability to block that transmission could stop an infection or autoimmune reaction at its source.

"While existing injectable vaccines are able to prevent serious conditions from developing, they are not effective enough to defend against infection," notes program director, Toshinori Nakayama.

FROM BASIC RESEARCH TO CLINICAL APPLICATIONS

Before new treatments can be developed, however, much more needs to be learned about the molecular architecture of the mucosal immune system. That is why the International Center of Excellence is focusing on basic research while simultaneously advancing clinical applications. It is also strengthening ties between researchers and industry in the hope of translating its discoveries into therapies for patients.

To this end, Nakayama is building a robust pipeline of talented scientists who can move research findings seamlessly from the lab bench to the hospital bedside.

"The research system we are creating is unprecedented," says Nakayama, who is also vice president of Chiba University and dean of the Graduate School of Medicine and the Faculty of Medicine.

Projects at the International Center of Excellence fall into three categories: Hiroshi Kiyono is studying the basic mechanisms of mucosal immunology in response to microbial infections and assorted diseases; Nakayama and colleagues, including Atsushi Onodera, Motoko Kimura and Osamu Ohara, are focusing on allergic reactions and novel treatments that target the mucosa; and Hiroshi Nakajima and colleagues belong to the clinical research team that is developing new vaccines and adjuvants for pathogens endemic to Japan and around the world.

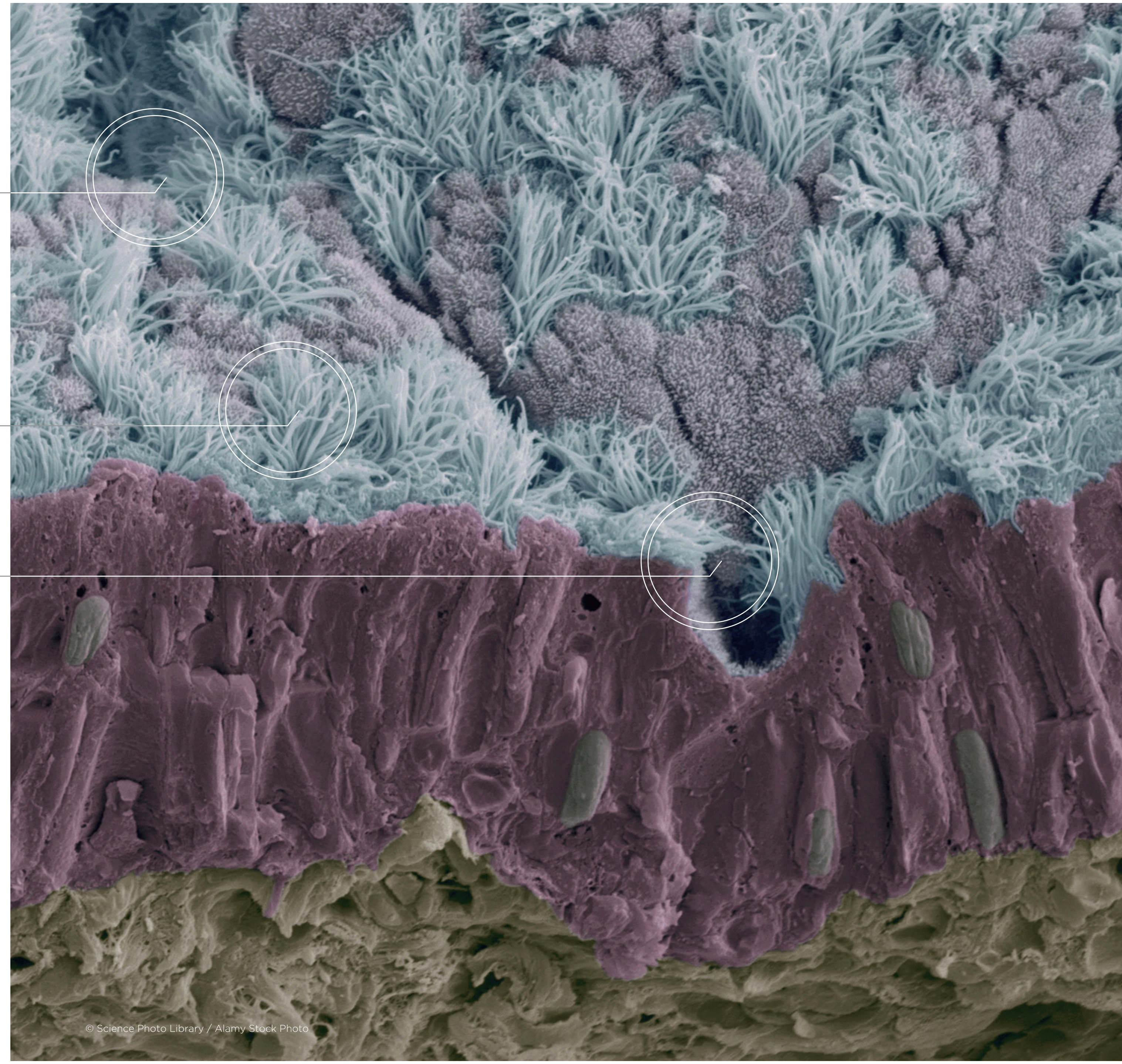
Chiba has initially committed US$2 million over five years to this alliance. Together with a matching contribution from UC San Diego, the project will facilitate joint research and exchanges between investigators and students on both sides of the Pacific.

MUCOUS MEMBRANE IN THE AIRWAY

Mucous coat layered with tiny hairlike cila.

Immune cells in the mucous membrane protect the body against invasion by pathogens such as bacteria and viruses. However, if they are too vigilant, they can cause diseases.

Vaccines that directly target the mucosal surface could provide more protection than a typical injection.



Members

Toshinori NAKAYAMA
Professor, Graduate School of Medicine

Hiroshi NAKAJIMA
Osamu OHARA
Atsushi ONODERA
Yosuke KURASHIMA
Hiroshi KIYONO
Motoko KIMURA
Akira SUTO

CHIBA RESEARCH

INTERNATIONAL CENTER FOR HADRON ASTROPHYSICS

REVEALING HIDDEN MESSAGES FROM THE COSMOS

Research Keywords:
Neutrino Astronomy, Cosmic Rays, South Pole, Elementary Particle Experiment

—From a remarkable observatory buried deep in the south polar ice, Chiba University astrophysicists are helping to explore the origins of the Universe.

Amundsen-Scott station in Antarctica.

Humans have been observing the stars for tens of thousands of years, first with our eyes, then with optical telescopes, and more recently using devices that can detect light at the extremes of the electromagnetic spectrum far beyond the visible range. Yet despite phenomenal progress in astronomy over the past half century, much of the Universe remains completely hidden from view, obscured by other matter, other radiation sources, and light's interaction with the interstellar medium. Now, scientists are on the verge of being able to peer into some of the most mysterious corners of the cosmos using not light but neutrinos — near-massless subatomic particles that travel close to the speed of light across the Universe without being deflected by magnetic fields or absorbed by matter.

The International Center for Hadron Astrophysics (ICEHAP) led by Shigeru Yoshida is part of the global collaboration responsible for managing the IceCube Neutrino Observatory deep in the ice at the South Pole's Amundsen–Scott station. "One of the longest standing puzzles in astrophysics is the origin of high-energy cosmic rays and neutrinos," says Yoshida. "The new windows to our Universe opened by neutrino observations, combined with powerful computer simulations of cosmic plasma, have great potential to finally resolve this mystery."

THE ICECUBE COLLABORATION

Neutrinos are the most abundant particles in the Universe after photons (light particles). They originate in some of the most violent and least understood cosmological phenomena like supernovas, galactic cores and black holes. After their birth, they travel in straight lines from their source with almost no deflection or absorption, making them ideal messengers from the heart of these mysterious astronomical objects. But these same properties also make them exceedingly difficult to detect.

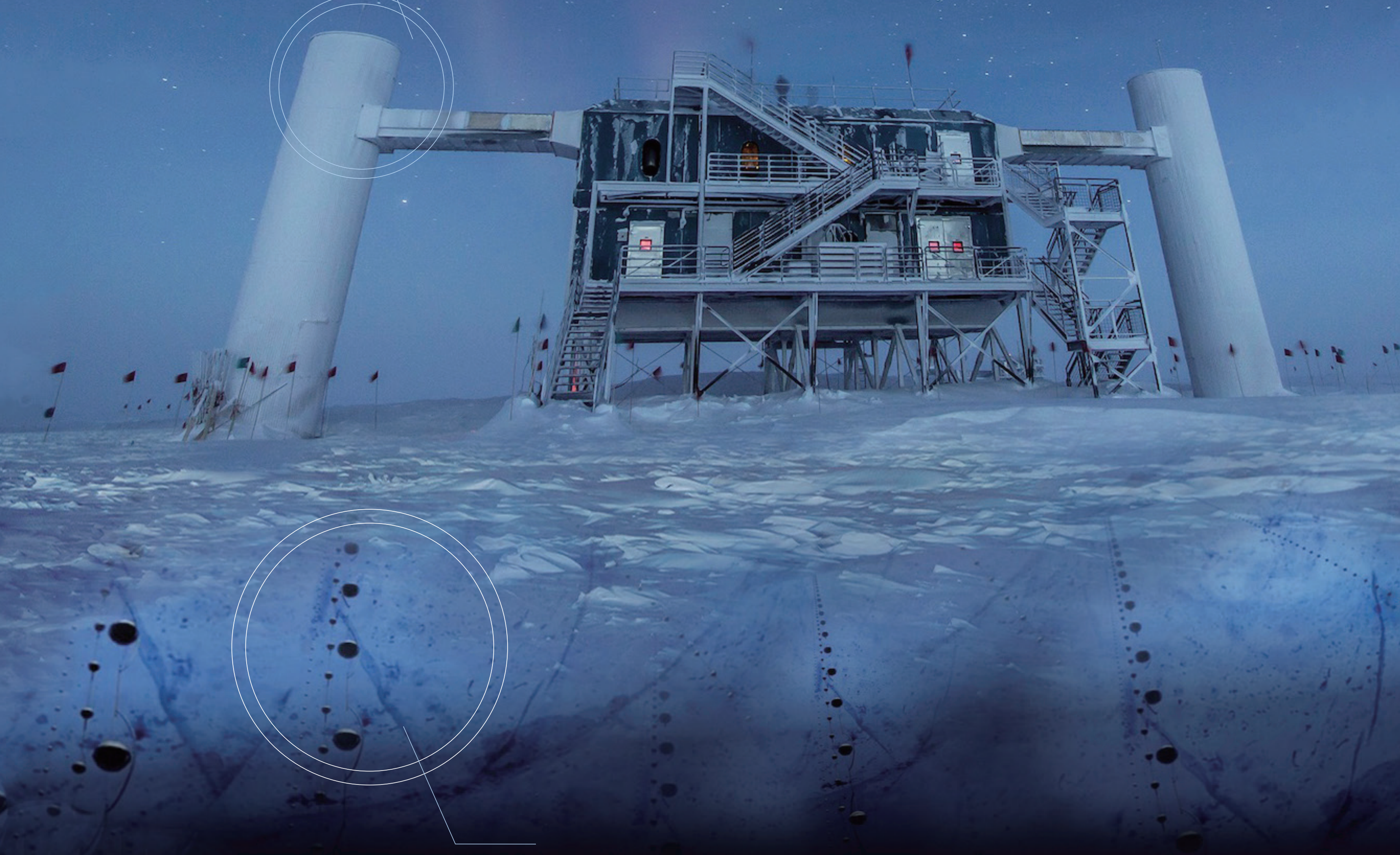
The IceCube collaboration, involving 300 physicists from 53 institutions in 12 countries, has gone to extreme lengths to detect these ghost-like, high-energy particles.

The IceCube observatory is a cubic kilometer of crystal-clear ice, deep below South Pole Station — the only place on Earth where such large volumes of clear, pure and stable ice can be found along with the infrastructure needed to support scientific research. By suspending thousands of delicate photodetectors on strings in a network of vertical holes drilled through the ice, physicists can capture the rare explosion of energy that occurs when a neutrino collides with an oxygen or hydrogen nucleus. Of the trillion, trillion neutrinos that pass through IceCube every day, the facility records just a few hundred collisions from high-energy neutrinos — a minute fraction of the neutrino flux but more than enough to stimulate some very exciting research. "We are proud of having been key players in the discovery of high-energy cosmic neutrinos, which astrophysicists have been dreaming about for more than 30 years," says Yoshida talking about his team members in ICEHAP.

Another important contribution of ICEHAP to understanding the high-energy Universe is its supercomputer-based massive numerical simulation program for deep investigation of the physical mechanisms behind high neutrino production. "Through our simulations we are helping to uncover the hidden messages carried by these neutrinos and to reveal the physical mechanism by which high-energy cosmic rays are accelerated at their source," says Yoshida. In 2018, the IceCube collaboration has finally discovered that a special type of galaxy, TXS 0506+056, is a birthplace of cosmic neutrinos. This achievement was selected as one of the top breakthroughs by *Science*. In 2022, the team's new detectors called "D-Egg" will be used at the South Pole. It clearly shows the steps being taken forward.

Two towers receive information from 5,160 light-detecting sensors buried 2,500 meters beneath the South Pole.

The IceCube Neutrino Observatory, at the South Pole's Amundsen-Scott station. The International Center for Hadron Astrophysics is part of the global collaboration constructing IceCube.



Neutrinos are subatomic particles that typically pass freely through matter. Other particles cannot penetrate the Earth, so below the 'Dark Sector' near the South Pole, free from every other interference, it is quiet enough for the neutrinos to be detected.

Members

Shigeru YOSHIDA
Professor, Graduate School of Science

Aya ISHIHARA
Lu LU
Colton HILL
Ryoji MATSUMOTO
Tomoyuki HANAWA
Hideyuki HOTTA
Ryo NAGAI
Kenichi KIN
Maximilian MEIER
Yosuke MATSUMOTO
Tomoaki ISHIYAMA

CHIRAL MATERIALS SCIENCE

USING LIGHT TO ESTABLISH A NEW FIELD OF CHIRAL MATERIALS

Research Keywords: Applied Optics, Optical Vortex, Chirality

—Understanding the universal property of chirality could lead to new materials and technologies for photonics and other applications.

