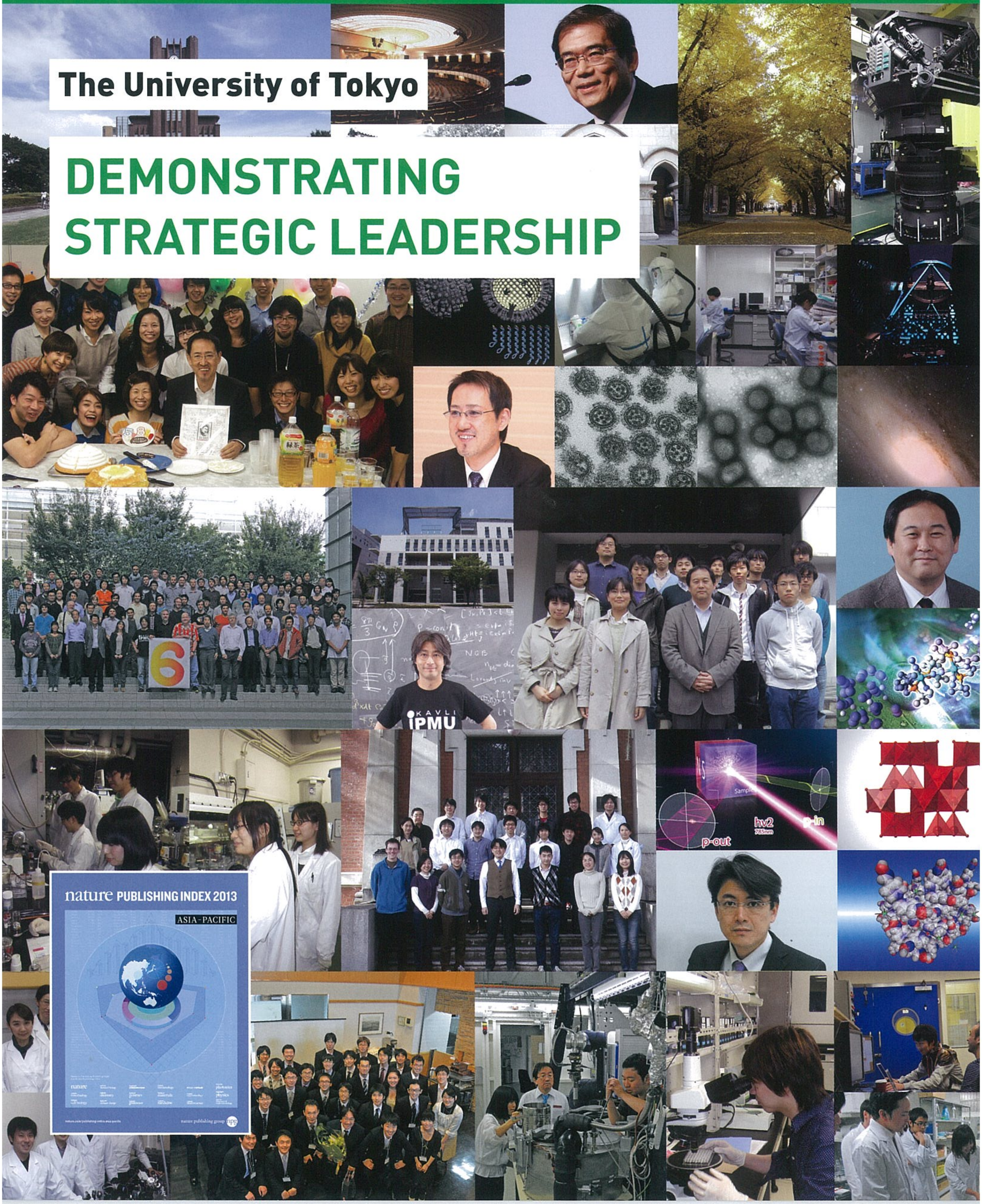
The University of Tokyo

DEMONSTRATING STRATEGIC LEADERSHIP



The University of Tokyo

DEMONSTRATING STRATEGIC LEADERSHIP

When, in 1877, the University of Tokyo was established, it was a leading force in the government's efforts to modernize Japan. Now as Japan struggles to redefine itself in a new and complicated international setting, where academic activity is inherently a global and competitive activity, that leadership role is just as significant, says Yoichiro Matsumoto, the university's executive vice president. Its mission is big: to define what Japan's future will be.