Members

Takashige OMATSU
Professor, Graduate School of Engineering

Hisao ISHII
Takeshi MURATA
Kazuyuki SAKAMOTO
Kenichi OTO
Nobuyuki AOKI
Takayoshi ARAI
Akira YANAGISAWA
Shiki YAGAI
Tetsuhiro NEMOTO
Akira MATSUURA
Kohji ITO
Daisuke UMENO
Keisuke IIDA
Masami SAKAMOTO
Peter KRÜGER
Hiroyuki YOSHIDA
Toyokazu YAMADA
Kazuki NAKAMURA
Atsushi NISHIDA
Midori ARAI
Kazuhiro YOSHIDA
Motohiro AKAZOME
Yoshihiro NISHIDA
Hiroki TAKAHASHI
Naohiko ANZAI
Satoshi OGASAWARA

Of the many mysteries still to be unraveled in the natural sciences, one of the most compelling is the origin and power of chirality — the property of a molecule or object that has two mirror-image forms — like our left and right hands.

Chirality is universal in biology, chemistry and physics. It critically affects the biochemical processes underpinning life, is a vital aspect of drug discovery, and crops up in particle physics. Light can have chiral properties that affect how it interacts with matter. But how can the power of chirality be harnessed and controlled? And what new discoveries and technologies might this give rise to? These are some of the questions Takashige Omatsu and his team are asking.

Light beams can be chiral when they are imparted with so-called helical wavefronts, that is, polarity that rotates either left or right. "We can use 'optical vortices' to twist the physical properties of metals, semiconductors and organic materials on the nanoscale to create chiral nanostructures with unique features," says Omatsu. "Our goal is to establish chiral photonic materials as an original research field and to pioneer new technologies such as chiral plasmonics and metasurfaces for nanoscale chiral chemical reactors, chiral-selective imagers and chiral sensors," he explains.

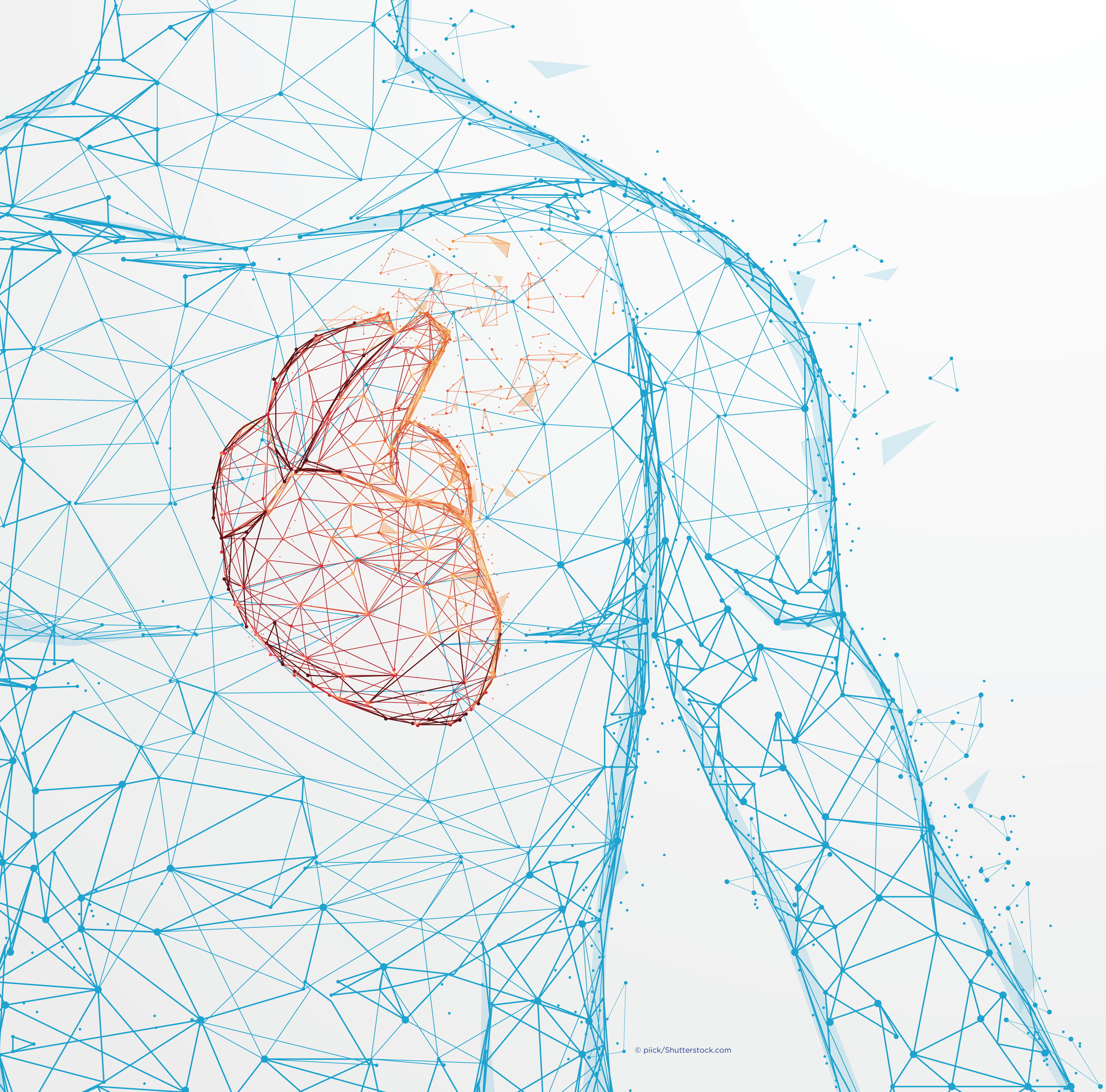
LIGHT CORKSCREWS

Omatsu's team focuses on the interaction between helical light and materials, and the physical properties and potential uses of such modified materials. The electromagnetic field of helical light rotates as the light moves through space. When this field interacts with conductive materials like metals, nanoscale corkscrew-like variations in physical properties can be inscribed on the material's surface. The modified surface can then react differently to left- and right-handed chiral molecules or helical light, giving rise to a range of interesting possibilities for chemical sensing, synthesis and imaging.

"We can use helical light to create nanostructures such as twisted needles, twisted reliefs and twisted fibers," says Omatsu. "We have also found that the same process can polymerize fullerene — a well-known functional organic molecule that is normally not conductive. This causes fullerene to form a novel conductive metallic phase, which could be used as the basis for fabricating electronic devices without metals and semiconductors."

Omatsu believes 'nanovortices' will one day be used for nanoscale precision control of light polarization, electron orbital motion and the aggregation of chiral molecules. "Our research will lead to materials for next-generation photonics and electronics, and new applications in chemical synthesis, pharmacy, biology and medicine," he says. "It might also allow us one day to answer the scientific mystery: 'Why does handedness exist in nature?'"

Omatsu has collaborated with many Japanese and international researchers, and is always looking for students and early career researchers. "Our research center brings together physicists, chemists, biologists and even medical doctors, and we frequently have brainstorming meetings to think up ideas for new projects," he says. "Several international researchers work here. There is a wonderful diversity of backgrounds and expertise."



Humanities and Social Sciences

CHIBA STUDIES ON GLOBAL FAIR SOCIETY

Forging a Fairer World

SMALL AREA ESTIMATION AND ITS APPLICATION

Improving Datasets Using Small Area Estimation

TRANSLATIONAL RESEARCH PROGRAM OF PSYCHIATRY AND PSYCHOLOGY

Cognitive Behavioural Theraphy Comes of Age in Japan

MIGRATION AND REFUGEE STUDIES

Living with People with Foreign Backgrounds

CHIBA STUDIES ON GLOBAL FAIR SOCIETY

FORGING A **FAIRER WORLD**

Research Keywords: Global Welfare Society, Multidisciplinary Social Science, Fairness

—A multidisciplinary team of researchers looks at how to create a fair society — on a global scale.

With globalization comes the need to ensure that people from all cultures, countries and backgrounds are treated fairly and equally. The drive to create a just global society requires solid foundations in all countries, backed by informed government policies and strong support networks at local, regional and national levels.

Much previous research into justice and social change has been dominated by studies of Western societies, but the rapid changes experienced by Asian countries in recent decades have spawned a growing field of research focused on building fair societies in Asia.

Researchers in law, politics, economics and social sciences have recently established the Chiba Studies on Global Fair Society project, with the aim of creating an interdisciplinary research base to inform future local, national and international policies.

Lead researcher on the project, Jiro Mizushima, says the key concept is fairness. "We define fairness as the basic element of justice," he explains. "In fact, we argue that it exceeds justice in most cases. At the same time, we embrace values such as equality and liberty."

Mizushima, whose research interests lie in welfare state reform in Europe, says the project aims to go beyond the traditional discussion of equality — it seeks to construct new principles that value diversity among people in a global society.

HOW DO WE ACHIEVE A FAIR SOCIETY?

The project consists of four interrelated research groups and a further six teams working to publicize the findings to a wide audience. Their focus is on challenging and overcoming unfair practices on all scales, investigating issues such as gender inequality, widening income gaps, migration, and the collapse of regional and marginal communities, both in Japan and around the world.

In particular, the researchers believe that proposals and practices aimed at closing the gap between large cities and local cities and resolving gender gaps are essential to overcoming the divides.

The key aims of the project are to investigate the development, transformation and limitations of existing welfare state models and to provide empirical evidence for how a fair society can be achieved in the 21st century.

Mizushima has spent considerable time researching aspects of the welfare state in the Netherlands, including how it has responded to social challenges such as global economic fluctuations and an aging population.

"Fairness has been the core of legal and political philosophy since ancient times, and so one of our teams is examining equality and fairness from a historical perspective, comparing political, economic and legal standpoints over time," he says. "Another group will analyze the meaning of fairness in the 21st century, providing us with fundamental guidelines to underpin our program."

The team plans to form networks of academics across the globe. To this end, they have hosted five highly successful international symposiums. "Many of our members are involved in local and national policymaking committees, and they are key to informing policy makers of our work," says Mizushima.

The project has published books and papers both in Japanese and English based on their research outcomes, and welcomes those interested in all aspects of social science, from law and politics to sociology and economics.

Members

Jiro MIZUSHIMA
Professor, Graduate School of Social Science

Masaya KOBAYASHI
Hikari ISHIDO
Hiroyuki MINAGAWA
Iwao FUJISAWA
Takayuki KAWASE
Reiko OGAWA
Akiko OISHI
Masahiro OGIYAMA
Seiichi IGARASHI
Kentaro SATO
Chiyo YONEMURA
Li XIANG

SMALL AREA ESTIMATION AND ITS APPLICATION

IMPROVING DATASETS USING SMALL AREA ESTIMATION

Members

Genya KOBAYASHI
Associate Professor, Graduate School of Social Science

Yuki KAWAKUBO
Shouto YONEKURA
Tsubasa ITO
Ryota YUASA
Yukiko OMATA
Eisaku SATO
Hiromi SAITO
Yuta YAMAUCHI
Syonosuke SUGASAWA

Research Keywords: Economic Statistics, Baysian Statistics, Small Area Estimation

—Statistical techniques can improve the accuracy and scope of limited information, saving time and money.

Collecting comprehensive data on populations is not always possible, or even the best use of resources. Surveys can be expensive and time-consuming, so improving the accuracy of data with "small area problems" can stretch data resources further.

"Small area problems happen when an estimator, such as sample mean for a small area, becomes very unstable because of small sample sizes," explains Associate Professor Genya Kobayashi, who is part of a new Chiba project called Small Area Estimation and Its Application to the Analyses of Poverty, Public Health and Disaster.

His group is focused on overcoming such issues by developing small area estimation (SAE) techniques that borrow statistical strength from supplementary data.

OVERCOMING INEQUITY AND PUBLIC HEALTH INSIGHTS

While the applications of SAE are broad, "small area problems arise particularly within official statistics on which governments make important political decisions. Hence, small area estimation techniques could lead to more effective policy making," notes Kobayashi.

An example crops up in the monthly Family Income and Expenditure Survey (FIES) conducted by Japan's Statistics Bureau. Although FIES provides the latest information on household income and expenditure, at a small area level, such as a city level, the sample size of FIES becomes so small that direct estimators are unstable and can't grasp detailed trends.

But FIES, says Kobayashi, can borrow statistical strength from data in the National Survey of Family Income and Expenditure (NSFIE). The sample sizes in the NSFIE are much larger than in the FIES and thus more reliable, but because the survey is time consuming and costly, it's only carried out every five years.

The FIES and the NSFIE collect area-level aggregated data, so Kobayashi's group used the Fay-Herriot, a mixed regression model routinely used in SAE.

However, when data is in other formats more appropriate SAE models must be developed. Recently, for example, Kobayashi's group has been working to improve an income map of Japan based on the Statistic Bureau's Housing and Land Survey (HLS). Using a new statistical model that accounts for the grouped data format of the HLS and additional data from the Population Census, they measurably reduced the uncertainty of the HLS's income estimates.

SAE's scope isn't limited to stabilizing data, adds Kobayashi. SAE techniques can add information. For example, the HLS model could also infer income in areas where data is missing. Using a mixture modeling approach, the team recently estimated the distribution of land prices around train stations in and around Tokyo by making inferences across areas.

Contributing to public health discussions, in 2018 Kobayashi collaborated on a paper that used a spatial Poisson regression model to look the links between access to clean water and dropping mortality rates in the early 1900s. Kobayashi and collaborators at the Tokyo Institute of Technology and Duke University in the United States looked at death rates in Tokyo in 1930 against a dataset of taps. The group found that access to clean water accounted for 41.3 percent of the improvement in Tokyo's crude death rate between 1921 and 1937. This paper adds to discussions on the relative importance of nutrition and clean water on mortality.

Kobayashi hopes that everyone from policy makers to businesses will soon come to the group to add a finer resolution to their datasets.

TRANSLATIONAL RESEARCH PROGRAM OF PSYCHIATRY AND PSYCHOLOGY

COGNITIVE BEHAVIOURAL THERAPHY COMES OF AGE IN JAPAN

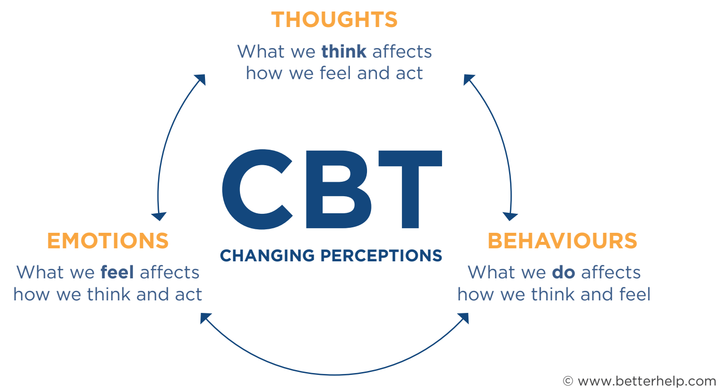
Research Keywords: Psychiatry, Psychology, Cognitive Behavioral Therapy

—Better access to mental health care in schools, at work and online could help people of all age groups suffering from anxiety, depression and other related conditions.

Members

Eiji SHIMIZU
Director and Professor, Research Center for Child Mental Development

Eiji KIMURA
Chikae ISOBE
Fumiko SUNAGAMI
Tomihisa NIITSU
Yoshiyuki HIRANO
Kenichiro SHIMAI
Makoto ICHIKAWA
Miho IWATA
Keito NAKAMICHI
Aika TOMOTO
Toshiyuki OTANI
Kensuke YOSHIMURA



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Major efforts are underway to help treat and prevent anxiety-related disorders in Japan —where as many as one in four people experience mental health problems during their lifetime.

Social Anxiety Disorder (social phobia), one of the most prevalent, is characterised by an intense fear of social situations. In some cases, social phobia can lead to addiction, depression or suicidal behaviour.

Many doctors, legislators and patients now recognise cognitive behavioural therapy (CBT) as an effective treatment for social phobia. By changing negative patterns of thinking and behavior, CBT can help children overcome anxiety and the fear of uncertainty, adolescents better manage depression and irritability, and adults deal with a host of stressful life experiences.

A LEADING CENTRE FOR CBT RESEARCH AND EDUCATION

We are now actively trying to increase the number of CBT experts in Japan," says Eiji Shimizu of Chiba University's Research Center for Child Mental Development and Chiba University Hospital's Cognitive Behavioral Therapy Center. "However, CBT resources in Japan are still relatively scarce." Chiba University and its affiliated hospital are spearheading efforts to address this.

The Chiba Improving Access to Psychological Therapies (Chiba-IAPT) program, adapted from a UK model, became the first post-qualification training course of its kind in 2010.

"It's important to tailor treatments to reflect not only cultural differences, but also personal differences," Shimizu adds. His team are developing new tailored interventions, such as internet-based CBT (iCBT), which are low-cost, easy to use, and provide optional anonymity.

In 2017, his group released a study protocol for iCBT on patients with persistent insomnia. They have also produced a simplified, five-minute program that can be used to help reduce depressive symptoms.

As part of his wider research, Shimizu contributed to the first study that visualised changes in brain activity during psychotherapy in 2015. Using functional magnetic resonance imaging (fMRI), the results indicated that the left posterior parietal cortex plays a vital role in cognitive restructuring — a process used in CBT that enables people to challenge existing beliefs.

In 2016, Shimizu and his colleagues showed that CBT can help reduce social anxiety for patients ineffectively treated with antidepressants.

In recognition of the growing need for professional CBT care, at the end of 2018 the Japanese government began to certify licensed psychologists. The national health insurance system has been updated to cover doctor-administered CBT for patients with depressive disorders, anxiety disorders and bulimia nervosa.

There are also moves to introduce CBT-based anxiety prevention programs in Japanese elementary schools.

A 2018 study, designed by Yuko Urao and supervised by Shimizu, examined the effectiveness of an anxiety prevention program named Journey of the Brave, targeted at children aged 10–12 years. Consisting of ten 45-minute sessions held during school hours, the program involved deepening understandings of anxiety, monitoring feelings, and developing assertiveness skills to reduce social stress.

While further follow-up studies are planned, preliminary results indicate that the program can help children manage their anxiety levels. "Our hope is that in ten years' time, all children in Japan will have access to this program," Shimizu says.

MIGRATION AND REFUGEE STUDIES

LIVING WITH PEOPLE WITH FOREIGN BACKGROUNDS

Research Keywords: Globalization, Migration and Refugee Studies, Multicultural Coexistence

—The Global-Local Nexus

THE INCREASED TRANSNATIONAL MOVEMENT OF PEOPLE

Until countries started closing their borders due to COVID-19, the cross-border mobility of people was part and parcel of everyday life in a globalized world. Some crossed borders for study or work, while others had no choice but to flee across boundaries to escape conflict and persecution. Globalization has increased the number of migrants and refugees, creating numerous impacts worldwide that lead to the burgeoning of research in the field of humanities and social sciences on migration and transnational mobility of people.

As witnessed in the 2015 Syrian refugee crisis in Europe, Britain's withdrawal from the EU, the massive flow of Rohingya refugees from Myanmar to neighboring countries, the movement of people has significantly influenced and altered the society.

As of late 2019, approximately three million registered foreign residents are living in Japan, led by several policy initiatives including the amended Immigration Control and Refugee Recognition Act and the "300,000 International Students Plan", which aimed to increase the number of international students.

Migrants are engaged in different types of work that sustain our daily lives and contribute to the economy. However, their contribution is not always visible. Migrants include people of various backgrounds and Japanese society is in fact quite diverse; however, sharp boundaries are often drawn between "Japan/ Japanese" and "foreign countries/ foreigners". There is also a tendency to perceive people in terms of prejudice and stereotypes based on the intersections of race, class, and gendered hierarchies that exists in Japan.

Led by Reiko Ogawa, this research group aims to integrate the transnational mobility of people with practical initiatives in the local area. It comprehensively studies the background for this global mobility, networks that enable it, policies and institutions, education and employment of migrants in Japan to identifying the challenges affecting multicultural coexistence in Chiba.

First, we study the migration trajectories through multidisciplinary approach. Backgrounds, global norms and networks provide the context in which mobility has been shaped, facilitated or hindered. Second, we focus on education and employment of migrants and children with foreign roots in Chiba.

Taking a multidisciplinary approach encompassing international relations, history, sociology, economics, management, educational studies, law and area studies, we present the research findings, facilitate networking and policy advocacy.

INTERGRATING EDUCATION AND EMPLOYMENT

The keyword of this research is multicultural coexistence. "The term 'multicultural coexistence' is often used to mean the integration of migrants into society. In contemporary Japan, the critical issue is to ensure the rights of migrants and integrate education and employment," says Ogawa. Japan has ratified many international treaties, but the failure of international norms to penetrate domestic affairs has caused many challenges. One of these challenges is education for children with foreign roots. Thus far, education policies in Japan have not given a clear place to these children. Therefore, low education levels, drop out and unemployment have become pressing issues. Many studies have shown that a lack of educational opportunities causes a lifelong impact and results in severe losses for society. Instead of marginalizing and excluding children with international backgrounds, we must provide an environment in which they can apply their latent skills. "As the Japanese population shrinks at an accelerating rate, it has become urgent to create a positive cycle that integrates the education and employment of migrants. This is a significant undertaking, both academically and policy wise," says Ogawa.

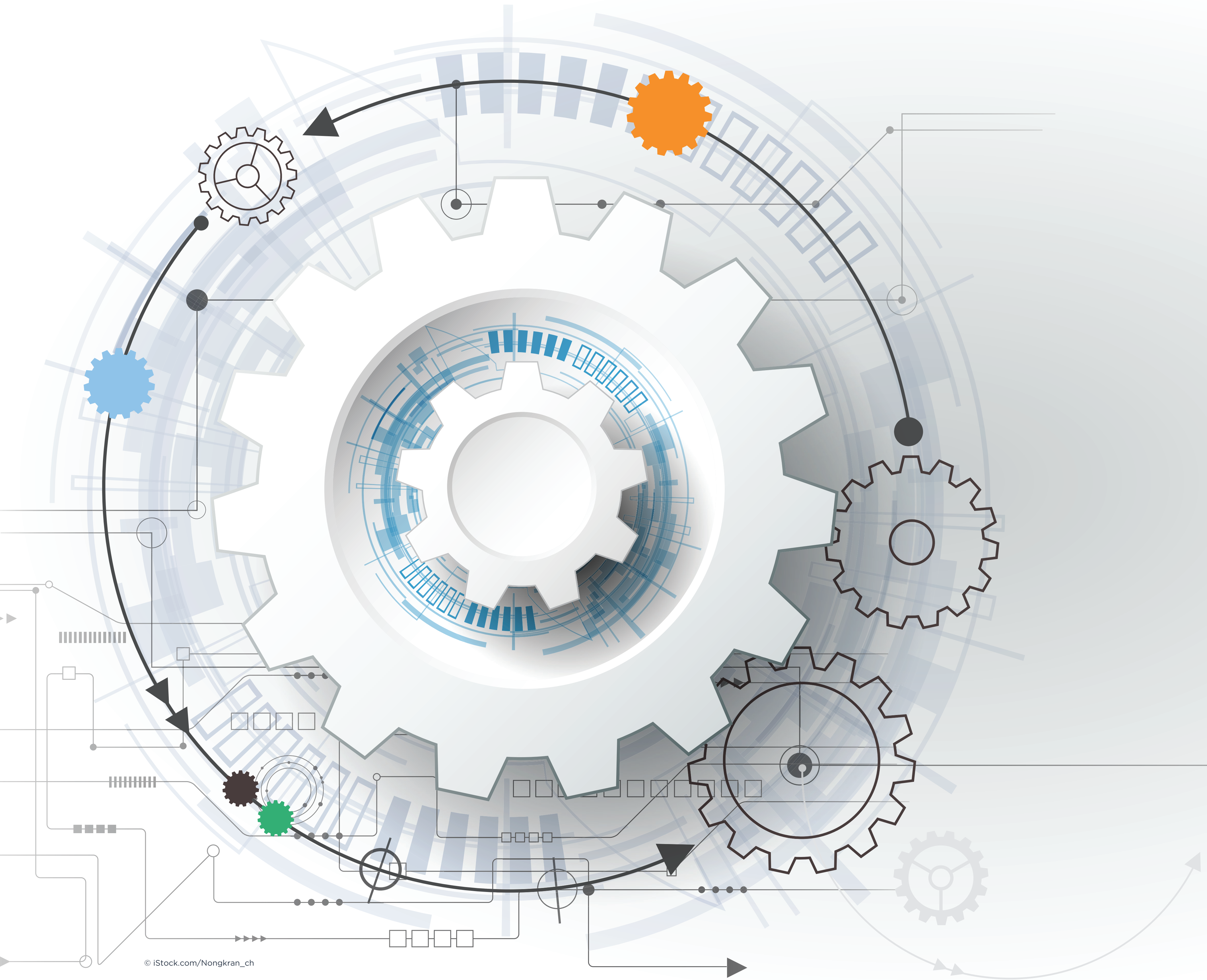
A society that recognizes diversity and where different cultures coexist would be a better one not only for migrants, but also for the Japanese, who are themselves diverse in terms of class, gender, ethnicity, social position, and physical and mental challenges.

Members

Reiko OGAWA
Professor, Graduate School of Social Sciences

Ayako SASAKI
Chihiro NAKAMURA
Harumichi YOKOO
Satoko KOBAYASHI
Yoshie TAKAMITSU
Keiko SAKAI
Ken ISHIDA
Tomoko FUKUDA
Kaoru SHIMIZU
Yuichi TSUCHIDA
Naoki SAKIYAMA
Ai SAITO
Hiroko GOTO

CHIBA RESEARCH



Science and Engineering

NEXT-GENERATION THREE-DIMENSIONAL DISPLAY AND MEASUREMENT

FUTURE IMAGES **MORE THAN MEETS THE EYE**

Research Keywords: Computer Holography, Volumetric Display, High Performance Computing

—Advances in three-dimensional image display and measurement techniques have applications in multiple fields, from medicine to communication and entertainment.

Members

Tomoyoshi SHIMOBABA
Professor, Graduate School of Engineering

Takashi KAKUE, Takashi OKAMOTO, Atsushi SHIRAKI, Tomoyoshi ITO, Seiichi KOAKUTSU, Michiko TAKAGAKI, Shigeo SHIODA, Yota YAMAMOTO

Technologies based on three-dimensional (3D) image displays and holography may conjure up visions of science fiction, but the Next-generation Three-dimensional Display and Measurement program aims to make these advanced tools part of everyday life.

Holograms create true three-dimensional images, which allow the viewer to see an object from all angles. They are created using coherent light sources such as lasers, which can store the complex light interference patterns required to accurately recreate an entire 3D object in full color. However, the main drawback of holography is the immense computational burden of producing high-quality holograms, not to mention creating moving 3D video images in real time.

Leader of the 3D program, Tomoyoshi Shimobaba says his team is developing ultrafast algorithms and dedicated computers for holography to create the world's first real-time holographic 3D display system.

"These dedicated computers will have a computational speed three or four orders of magnitude higher than the household computers of today," adds Tomoyoshi Ito, advisor on the project. "Based on this dedicated technology, we will investigate holographic projection, digital holographic microscopy and ultrarapid holographic imaging techniques."

Among the team's recent successes is a small, inexpensive, zoomable holographic projection system, suitable for use in classrooms, medical applications and entertainment products. Shimobaba's team refined mathematical image manipulation techniques to ensure a high-resolution, non-grainy holographic image even when zooming in and out. The researchers are further developing algorithms that can reduce 'speckle noise' in reconstructed images to avoid degradation in image quality.

ONE IMAGE, MULTIPLE VIEWS

Another aim is to reconstruct large 3D images with a large viewing angle — something that is difficult to realize using current technologies.

"We are also developing accurate holographic measurement systems, which will be invaluable in medical science because they allow researchers to image and measure samples in 3D alongside visualizing moving phenomena in real time," explains Shimobaba.

In another exciting field of research, the team is exploring a form of 3D image creation called volumetric displays — the difference being that, while holograms can only be seen clearly by a few people at a time, volumetric displays can be viewed by multiple people from different viewpoints. And, in an even more challenging concept, they are trying to create multi-viewpoint images with plural information appearing in specific directions. In other words, one person standing at one place will see one piece of information, while another standing somewhere else will see completely different information.

"Our volumetric display simultaneously provides several observers with different information," explains Shimobaba. "This very exciting feature is quite new, and we are considering new applications for using it, such as developing multi-language signage for the Tokyo Olympics in 2020," he says. Such 3D displays may benefit from advanced aerial projection techniques, also under development by Shimobaba's team.

"Networking is the key to our success," says Shimobaba. "Many students who have graduated from our laboratory move on to conduct research in academia or in private companies, and we continue to work with them. In this way, we expand our project and build fruitful working relationships across academia and industry."

MULTIMODAL MEDICAL ENGINEERING

TOWARD IMAGE-BASED **DISEASE DIAGNOSTICS**

Research Keywords: Medical Engineering, Physical Measurement, Multimodality

—Novel, high-precision imaging techniques are being used to provide non-invasive disease diagnosis and guide future treatments.

Members

Hideaki HANEISHI
Professor, Center for Frontier Medical Engineer

Tadashi YAMAGUCHI, Hideki HAYASHI, Kenji YOSHIDA, Kazuyuki SAITO, Kazuya KAWAMURA, Takashi UNO, Toshiya NAKAGUCHI, Mikio SUGA, Takashi ONISHI, Yuzuru IKEHARA, Yasuo IWADATE, Koichi HAYANO, Hao LIU, Ken-ichi TSUBOTA, WenWei YU, Hiroki SUYARI

Non-invasive, precise diagnosis of diseases using advanced medical imaging technologies could one day replace traditional techniques based on biopsy and dissection. With this prospect in mind, researchers at the Multimodal Medical Engineering program are combining medical and engineering expertise to create novel, noninvasive imaging-based methods for diagnosing and treating disease.

The program uses various scanning techniques, or 'modalities', including computerized tomography, magnetic resonance imaging (MRI) and ultrasound, to analyze cellular and organ variations caused by different diseases.

The program's goal is to develop highly precise, non-invasive imaging methods, while boosting existing imaging techniques to improve resolution and enable more-detailed tissue analysis, says program leader Hideaki Haneishi.

"Many current disease diagnostics, particularly for cancer, involve highly invasive, unpleasant procedures to clarify the type and stage of the disease," explains Haneishi. "We are investigating, for example, the development of a system to diagnose breast cancer using very-high-frequency ultrasound."

Rather than physically sampling and dissecting lymph nodes from potentially cancerous tissue, his team has shown that it is possible to analyse cell characteristics of lymph nodes using ultrasound. Their technique highlights metastasis positive and negative cells in lymph nodes, enabling rapid, painless diagnosis.

Haneishi and his team are also devising ways to combine data from two or more modalities. For example, in 2016 they developed an image registration method that transforms two data sets into one coordinated system using MRI and pathological images of brain tumors.

"If we can establish the technology for registering two kinds of images, then MRI features that are strongly related to the pathological features of tumors can be highlighted. This may eventually allow us to diagnose using only MRI," says Haneishi. "Determining the relationships between different data sets helps us build up detailed pictures of what is going on inside the body, not only for diagnosis but also to improve our understanding of disease development," he adds.

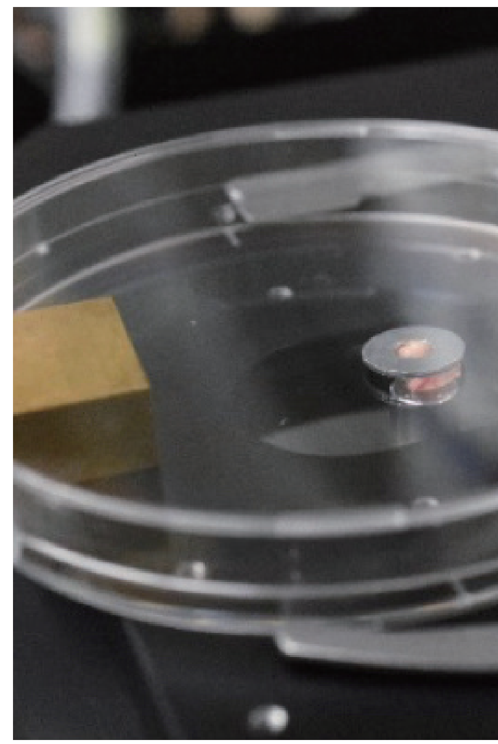
NOVEL OPTICAL PROBES

Alongside conventional imaging techniques, the researchers are also exploring novel optical probes. One example involves a method for monitoring microcirculation — the flow of red blood cells — in the body. The probe comprises multicolored light-emitting diodes (LEDs). As the LED light is scattered through the tissue, it is partly absorbed by molecules in the red blood cells, generating a clear, detailed picture of the cells and their microcirculatory network.

Building on previous work, the team hopes to use this probe to estimate features such as the oxygen saturation of each blood vessel in areas around suspected tumors in real time. This could aid diagnosis and further our understanding of vascular behavior in and around tumors. "Ultimately, we would like to build on these imaging techniques and use machine learning and artificial intelligence technologies to relate measured signals and diagnoses, to develop a comprehensive understanding of different diseases," says Haneishi.

The Multimodal Medical Engineering program has access to highly specialized equipment and technologies that can help realize researchers' ideas.

"We welcome engineers and medical researchers who wish to work at the cutting-edge of research and development with direct clinical applications," says Haneishi.

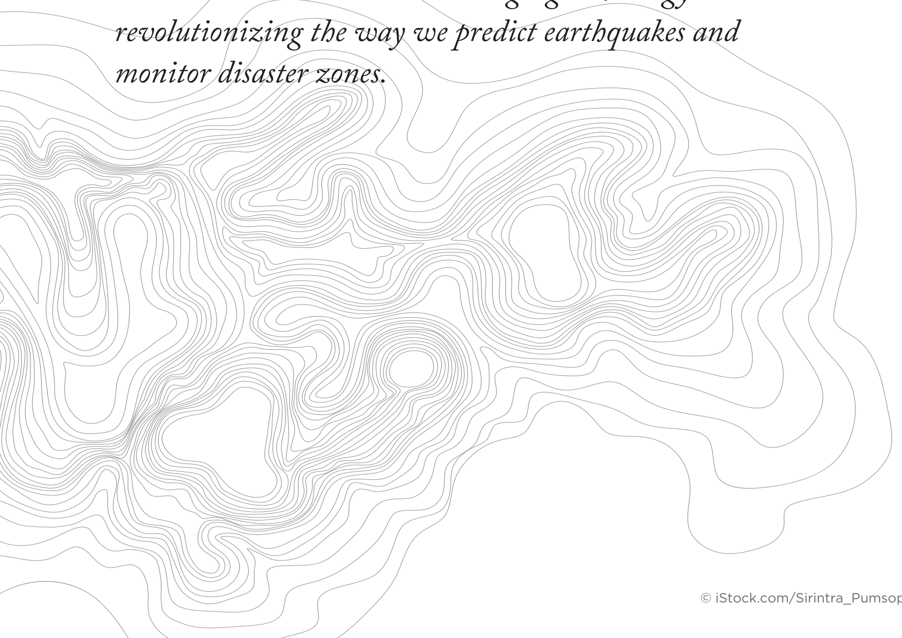


CENTER FOR INNOVATIVE MICROWAVE REMOTE SENSING

THE NEXT WAVE IN REMOTE SENSING

Research Keywords: Microwave Remote Sensing, Synthetic Aperture Radar, Environment and Disaster Monitoring

—Microsatellites and remote imaging technology are revolutionizing the way we predict earthquakes and monitor disaster zones.



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The Microwave Remote Sensing Laboratory is far more than a laboratory. It is an experimental aerospace workshop where world experts in remote sensing collaborate with mechanical and aerospace engineers to construct state-of-the-art microsatellites, unmammed aerial vehicle (UAV), and airborne sensors. The research team specializes in microwave-radar technology for detecting ground movements and earthquake predictors as part of a new generation of remote sensing technologies.

“Microwave radiation is particularly useful for remote sensing because it penetrates cloud, haze and fog, allowing us to observe the Earth’s surface from space,” explains Josaphat Tetuko Sri Sumantyo who leads this research project. The core area in this research project is the development of synthetic aperture radars (SARs) for microwave remote sensing to monitor land deformation. SAR emits a microwave signal in the direction of the target and then detects microwaves scattered from the target. By comparing SAR images obtained before and after a change such as an earthquake or a landslide, researchers can determine how much the land has moved.

The research team has a well-developed research-and-development program with 15 researchers, 25 students and facilities for designing, manufacturing, calibrating and operating SAR for UAV, aircraft, and microsatellite applications.

ADVANCED AEROSPACE FACILITIES

“Our facilities include an anechoic chamber for calibrating sensors, a satellite–ground communication system, and microsatellite calibration and measurement systems. We also have a simulator for designing microwave circuits and antennas, along with a suite of manufacturing equipment,” says Sri Sumantyo. “We even have our own 6-meter experimental UAV, the JX, which we developed in this laboratory.”

They have already developed SAR sensors for circularly polarized (CP) microwave radiation in the L, C and X bands, which have been deployed on both large and small aircraft, as well as on the JX UAV. The CP-SAR sensor is the first of its kind, utilizing interference between left- and right-handed circularly polarized light to obtain precise information about the Earth’s surface in a compact, lightweight and inexpensive sensor.

We have developed several techniques based on SAR imaging to monitor infrastructure and areas affected by disasters such as forest fires, landslides, subsidence and volcanic eruptions,” says Sri Sumantyo.

Engineers in this team are developing two novel microsatellites. One is equipped with radio occultation and electron density temperature probe sensors for measuring the atmospheric signatures thought to precede earthquakes, while the other is a CP-SAR satellite with lightweight gold-coated mesh antenna. These satellites are poised to take the lab’s research beyond the stratosphere.

“Our microsatellite program is very exciting for future SAR sensor applications and planetary exploration,” says Sri Sumantyo. “We eventually aim to have five microsatellites in orbit, which will provide real-time monitoring for global disaster mitigation and research.”

The team has strong collaborations with Japanese and overseas research institutions and industry — it has more than 50 agreements with research and industry partners throughout the world. The group also encourages short- and long-stay programs, and Double Degree Program for Master and Doctoral Courses under various government programs, through which more than 500 students and researchers from many different countries have worked at the lab.

Members

Jasaphat Tetuko SRI SUMANTYO
Professor, Center for Environmental Remote Sensing

Kazuteru NAMBA
Katsumi HATTORI
Chiharu HONGO
Wen LIU
Hiroyuki NAKATA
Akira KATO

IMAGING SCIENCE AND TECHNOLOGY FOR MATERIAL APPEARANCE AND AFFECT

AFFECT AND REALNESS IN DIGITAL IMAGES

Research Keywords: Engineering for Material Appearance, Image Sensing, Visual Psychology

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—Understanding how the human brain interprets images could underpin the future of internet shopping, virtual communication, digital fabrication and even non-invasive medicine.

When internet purchases arrive and seem nothing like their picture, it can be a disappointing experience for shoppers. So, while big e-commerce players are increasingly investing in technologies to help personalize products or shop via phone or virtual reality headset, a significant stumbling block is rendering realistic, digitally produced images.

“To achieve a realistic rendering of something, we also need to deeply consider human perception,” explains Keita Hirai, a member of the “Creation of Material Appearance and Affective Imaging” group at Chiba University’s Graduate School of Engineering. How we perceive a material, he says, can also be linked to cognition, not just physical phenomena.

To examine the complex effect of the mind’s eye, Chiba University have drawn from a diverse range of researchers, including engineers, psychologists, and medical and cognitive scientists.

Recently, Hirai’s team developed a new system for texture evaluation, and through participant feedback have devised a set of algorithms that can produce more realistic digital representations of patinas and colours overlaid onto textured fabrics in digital images. The aim, he says, is to one day digitally simulate photo-real fabric appearance via a smart device. Hirai points out that this will not only be helpful to internet shoppers, but that these algorithms could also find applications in rapidly advancing digital fabrication techniques, such as printing digital patinas onto fabrics or objects, and manufacturing representative digitally-designed 3D products. In fact, the group aims to contribute to industries as diverse as cosmetics and medicine.

UNDERSTANDING THE MECHANISM OF MATERIAL APPEARANCE AND AFFECT

Among the work done by the diverse group is a study analyzing affects and emotions. A research team led by Norimichi Tsumura, who is also the leader of this research project, has developed a technology to visualize the amount of hemoglobin, which carries oxygen in the blood, on the images taken with a smartphone camera. If you take a video of your face using this technology, you can also measure your heart rate based on the increase or decrease in the amount of hemoglobin. Furthermore, by capturing a slight change in the interval between heartbeats, it is possible to grasp the respiratory rate and the balance between the sympathetic nerve and the parasympathetic nerve. It is expected as a technology for measuring human affects and emotions.

Another group found that our perception of colour is affected by our understanding of its dimensionality. The same viewer looking at the same image saw colours differently depending on whether they interpreted the image as two dimensional or three dimensional. Viewing images with one eye or both, and whether the image or the viewer’s head was moving, also affected how natural the image seemed. This work, says Hirai, is important for better smart device production. “A more informed colour management system, for example, may help realize more accurate colour reproduction between different devices: displays, cameras and printers,” he explains.

Hirai says the group’s work will influence the most cutting-edge imaging technology, such as the omni-directional 3D camera systems and virtual reality headsets coming from technology giants such as Sony, Panasonic, Canon and Nikon. While he also mentions cosmetics and automotive painting, one team have already had some remarkable success in one crucial, but quite unique area — medical diagnostics. The pulse measurement technology developed by the research team of Tsumura has already produced remarkable results in medical diagnosis via the internet communication. It is expected to be applied to a wide range of use, from non-invasive medical diagnosis to improving understanding of physical exercise using a simple smartphone app. Furthermore, this research project connects the expertise of various researchers in order to establish new imaging technologies that integrate material appearance and affective engineering, which monitors human emotional states and provides images with high quality material appearance.

Members

Norimichi TSUMURA
Associate Professor, Graduate School of Engineering

Takahiko HORIUCHI
Yoko MIZOKAMI
Michinari KOHRI
Toshihiko MATSUKA
Rumi TOKUNARA
Eriko KOBAYASHI
Shunji KOTSUKI
Keita HIRAI
Shoko IMAIZUMI
Noriko YATA
Kensuke YOSHIMURA
Ayumi AMEMIYA
Kazuki NAKAMURA
Shinichi INOUE

INSECTS-INSPIRED BIG INNOVATION

LOOKING TO NATURE TO **REVOLUTIONIZE FLIGHT**

Research Keywords: Bioinspired Engineering, Biological flight, Drone

—The beating wings of insects hold the secrets to controlled low-speed flight and Micro Aerial Vehicles.

Members

Hao LIU
Professor, Graduate School of Engineering

Akio NAMIKI
Toshiyuki NAKATA
Toshihiko MATSUKA
Arii WATANABE
Hiroyuki ISHIKAWA
Kazuya OKAWA
Michinari KOHRI
Tomokazu USHITANI
Yuma TAKAHASHI
Akira KATO

Inspired by the fascinating flying ability of insects and humming birds, Chiba University's Biomechanical Engineering Laboratory has been conducting pioneering research on beating-wing flight for more than 20 years. Headed by Professor Hao Liu, the lab is on the verge of revolutionizing the very concept of flight itself.

"Insects have this amazing ability to hover and execute highly controlled flight in both still air and turbulent wind gusts," says Liu. "Scientists once knew very little about how insects generate aerodynamic force in turbulent environments, and even less about how they are able to maintain such agile control in flight."

BIOLOGY INSPIRES MICRO AIR VEHICLES

Conventional flight is based on the uninterrupted flow of air over the curved upper and lower surfaces of a wing, which causes a 'suction' effect that lifts the wing upward. "Fixed wings need smooth airflow to generate lift," explains Liu. "Turbulence over the wing can lead to disaster. Our first major breakthrough in unravelling the mystery of insect flight was that most flying insects in fact generate most of their lift force by creating a vortex on the leading edge of the flapping wing. It's a completely different principle of flight to conventional flight."

It all started in 1996 with Liu's development of the first computational fluid dynamics simulation for insect flight, which led to the discovery of the universal leading-edge vortex mechanism in insect and bird flight. To delve deeper, the laboratory installed an ultra-low-speed wind tunnel capable of airflow as slow as half a metre a second. They use it to observe and analyse the flight of live birds and insects such as moths, beetles and dragonflies, as well as micro air vehicles (MAVs), very small drones with potential uses in disaster relief and covert operations.

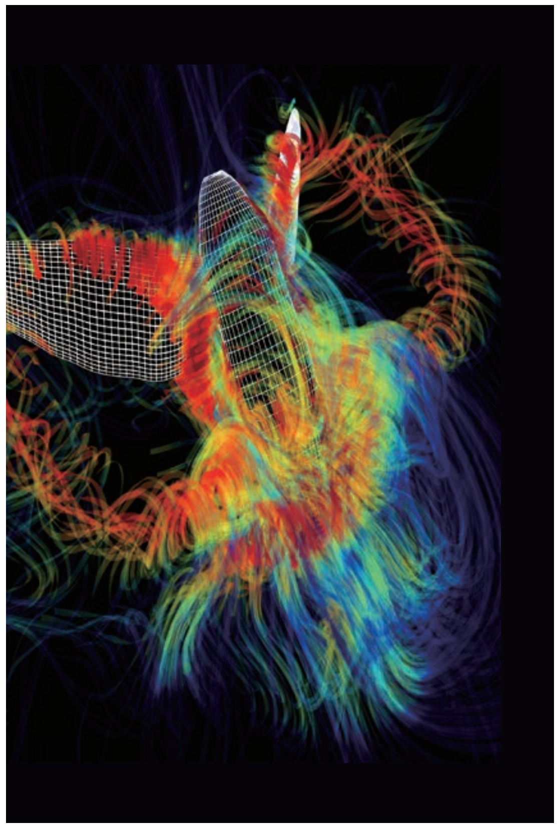
"Using high-speed imaging and particle image velocimetry data, we were able to create a computer model of an insect and its flight mechanism, and from there we made an experimental robot insect that actually flew. That was another pioneering breakthrough," says Liu.

"Our research brings together biology, engineering, computational physics, biorobotics and neuroscience, and we collaborate with the likes of Cambridge and the University of London on some really interesting international, cooperative projects. Chiba is definitely a world leader in this area with a strong interdisciplinary team and world-class facilities."

The lab's research now focuses on developing insect-inspired flight systems, which he expects to lead to big developments in the design of insect- and bird-size MAVs.

"For example, we think it's wing flexibility that gives insects much of their resilience to wind gusts, but we are also seeing that insects use their body much more than we thought to control direction and movement, both actively and passively. This is completely different to the conventional wing-based control used by planes today and has the potential to revolutionize flight control strategies in general," says Liu.

"Ultimately we want to develop an insect-inspired autonomous drone that is far more reliable and agile than anything based on today's rotor-based technology. In 2019, we established the Center for Aerial Intelligent Vehicles, aiming at creating innovation from a new mechanism of flight. In the meantime, we continue to collaborate on the development of advanced, flapping MAVs, as well as help improve the reliability of rotor-based drones by introducing flexible wing technology."



SOFT MOLECULAR ACTIVATION FOR INTELLIGENT MATERIALS

CATALYZING THE FUTURE OF **SMART MATERIALS**

Research Keywords: Synthetic Chemistry, Catalytic Reaction, Iodine Bond

—Catalysts developed from soft iodine, graphene and metal complexes could transform smart material technologies.

Members

Takayoshi ARAI
Professor, Graduate School of Science

Hirofumi KANOH
Katsuhiko MORIYAMA
Nobuyuki ICHIKUNI
Yasuhiro YAMADA
Takeshi MORITA
Fumio SAKANE
Takuya HASHIMOTO
Kazuhiro YOSHIDA
Hideaki SHIROTA
Shinji HARADA
Tomoya UEHARA
Keisuke IIDA
Manabu TSUKADA
Shoji MATSUMOTO
Yasushi YOSHIDA
Tomonori OHBA
Shoichi KATSUTA
Hyuma MASU
Takeshi MURATA
Shigeru ARAI
Takashi MINO
Masaya NAKAJIMA
Shingo HARADA
Mamoru TAKADA
Yasuhiro YAMADA

The very idea of materials that change their shape or function as required sparks the imagination. Smart materials are impressive artificial molecules, often inspired by naturally occurring chemicals, which have the potential to revolutionize design. They undergo changes that are reversible and repeatable, meaning they can function as molecular switches, valves and sensors. Other smart materials include shape-memory alloys that return to their original shape after bending, metal-bearing polymers that can switch from insulator to conductor and drug-delivery systems that slowly release pharmaceuticals where and when they are needed.

Researchers at the Soft Molecular Activation for Intelligent Materials program are leading investigations into catalysts made from soft molecules that could one day transform smart material design.

Lead researcher Takayoshi Arai says the program is focused on developing powerful catalysts to create novel smart materials using three catalyst types. "Firstly, soft halogen catalysts, predominantly using iodine, can be used to develop highly targeted medications," he explains. "A second type is 'soft ∏-electron' using carbon nanotubes and graphene, which would provide a unique reaction sphere for catalysis. The third type, 'soft metal' catalysts allow us to introduce soft elements such as gold and copper into target molecules."

NEW CATALYST DESIGN

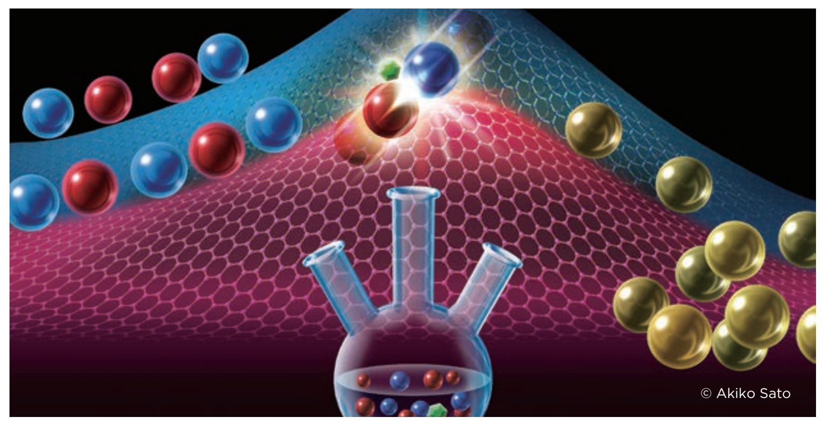
Arai says one of the main goals of the program is to create new asymmetric catalysts, which are used to generate large numbers of very specific molecules. Most biological molecules are chiral, meaning they exist in one of two mirror-image forms called enantiomers. Many drugs and smart materials use just one specific enantiomer, and so catalysts are needed to direct the chemical reactions toward forming the correct enantiomer.

For example, iodine has been used to help synthesize specific enantiomers of cyclic and ring-shaped molecules. "We are lucky that Chiba prefecture in Japan is one of the world's leading producers of iodine," says Arai. "In fact, the Chiba Iodine Resource Innovation Center (CIRIC) has opened at Chiba University in July, 2018. A key goal of our program is to perfect iodine-based soft molecular activation."

Recent success for Arai's team includes the development of an aminoiminophenoxy-copper carboxylate catalyst that can trigger high yields of O-cyclized molecules. These can, in turn, be used to generate a particular chiral compound that is invaluable for use in antimicrobial and antiosteoporotic compounds.

"A crucial part of our research is designing catalysts that can be reused multiple times, thereby creating cost-effective, sustainable methods for generating useful compounds," says Arai. His team recently designed a recyclable catalyst made from a zinc-polymeric ligand complex. The polymeric ligand allows the catalyst to be separated from the final product by a simple filtration process, meaning it can be reused — indeed, poly-Zn remained a stable and active catalyst for creating iodine-based ring-shaped molecules more than five times.

"By introducing soft elements to target molecules, our research will facilitate the development of smart materials with smooth and rapid responses," says Arai. "We welcome anyone interested in research at the forefront of iodine-related soft molecular activation chemistry to come and work in this diverse and challenging field at Chiba."



ADVANCED BONE-CONDUCTION COMMUNICATION

BONE-CONDUCTION TECHNOLOGY BEYOND HEARING AID

Members

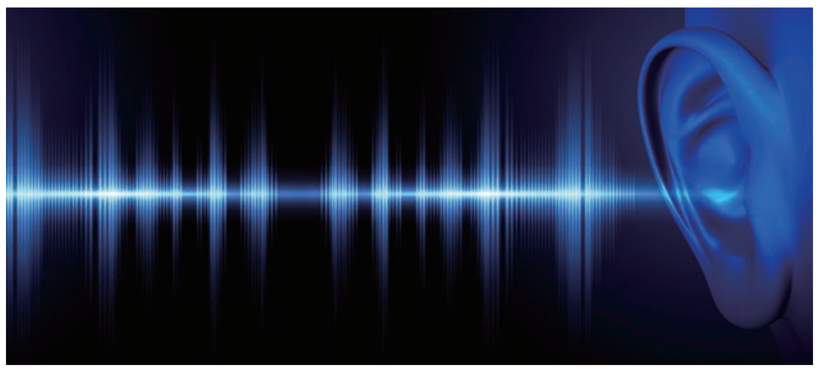
Seiji NAKAGAWA
Professor, Center for Frontier Medical Engineering

Shingo KUROIWA
Yasuo HORIUCHI
Sho OTSUKA
Masashi SEKINE
Yoshihiro SHIMOMURA
Keita ISHIBASHI
Satoki ZENBUTSU

Research Keywords: Bone Conduction, Hearing Aid, Biomedical Engineering

—Elucidating the perceptual mechanisms of ultrasonic bone conduction and cartilage conduction with a view to new device development.

Against the background of the aging society and diversifying lifestyles, there is a growing need for a broader range of options in hearing aids and audio devices. Among the various technologies used for hearing aids, bone conduction has mainly been used for compensating conductive hearing loss caused by middle or outer ear disorders. In recent years, the incidental benefits of bone conduction technology, such as benefits in speech perception under noisy conditions, less sound leakage, and usability in water, have come to attract attention. However, the perceptual mechanism of bone conduction is complicated and has yet to be fully understood.
“The sound we usually hear through our earholes is called air conduction. While there is only one pathway for air conduction, there are at least four pathways available for bone conduction,” says Seiji Nakagawa. “The perceptions of bone-conducted sound largely changes according to frequency and location, and at times differ largely from the sound perceptions by air conduction.” Nakagawa and his team are working to elucidate auditory perceptual mechanisms with a focus on ground-breaking bone conduction phenomena, including ultrasonic bone conduction and cartilage conduction, and try to apply them to hearing aids and smartphones.



PERCEPTUAL MECHANISMS AND DEVICE DEVELOPMENT

Bone-conducted ultrasonic waves can be perceived as a sound even by severely hearing-impaired people who cannot hear even with the use of a conventional hearing aid. Prototype testing of an ultrasonic bone conduction hearing device showed that, with the use of this device, about half of severely hearing-impaired persons were able to perceive verbal sounds, and around 30% were able to identify the words being spoken. The cartilage conduction is technology in which the vibrator is attached to the pinna cartilage, and now it is applied to hearing aids for patients with atresia of the ear canal and also to speakerless smartphones.
The cartilage conduction and the ultrasonic bone conduction are both ground-breaking approaches. There are still some challenges before applying them to practical products for widespread use: improvement of sound transmission performance, wearability and comfort of use, and development of industry standards and hearing-related safety standards. Fundamental understanding of the perceptual mechanisms is essential to solving these challenges.
“Research on ultrasonic bone conduction and cartilage conduction have just begun, and most of their perceptual mechanisms are still unknown. For example, the mechanisms of how the bone-conducted ultrasonic waves are propagated and easily perceived are unclear when the vibrator is attached to the neck, chest, or even the upper arm. Most of the technical challenges of bone conduction cannot be solved without understanding the perceptual characteristics and propagation process of bone conduction.”
Nakagawa believes that if he advances bone conduction technology based on a deep understanding of such mechanisms, it opens up possibilities for new applications.
“For example, we are now going to develop bone conduction headphones and microphones that can be used even under severely noisy conditions, and an earphone for infants who often resist the use of conventional earphones or headphones. Furthermore, bone conduction is also suitable as an interface for smart glasses, which people think to be the next-generation information terminal.”
“Chiba University has many faculty members with expertise and knowledge in human interface technology and acoustic signal processing. We can develop new devices by bringing those strengths together for projects centered on bone conduction technology. We also have collaborative partnerships with businesses in Japan and abroad and hope to achieve innovation by pursuing fundamental research for mechanism elucidation as well as the development of practical applications,” says Nakagawa.

LYMPHEDEMA MONITOR

MAKING INVISIBLE **LYMPHEDEMA** VISIBLE

Members

Masahiro TAKEI
Professor, Graduate School of Engineering

Shinsuke AKITA
Yoshihiro SHIMOMURA
Nobuyuki MITSUKAWA
Takafumi SANGAI
Tadashi YAMAGUCHI
Mikio SUGA
Ryoji YAGI
Michiko SUGAWARA
Akira MITSUHASHI
Takuro HORIKOSHI
Ichiro MANABE
Kenji YOSHIDA

Research Keywords: Electrical Impedance Tomography (EIT), lymphedema, Cloud Computing

—A low-cost and easy-to-use tomography device can ensure early detection and proper understanding of lymphedema.

“Lymphedema,” or stagnant lymph flow and abnormal swelling of the arms and legs that may occur following the removal of lymph nodes by surgery or radiotherapy, occurs in about 30% of patients who had surgery for gynecological cancers such as breast cancer and uterine cancer. “It has been considered as an abandoned sequela for a long time and has only recently garnered the attention of researchers,” says Masahiro Takei. “The risk of lymphedema onset lasts for a lifetime, and the condition cannot be fully cured if detected late, so the patients are forced to have a significant psychological burden. For a good prognosis, early detection of stages 0 and 1 of lymphedema is critical, but there is still no effective detection device for this purpose.”
Takei is now forming a research team of engineering, medical, pharmaceutical, and scientific experts from Chiba University, aiming to improve the accuracy of detection by developing IoT lymphedema tomographic monitor with artificial intelligence (AI) system that can be used at home.

A SMALL ELECTRIC TOMOGRAPHY

As a mechanical engineer, Takei’s belief is “to make invisible things visible by using a machine.” So far, he has been working on developing hardware and software related to electrical tomography. Tomography refers to cross-section visualization measurement, as in computed tomography (CT). Medical CT is a large machine that costs hundreds of millions of yen, and it is impossible for patients themselves to use it easily at home. This challenge has been recognized around the world. In the 1990s, the theoretical construction of a new electric tomography began at the University of Manchester, UK. Takei had also participated in this project called “European Action.” Several challenges occurred during this project, and the member researchers tried to solve these problems one by one. They developed the sensors, the electrical circuits to reduce noise and speeding up, the image reconstruction software with mathematical inverse problem-solving capability, and proceeded with developing the appropriate procedures for industrial and biological use. However, the prototype equipment had cost millions of yen, and the accuracy was not sufficient for practical use.
“At that time, I thought it would be innovative if we could easily see our inside of the body with a machine that costs around tens of thousands of yen,” says Takei. Thus emerged the breakthrough technology—a small electric tomography with diagnostic function. The new system works as follows: several electrodes are placed on the body, and a weak electric current is passed through the body. The system produces images showing the distribution of conductivity and dielectric constant in the body at each frequency using a wearable sensor to measure the potential, small hardware, and mathematical algorithms.
Currently, Takei’s research team is working on developing an easy-to-use IoT lymphedema tomographic monitor. First, with the monitor, impedance data measured by a small unit from the multi-electrode winded sensors are sent to the cloud computing unit. Next, 4D images of limb cross-sections are reconstructed at high speed on the cloud using specialized software. Finally, edema (including early-stage edema) is diagnosed using machine learning and big data analysis of the lymphedema images. With this device, patients can check their edema stage by themselves at home.
To elucidate the mechanism of development and progression of lymphedema, not only engineering and medical knowledge but also pharmaceutical and scientific considerations are crucial. By implementing the knowledge gained from such integrated research to the prototype, Takei’s team aim to improve the accuracy and convenience of the machine. “Ultimately, we want to visualize the medical condition in real-time on a mobile device and to reduce the pain of patients.”

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Medical and Pharmaceutical Sciences

PHYTOCHEMICAL PLANT MOLECULAR SCIENCES

UNLOCKING THE POTENTIAL OF PHYTOCHEMICALS

Research Keywords: Plant Molecular Science, Phytochemical, Gene

—Advanced genetic and genomic techniques are transforming our understanding of how phytochemicals can improve human health.

Members

Kazuki SAITO
Director, Plant Molecular Science Center

Mami YAMAZAKI
Amit RAI
Daisuke UMENO
Hajime SATO
Masami ISHIBASHI
Akiko TAKAYA
Tomoko IGAWA
Eiji GOTO
Takashi SHIMADA
Yasumasa HARA
Taira MIYAHARA
Naoko YOSHIMOTO
Hiroki TAKAHASHI
Takashi TSUCHIMATSU
Kohji ITO
Mariko KITAJIMA
Noriyuki KOGURE
Mitsumasa HANAOKA
Natsuko KAGAWA
Hidenori SASSA
Shinji KIKUCHI
Takanori SAITO

Since ancient times, people have used the natural compounds in plants, known as phytochemicals, for medicinal and nutritional use. Now, scientists at Chiba University are using advanced genetic and genomic techniques to verify how phytochemicals are generated in plants, how they can be manipulated to optimize certain plant groups, and how they may help tackle lifestyle- and aging-related diseases.

Plants naturally generate chemicals for various purposes, including for attracting pollinators and defending themselves. These specialized metabolites allow plants to colonize specific niches in the food chain, adapt to new environments and evolve to survive potential stressors. Crucially, phytochemicals also exhibit properties that can help treat human diseases. Examples in modern medicine include morphine, the antimalarial drug artemisinin and chemotherapy agents derived from taxanes.

ENLISTING PHYTOCHEMICALS TO FIGHT DISEASE

Kazuki Saito, who leads the Phytochemical Plant Molecular Sciences program, says that because phytochemicals display considerable natural diversity, they have huge potential to fight disease. "Although phytochemicals have been used in pharmaceuticals and ancient remedies for many years, it is only now, with the advent of next-generation DNA sequencing, that we can really begin to understand how they work and unlock their full potential," says Saito.

The program consists of three collaborative research groups, each working on a specific theme.

One group is focusing on the genomics of medicinal plants and food crops with the key aim of revealing the genomic principles of phytochemical production. Employing state-of-the-art technologies, the researchers identify and clarify the roles of unknown genes, as well as investigate plant metabolism. In 2016, Saito's team assembled a draft genome for licorice (*Glycyrrhiza uralensis*), which is used worldwide as a natural sweetener and a medicinal component.

They identified several components known to play a positive role in human health within the plant, while pinpointing key genes, the manipulation of which could lead to crop improvements.

The second team is identifying novel phytochemicals and active products in a wide variety of plants, searching for drug components to tackle diseases such as cancer, dementia and diabetes. As well as isolating and analyzing promising molecules, the group conducts animal trials to assess the pharmaceutical potential of molecules. In particular, they have extensively investigated Lycopodium alkaloids (LAs), molecules found in the vascular plant Lycopodiaceae, which may help to treat Alzheimer's disease and schizophrenia.

The third group is investigating how plants respond to different environmental stresses by growing plants in different artificial environments and monitoring their responses to change.

"Our aim is to optimize plants so that they produce high-quality phytochemicals that we can harvest for use in medicines and functional foods," explains Saito. "Our insights will enable us to grow rare plants more successfully and will also inform agricultural practices for commercial crops in the future."

While the group is focusing on phytochemicals, it also conducts wide-ranging interdisciplinary studies and hence welcomes researchers and students with backgrounds in chemistry, horticulture, genetics and pharmacy who are interested in this exciting and rapidly developing area of research.

CHIBA RESEARCH

CANCER EPIGENOME CENTER

A DIFFERENT APPROACH TO FIGHTING CANCER

Research Keywords: Cancer, Epigenome, Inhibitor

—A new center aims to combat cancer by rewriting the epigenetic modifications harbored by tumor cells.

Members

Atsushi KANEDA
Professor, Graduate School of Medicine

Ichiro MANABE
Tetsuhiro NEMOTO
Hisahiro MATSUBARA
Hideki HANAOKA
Hiroyuki MATSUE
Toyoyuki HANAZAWA
Tomoaki TANAKA
Kiyoe URA
Ichiro YOSHINO
Tomohiko ICHIKAWA
Emiko SAKAIDA
Yoko SHINAGAWA

Cancer is thought of as a genetic disease, with mutations to a cell's DNA causing a normal cell to give birth to a malignant tumor. Yet epigenetic alterations, which leave the DNA sequence intact, can be just as important in a cell's transformation to cancer. Even though epigenetic regulation through mechanisms such as methyl tags and histone modifications does not alter the DNA sequence, it can chemically modify the genome to signal which genes should be turned on and off. When tumor-suppressor genes are silenced or oncogenes are activated in this way, many different forms of cancer can result.

Fortunately for medicine, epigenetic alterations are not permanent. They can be undone to prevent or reverse cancer, leaving a cell with its entire complement of normal DNA intact.

This is exactly what researchers at the Cancer Epigenome Center are striving to do. Led by Atsushi Kaneda, the center is seeking to understand the various epigenetic drivers that contribute to different types of cancer and then develop new drugs that overturn these effects.

"We will explain key epigenomic aberrations and their molecular causes," says Kaneda. "And then, taking advantage of small molecules that bind to DNA in a sequence-specific manner, we will develop drugs that can rewrite the accumulated epigenomic aberrations or prevent them accumulating in targeted genomic regions."

UNRAVELING MOLECULAR MECHANISMS

Kaneda points to ongoing investigations of gastric cancer as an example of this strategy in action. Patients with this cancer exhibit different levels of DNA methylation in their tumor cells, depending on the pathogen responsible for the disease. The cancer-causing bacterium Helicobacter pylori is one source of irregular methylation. Epstein-Barr virus is another pathogen of gastric cancer, which not only inactivates tumor suppressor genes by inducing extreme DNA hypermethylation, but also activates proto-oncogenes via an epigenetic mechanism the research group has named "enhancer infestation" (*Nat Genet* 2020).

Kaneda and his colleagues are using clinical samples and cell experiments to unravel the molecular mechanisms that induce hyperactive methylation patterns following infection with these pathogenic agents. They ultimately hope to stop the process in its tracks. Similar projects are ongoing to combat colorectal cancers — which Chiba researchers have shown can be categorized into three types, depending on methylation levels — as well as blood cancers and other types of tumor.

With an eye to developing novel therapeutics, chemists at the Cancer Epigenome Center are working on new methods to efficiently synthesize molecules that can act on epigenetic aberrations. One such group of molecules is the pyrroleimidazole polyamides. These molecules can bind to DNA at specific sites in the genome, and when coupled to an epigenetic inhibitor they can prevent methylation-based gene silencing. Kaneda hopes to deploy the molecules to edit the epigenome at targeted regions to regulate tumor formation.

The Cancer Epigenome Center includes researchers from a wide range of backgrounds and specialties. This multidisciplinary team approach, says Kaneda, is essential for turning the center's discoveries into clinically meaningful treatments and diagnostic tools. "We will help determine the mechanisms of cancers and develop new cancer drugs through collaborating with experts in medicine, physics and pharmacy," he says.

MEDICAL MYCOLOGY RESEARCH CENTER

MANIPULATING MICROBES FOR HUMAN HEALTH

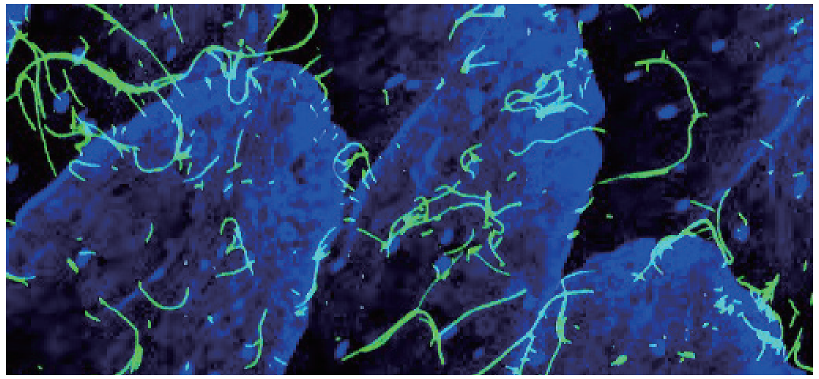
Research Keywords: Infection and Immunity, Microbiota, Superorganism

—Detailed investigations of host–microbe interactions could yield new therapies against infectious agentsand autoimmune diseases.

Members

Mitsutoshi YONEYAMA
Professor, Medical Mycology Research Center

Shinobu SAIJO
Tomohiro TAMACHI
Yoshiyuki GOTO
Kinnosuke YAHIRO
Koji ONOMOTO
Koichi HIROSE
Akiko TAKAYA
Hiroshi ASHIDA
Arifumi IWATA



The human body is made up of a staggering 30 trillion cells or so. But just as numerous, if not more so, are the several hundred trillions of microbial co-inhabitants that teem in and on us. These microbiotas are essential to our well-being, and a distortion in its balance can trigger a wide range of disorders.

Only recently, however, have scientists come to appreciate just how critical this collection of microbiota is for determining human health and disease. They are also becoming excited about the prospect of how manipulating this microbial ecosystem could form the basis for the next generation of life-saving therapeutics. Led by Mitsutoshi Yoneyama, researchers at the Medical Mycology Research Center have launched a comprehensive research effort to dissect the intricacies of host-microbe interactions in the skin, lung, intestines, and bone marrow.

"Dysregulation of host-microbe interactions can give rise to a wide variety of human disorders, including opportunistic infections, allergies, and autoimmune disease," explains Yoneyama. "It is hence crucial to understand how hosts and commensal microbes communicate as a superorganism."

Creating a superorganism is an apt metaphor for what Yoneyama is trying to achieve because, through the melding of minds from across Chiba and around the world, the center can make a far greater impact than any individual scientist working independently.

At Chiba University, the investigators come from the Medical Mycology Research Center, the Graduate School of Medicine, and the Graduate School of Pharmaceutical Sciences, while external collaborators are based in the United States, Germany, and elsewhere in Japan. These scholars, together with others from around the world, convene each November at the Medical Mycology Research Center for the annual Global Network Forum on Infection and Immunity.

EXPLORING HOST–MICROBE INTERACTIONS

The team that Yoneyama has put together is roughly divided into four groups, each studying molecular interactions in different host-microbial systems. One, led by Shinobu Saijo, is focused on fungal and bacterial infections in the skin of mice and humans; another, led by Koichi Hirose, Tomohiro Tamachi, and Arifumi Iwata is investigating the microbes — both good and bad — that reside in the respiratory tract. A third group, which includes Yoshiyuki Goto, Hiroshi Ashida, and Kinnosuke Yahiro, is concentrating on the gut microbiome and how opportunistic intestinal infections gain a foothold; while the fourth, led by Akiko Takaya, is working on more basic mechanisms of immunological memory in response to microbial invaders.

"Results obtained from our projects will help efforts to create innovative new therapeutics against infectious diseases and will eventually lead to improvements in human health," says Yoneyama, whose own research focuses on the mechanisms of innate antiviral immunity with Koji Onomoto.

To assist all these research projects, investigators from each group have access to the Japanese government's network of core facilities — a resource known as the Joint Usage/Research Center, which is staffed by specialized researchers and technicians who can run state-of-the-art experiments, including with fungi and other microbes. A bioinformatics unit at Chiba led by Hiroki Takahashi helps with computational analyses.

CHIBA RESEARCH

MEDICINE FOR RARE DISEASES

INNOVATIVE APPROACH OFFERS HOPE FOR INTRACTABLE PROBLEMS

Research Keywords: Rare Disease, Intractable Cancer, iPS Cell

—The ReDenim network is developing therapies to treat rare and intractable diseases.

Members

Shinichiro MOTOHASHI
Professor, Graduate School of Medicine

Hideki HANAOKA
Itsuko ISHII
Kiyoshi HIRAHARA
Sonoko MISAWA
Koji ETO
Masayuki KURODA
Kotaro SUZUKI
Katsunori FUJII

Scientists at Chiba University have a long track record of excellence in clinical research, particularly for investigations in patients with immune-related diseases. And Chiba University researchers have made a number of important breakthroughs in basic immunology and disease biology. However, connecting these two areas, a field known as translational research, has often been less successful.

That is a problem that Shinichiro Motohashi wants to fix. Motohashi leads Chiba's Research and Development Network of Innovative Medicine for Rare and Intractable Diseases — ReDenim. The network is aiming to provide the clinical support and resources needed to take discoveries from the lab to the clinic.

In particular, ReDenim has singled out two disease areas for which there are currently no good treatment options — deadly forms of cancer, such as head and neck tumors; and rare diseases that each afflict fewer than 50,000 people in Japan, but collectively affect about 10 percent of the population.

TWO-PRONGED APPROACH

Motohashi belongs to the tumor immunity team, which intends to capitalize on Chiba University's expertise in developing cell-based immunotherapies. Their approach uses tumor-destroying natural killer T-cells to search for combination therapies that can further modulate the tumor immune microenvironment in a favorable way. They also intend to identify biomarkers that can predict how individual patients will respond to these treatments.

Led by Sonoko Misawa, the rare-disease team, including Masayuki Kuroda and Katsunori Fujii, is using immune-modulating drugs and gene therapies to address immune-related peripheral nerve disease and hereditary disease. Kotaro Suzuki and Kiyoshi Hirahara are aiming to develop new treatments based on the analysis of pathological conditions using animal models of autoimmune diseases and tissue fibrosis. Koji Eto and his collaborators of orthopedics and plastic surgery, Seiji Ohtori, Sumihisa Orita, Yasuhiro Shiga, and Nobuyuki Mitsukawa, are developing a new method of wound healing using platelet-rich plasma derived from iPS cells. Kuroda is also working with the tumor immunity team to develop transgenic adipocyte technology that can be applied to cancer treatments, in addition to his research target, hereditary metabolic diseases.

Importantly, both teams will share research experiences, technology platforms and manufacturing facilities. "Sharing the know-how to treat each disease within the network will accelerate drug development," says Motohashi. And the two teams will also have access to support units at the university's Core Clinical Research Hospital, a designation granted to Chiba University under Japan's Medical Care Act. Hideki Hanaoka and Itsuko Ishii develop the support units to apply basic science toward therapeutic applications.

This support includes consultation services on issues such as intellectual property, project management, clinical trial design and other steps needed to fulfill the promise of translational medicine. "Our ultimate goal is to form a therapeutic cluster that can be applied to a wide variety of rare and intractable diseases," Motohashi says. He can even foresee a day when the infrastructure created through ReDenim could be used to develop new therapies for common diseases, such as diabetes or lung cancer.

Judging by the progress they have made so far, Motohashi and his coworkers are well on their way to fulfilling their dream, and their potential is widely recognized. ReDenim has already forged collaborations with some of the world's leading experts in cancer immunotherapy and rare diseases, and is working with Japanese drug companies to partner on additional research projects.

GLYCOMEDICINE RESEARCH CENTER

SUGAR SCIENCE'S **IMMUNOTHERAPHY PLAY**

Research Keywords: Immunology, Biochemistry, Glycobiology

Members

Hiroto KAWASHIMA
Professor, Graduate School of Pharmaceutical Sciences

Motoyuki ITOH
Hirofumi DOHI
Yasunori MATSUMOTO
Noritaka NISHIDA
Noritaka YAMAGUCHI

—By bridging the gap between glycoscience and medicine, major advances in immunology and drug development are imminent.

Lymphocytes are the body's warrior cells. They circulate through the bloodstream and arrive at sites in the body such as the spleen and lymph nodes, where they combat harmful bacteria, viruses and even cancer cells. Sugars, or glycans, are integral to this migratory process called lymphocyte homing, which is of intense interest to researchers. These scientists hope to target glycans to find new immunotherapies and drugs for autoimmune diseases.

"We now know that glycans — chains of sugar molecules that have diverse functions in our bodies — play an essential role in lymphocyte homing," says Hiroto Kawashima, a professor at Chiba University's Graduate School of Pharmaceutical Sciences, Laboratory of Microbiology and Immunology.

"These glycans are found on the surface of endothelial cells in lymph nodes," he explains. "Thanks to glycans, lymphocytes recognize and bind to the surface of those cells." Lymph nodes activate lymphocytes to fight disease.

In a study published in *Nature Immunology* in 2005, Kawashima and his colleagues in Japan and the United States showed that glycans produced by two enzymes — N-acetylglucosamine-6-O-sulfotransferase 1 (GlcNAc6ST-1) and GlcNAc6ST-2 — are essential for the binding of lymphocytes, and consequently play a vital role in controlling lymphocyte homing in mice.

After working on this study at California's Burnham Institute, Kawashima returned to Japan in 2005, bringing with him the 'knockout' mice (deficient in the two key enzymes) he had developed. At Chiba he has used these to continue hunting for new antibodies that target glycans.

GLYCOMEDICINE TAKES OFF

Today, the expanding fields of glycoscience (the study of glycans) and glycomedicine (combining glycoscience and medicine) are leading to breakthroughs in drug development and diagnostics for autoimmune diseases.

Chiba University's Glycomedicine Research Center, which opened in August 2017, marks a shift towards accelerating such breakthroughs in Japan.

"Many researchers here at Chiba University have been working independently on glycans," Kawashima says. "Some specialize in biological functions, while others focus on synthesis or analyze glycan structures. The idea is to bring all of these researchers together, build new collaborations and understand the function of glycans across many biological phenomena."

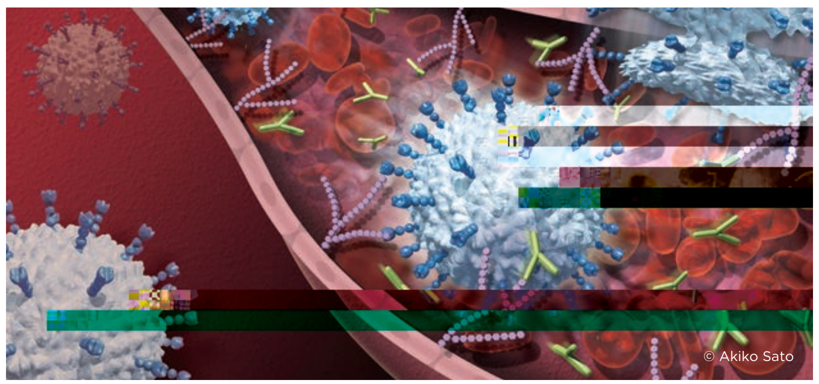
The new centre has plans to collaborate with teams both nationally, for example, at the Glycomedicine Technology Research Center and the National Institute of Advanced Industrial Science and Technology (AIST), and internationally.

Already, Kawashima has developed antibodies that will specifically bind to the building blocks of glycans and disable them in studies published in The Journal of Biological Chemistry in 2010 and 2015. This could halt the dysfunctions involved in autoimmune disease, in which the immune system is overreacting.

"Usually, it's very difficult to generate monoclonal antibodies against carbohydrates," says Kawashima. This difficulty in producing clones of these antibodies is because carbohydrate antigens are not generally very antigenic. "To get around this problem, we immunized knockout mice with cells expressing the missing sugar chains, which are highly prone to stimulating the production of antibodies."

The next step will be to further investigate and identify new ideas for drug development and to collaborate with pharmaceutical companies to bring them to market.

"Right now, there are lots of antibody drugs," says Kawashima. These immunotherapies target issues such as rheumatoid arthritis and cancer, but, he says, new advances are limited by a shortage of molecules to target. "Glycans have unexplored potential, so this is an exciting time to be looking into developing new candidate drugs based on glycoscience."



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CHIBA RESEARCH

LABORATORY OF DDS DESIGN AND DRUG DISPOSITION

BIG HOPES FOR NANOTECHNOLOGY BASED **DRUG DELIVERY SYSYEMS**

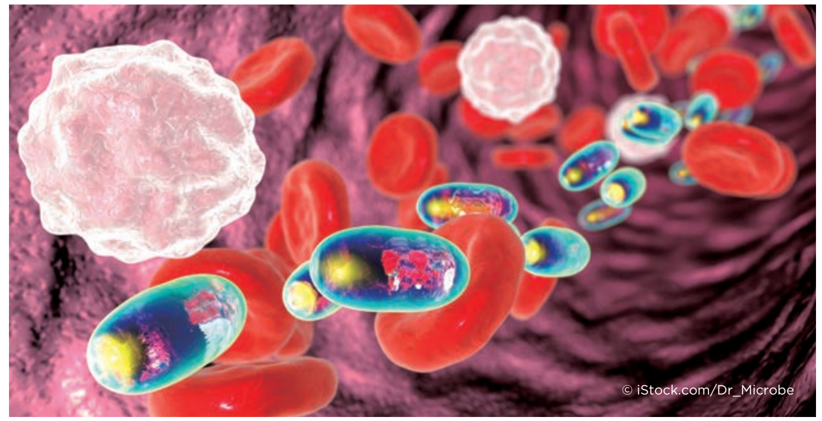
Research Keywords: Drug Delivery, Nanobio, Vaccine

Members

Hidetaka AKITA
Professor, Graduate School of Pharmaceutical Sciences

Akihiro HISAKA
Kousei ITO
Kunikazu MORIBE
Hiroki TANAKA
Keisuke UEDA
Hiroto HATAKEYAMA
Yu SAKURAI
Naohiko ANZAI
Takeshi MURATA
Satoshi OGASAWARA
Kenjirou HIGASHI
Shigeki AOKI
Hiromi SATO

—Drug delivery systems that nanocarriers could enhance the effectiveness of therapies ranging from genetics-based cancer treatments Alzheimer's medicines.



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Drug delivery systems that nanocarriers could enhance the effectiveness of therapies ranging from genetics-based cancer treatments to Alzheimer's medicines.

Personalised medicine — tailoring medical treatments to individual needs — may no longer be far-off.

Developments in nanocarriers have progressed rapidly, promising targeted delivery and release of nucleic acid-based drugs (NABDs), an emerging class of therapeutics designed to target diseases at the genetic level.

A BREAKTHROUGH MOLECULE

In 2013, Akita's group reported on SS-cleavable Proton-Activated Lipid-like Material (ssPalm), a molecule designed and tested over five years that showed promise for drug delivery.

The molecule itself consists of two main components: One, tertiary amines, are activated in response to an acidic environment, such as the endosome compartment inside the cells of plants and animals. These activated amines enable membrane destabilisation. The other, a disulfide bond (SS) that can be cleaved in a reducing environment such as in the cytoplasmic material inside cells, triggers the release of NABDs in specific cells.

In proof-of-concept studies in mice in 2016, the researchers showed that lipid-based nanoparticles, formed using ssPalm, enabled efficient delivery to the liver of a genetic treatment that uses small interfering RNA. They have since gone on to develop second-generation ssPalm, which uses Vitamin E as a waterproofing scaffold (ssPalmE).

One of the biggest challenges for cancer therapeutics researchers, Akita explains, will be "to develop DNA- and RNA-based vaccines that could target unique genetic changes in individual cancers."

The hope is that the versatility of ssPalm could help maximise drug efficacy while reducing side effects. For example, in mouse studies performed in 2018, Akita's group demonstrated that a plasmid DNA-encapsulating lipid nanoparticle (ssPalmE-LNP) induced anti-tumour effects. They also showed that ssPalmE-LNP enhanced the therapeutic effect of an antibody used to combat immune system supressing programmed cell death protein 1 (PD-1), raising hopes for combination therapies to combat cancer.

Brain disorder treatments also stand to benefit from nanocarriers. Recent studies suggest that using ssPalm as an alternative to viruses that deliver genetic material could improve treatments.

In experiments with Hokkaido University in 2018, Akita's team used ssPalm in the delivery of messenger RNA (mRNA) to neurons and astrocytes — star-shaped cells found in the brain and spinal cord increasingly implicated in neurodevelopment and disease.

By surpassing the limitations of other forms of delivery (such as DNA-based artificial gene carriers), mRNA therapeutics could be used to treat many conditions, including Alzheimer's, Parkinson's, Huntington's disease and other neurological disorders.

"Our strengths at the Faculty of Pharmaceutical Science include our expertise in characterizing physicochemical properties, and evaluation of pharmacokinetics and pharmacodynamics, as well as safety," Akita explains. These skills could potentially contribute to a wide range of fields he says, including immunology and cancer research.

"We need to keep our eyes open to societal needs," Akita adds. "Until now, we have been concentrating on materials science. We have only just begun to enter the arena of nucleic acid-based therapeutics. I believe innovations arise when you can look beyond your own particular filed, and apply original technologies in unexpected ways."

INTERNATIONAL HUB FOR METALLOMICS RESEARCH

UNDERSTANDING THE FUNCTION OF BIOMETALS FOR HUMAN AND ENVIRONMENTAL HEALTH

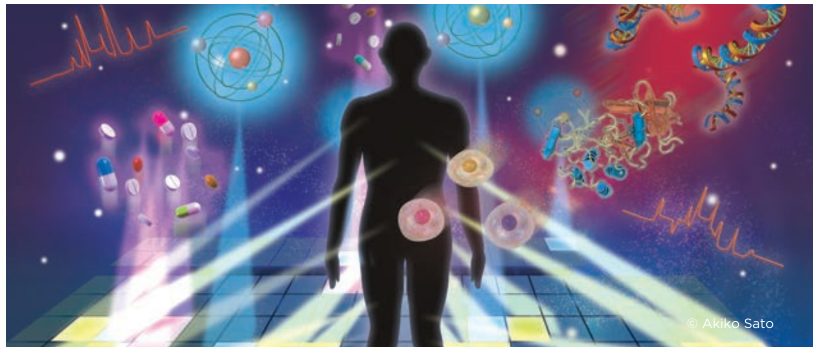
Research Keywords: biometal science, metallomics, theranostics

—Metallomics opens new frontiers in eco-toxicology, disease prevention, drug discovery, and medical diagnosis and therapy.

Members

Yasumitsu OGRA
Professor, Graduate School of Pharmaceutical Sciences

Tomoya UEHARA
Noriyuki SUZUKI
Yasunori FUKUMOTO
Yuki TANAKA



Biological phenomena are recognized as a collection of organic chemical reactions consisting of carbon, hydrogen, oxygen, and nitrogen.
A trace amount of metals, such as iron, zinc, copper, and selenium, play an important role in controlling these reactions. These metals specifically required for physiological reactions are called "essential metals." Contrary to the essential metals, some metals disturb the physiological reactions. Since there are many industrially useful "non-essential metals" in our daily life, some non-essential metals are the risk in human and environmental health. In addition, excess amounts of essential metals also disturb the physiological reactions. Hence, organisms have the mechanisms underlying the distinction of essential and non-essential metals, and the homeostasis of essential metals. The disturbance of the mechanisms results in critical problems in human and environmental health.
Metallomics is a study of metallome which means metal-containing biomolecules. Metals can induce various physiological and toxicological effects in a very small amount, in other words, the metal concentrations are very low in organisms. Thus, analytical techniques for a trace amount of metals are crucial to understand the biological and toxicological functions of metals.

RESEARCH IN METALLOMICS IS UNDERPINNED BY UNIQUE ANALYTICAL TECHNIQUES

The research group made discoveries based on a unique biometal analytical technique. "Our method is the only analytical technique for measuring biometals. We aim to expand applications by refining existing methods to enable biometal analysis at a single cell level, whereas prior biometal analysis was performed at the level of tissues or organs," says Yasumitsu Ogra, the leader of this project.
One of these single cell-level analyses specified the function of metal nanoparticles, or biogenic nanoparticles, which are produced by organisms. It has been generally understood that organisms take in, use, and secrete metals as ions, and they do not replace metal ions with metal elements. However, certain micro-organisms, higher-order plants, and animals show an exception.
"Our analytical technique revealed that higher plants and animals exhibit a common mechanism to convert metal ions into elements which involves detoxification of the ions of non-essential metals and excess amount of essential metals. In other words, they detoxify metal ions to elemental nanoparticles." Investigating this mechanism requires a technique that can measure metal nanoparticles in high-matrix biological samples. Ogra and others are confident that they can establish this technique and are looking ahead to apply it for bioremediation, resource recovery (bio-mining) and in the field of medicine. Previous technologies have used plants to eliminate toxic metals and recover useful metals from the environment. Recovering these metals as elements instead of ions will be significantly more efficient than existing techniques.
"The technique that we are trying to establish to measure metal nanoparticles can be developed for the accurate measurement of elements in individual cells." If a technique that quantifies the metal concentrations in individual cells can be established, we can have a more detailed understanding of pathologies involving metals. It is anticipated that in the future, applications will prevent diseases through AI using big data obtained from peripheral cells on elements in individual cells.
This research project also entails research on the production of metal-containing drugs using the unique physicochemical properties of elements in the bottom half of the periodic table, which have been seldom used as medication. They will conduct research on practical application of theranostics that employs radioactive metals to develop a novel medical technology for simultaneous diagnosis and treatment. Furthermore, the group led by Tomoya Uehara will continue their research in the field of diagnostics and treatment with radioactive metals, using a SPECT/CT device for small animals. This research project will serve as a comprehensive research hub that unravels the relationship between organisms and metals.

INSTITUTE FOR GLOBAL PROMINENT RESEARCH

To accelerate innovative research beyond the borders of academic disciplines, the IGPR was founded at Chiba University in 2016 as a core institution for world-leading research. IGPR has been actively supporting research projects with potential impact as a global hub for world-class research.

The institute is also focused on the capacity development of young researchers who will lead new research fields in the next generation. Currently, IGPR is supporting more than 20 research projects in diverse areas.

TEL : +81-43-290-2916
Mail : gp-office@chiba-u.jp
URL : igpr.chiba-u.jp/global

ACADEMIC RESEARCH & INNOVATION MANAGEMENT ORGANIZATION (IMO)

IMO was established in 2020 at Chiba University as a hub to enhance academic research and collaboration between industry, academia and government. IMO fosters innovation by strengthening fundamental and advanced research, cross-sectoral collaboration, and venture support system.

URL: imo.chiba-u.jp

Research Promotion Division
Tel: +81-43-290-3833
Mail: ccrcu@faculty.chiba-u.jp

Intellectual Property Strategy Division
Tel: +81-43-290-3831
Mail: beo3566@office.chiba-u.jp

Venture Support Division
Tel: +81-43-290-3519
Mail: bex4680@chiba-u.jp

RELATED RESEARCH CENTERS

- Center for Environmental Remote Sensing
- Medical Mycology Research Center
- Soft Molecular Activation Research Center, Chiba Iodine Resource Innovation Center
- Molecular Chirality Research Center
- Center for Frontier Medical Engineering
- Center for Environment, Health and Field Science
- Research Center for Child Mental Development
- Plant Molecular Science Center
- International Center for Hadron Astrophysics
- Center for Aerial Intelligent Vehicles
- International Center of Excellence in the Mucosal Immunology and Innovative Allergy Therapeutics
- Center for Artificial Intelligence Research in Therapeutics
- Shanghai Jiao Tong University and Chiba University International Cooperative Research Center

MESSAGE FROM THE DIRECTOR OF IGPR

Takeshi Tokuhisa
Director, IGPR and
President of Chiba University

It gives me great pleasure to inform you that the 2021 edition of *CHIBA RESEARCH* is now available. All of the research projects introduced in this issue have been carried out with the support of the Institute for Global Prominent Research (IGPR), a university-wide organization of Chiba University. IGPR was established in 2016 with the goal to enhance prominent international research projects of Chiba University and foster the development of young scientists who will lead the next-generation research. This is an original attempt to bring together research resources from all sources throughout the university, and support and promote high-quality research in a wide range of disciplines. The projects have produced many innovative research outputs and findings. Assistant Professor Toshiyuki Nakata, who is working on the bioinspired engineering research project, has proposed a new mechanism for detecting floors and walls by sensing airflow fluctuations generated by mosquitoes. This study was published in *Science* and widely featured in national newspapers. Professor Takayoshi Arai, who is leading the project on soft molecular activation, has succeeded in catalytic asymmetric iodoesterification from simple alkene substrates and carboxylic acids. Published in *Angewandte Chemie International Edition*, this new research was accomplished by precisely controlling multiple interactions in a single catalytic reaction and is expected to contribute to the development and improvement of medicines.
Professor Hidetaka Akita and Assistant Professor Hiroki Tanaka have been researching nanotechnology-based drug delivery systems. They have successfully developed a lipid-like material that self-degrades after being taken into cells. This study published in *Advanced Functional Materials* is expected to be applied in systems that deliver various drugs to target cells. The cancer epigenome research team led by Professor Atsushi Kaneda has studied the mechanism of how Epstein-Barr virus (EBV) infection causes gastric cancer. Published in *Nature Genetics*, this research will contribute to elucidation of the causes and establishment of treatment methods for cancers involving the virus. Due to the worldwide spread of the new coronavirus in 2020, we were required to take different measures to implement the projects. Associate Professor Genya Kobayashi, who is leading the project on small area estimation and its application, has analyzed the data of coronavirus infection using statistical models to estimate the effects of behavior change before and after the state of emergency declared by the Japanese government and to predict infection outbreaks.
Starting in October 2020, the bioinspired engineering research project led by Prof. Hao Liu held a VR exhibition on drones where you could learn the technology developed by the project as well as the history of aviation and the development of robotics technology. This unique and interactive virtual exhibition has attracted many visitors. In addition, IGPR held a symposium in November 2020 as part of IGPR's initiative to foster the development of next-generation researchers. The symposium served as a platform for young researchers engaged in IGPR research projects to brush up their skills and effectively communicate their findings to people outside of their specialization.
Through promoting world prominent research at IGPR, Chiba University continues to make vital contributions to society. I strongly hope that this issue of *CHIBA RESEARCH* will help you gain a deeper appreciation of the University's cutting edge research activities.

ABOUT THIS MAGAZINE

Design and layout:
Ikjoon Chang, Takumi Sato
Editing and coordination:
Midori Ishii, Ayako Shimura

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CHIBA UNIVERSITY

1-33 Yayoi-cho, Inage-ku,
Chiba-shi, Chiba,
263-8522 Japan
www.chiba-u.jp/e

WHERE IS CHIBA UNIVERSITY?

CHIBA Prefecture is located at the east edge of the South Kanto region. It has a population of approximately 6 million, the 6th largest among the 47 prefectures in Japan. Chiba is the center of Keiyo Industrial Area and has the well-developed industry. The three sides of the prefecture are surrounded by the sea, which helps Chiba's growth in the seafood industry as well.

Chiba University has 4 campuses in Chiba Prefecture.

Nishichiba Campus (Main Campus) is located between Narita International Airport and Tokyo Station. It takes about 30 to 40 minutes by train to Tokyo Station and also Narita International Airport.

PUBLIC TRANSPORT TO CHIBA

1. KASHIWA-NO-HA CAMPUS

5-min walk from the Tsukuba Express Kashiwanoha-campus Station.
Take the Tobu bus bound for National Cancer Center or Kashiwanoha Park from bus stop No2 at JR Kashiwa Station or near the east exit of Tobu Kashiwa Station.

2. MATSUDO CAMPUS

10-min walk from Matsudo Station
(JR Joban line, Tokyo Metro Chiyoda Line, Shin-Keisei Line)

3. NISHI-CHIBA CAMPUS

2-min walk from JR Nishi-Chiba Station to the South Gate of Nishi-Chiba Campus
7-min walk from Keisei Midoridai Station to the Main Gate of Nishi-Chiba Campus
10-min walk from Chiba Monorail Tendai Station to the North Gate

4. INOHANA CAMPUS

After arriving at JR Chiba Station or Keisei Chiba Station, a bus stop can be found in front of JR Chiba Station east exit 7. Take the bus bound for Chiba University Hospital or Minami-Yahagi and get off at the School of Medicine Entrance bus stop. To get to the university hospital, get off at the Chiba University Hospital stop.

CHIBA UNIVERSITY

Institute for Global Prominent Research

1-33 Yayoicho, Inage-ku, Chiba-shi, Chiba, 263-8522 Japan
E-mail: gp-office@chiba-u.jp
http://igpr.chiba-u.jp/global