The government has been struggling to do this. "What kind of country they want to make out of Japan and what kind of leadership role Japan will play in the world are not clear. There is also no strategy for bringing such a vision to reality," he says. The University of Tokyo seeks to fill this void under the strategic leadership of President Junichi Hamada.

Central to those efforts are the university's basic research projects. "Even if they take time to initiate and their significance is not immediately clear to some people, our basic research projects have helped to build an economic and cultural foundation at home and they have even become an asset for the whole region. The combination of inventions makes real innovation," says Matsumoto.

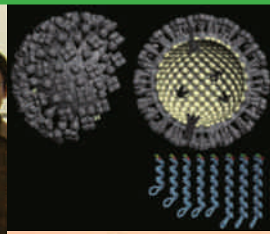
University researchers are leading several of the collaborative Center of Innovation programs recently selected by the government. These projects set priorities—such as mental and physical health and sustainability—for a Japan ten years in the future and seek innovative ways to make that vision a reality. The research is meant to be "high risk" and is accompanied by risk management policies. Hiroshi Kiyono, for example, is collecting health-related data from a million Japanese to create a health and longevity policy platform while ensuring ethical use of the data. Makoto Gonokami is harnessing coherent photon technology to create innovative manufacturing techniques—"without screws, welding and with little burden on the environment." The university also received funding from the Program for Leading Graduate Schools, which aims to overhaul graduate education while cultivating new academic and industrial leaders.

To carry out its research mission, the university will have to balance demands from the government that threaten to narrow, rather than expand, the focus of universities. Over the past several years, the government has tended to push universities to make profit and assume short-sighted governance policies.

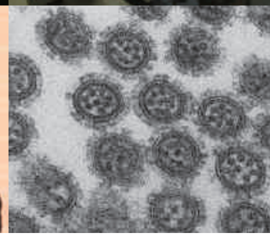
Indeed, times have been tough for Japanese universities. Full-time tenure positions are decreasing as universities rely more on temporary academic positions. Following severe budget cuts, one-half of funding for top universities now comes from competitive grants and other external funds, compared to one-third less than a decade ago. With an increased burden from administrative duties and grant-writing, professors have less time to spend on research even though they work longer hours.

The University of Tokyo and ten other top universities teamed up in 2009 to take stock of the situation. They are, for example, finding ways to increase the visibility of Japanese universities. They are also working with a consortium of top European universities to boost exchanges as part of efforts to reverse a worrisome trend—the drop in the number of Japanese students who go abroad.

The road ahead is full of challenges, but they are confident that the accumulated wisdom from the university's hundred plus years of history will offer "a view from a higher perspective," one that will "optimize the entire society."






THE UNIVERSITY OF TOKYO

Racing against viral evolution

The H7N9 strain that ripped through Shanghai killing dozens last spring tested our capacity to understand new viruses and China's ability to contain an epidemic. It was tragic—but through concerted efforts by health officials and researchers around the globe, a much worse scenario was averted. Such sustained, global efforts, rooted in a dynamic research network, have become crucial part of our efforts to avoid a pandemic.

Yoshihiro Kawaoka's laboratory at the University of Tokyo is a vital hub in this global battle. Kawaoka has set himself a challenge: to understand, and ultimately predict, the pandemic potential of influenza viruses by picking them apart at the molecular level. "Unless we unravel the viral and cellular determinants and mechanisms that define disease severity and transmissibility, we will not be able to predict the pandemic potential of novel strains, which would allow us to implement countermeasures to curtail future pandemics," he says.

His group was the first to figure out that the H7N9 virus can replicate in the lower respiratory tracts of nonhuman primates, offering an explanation of the virulence and high fatality rate witnessed last spring. The research, enabled by generous sharing of materials by scientists at the Chinese National Influenza Center that allowed Kawaoka to quickly obtain viral samples, also demonstrated that the virus can be transmitted by respiratory droplets in ferrets, suggesting that a global pandemic in humans was a real possibility.

Ferrets have become a seminal model for studying the molecular mechanisms involved in the transmission of influenza viruses thanks to Kawaoka's previous pioneering study of the H5N1 virus. Highly pathogenic avian H5N1 influenza viruses have circulated in parts of Asia for over a decade, infected more than 600 people, and killed more than 350 of them. But since sustained human-to-human transmission had not been witnessed, some dismissed these viruses as low risk. Kawaoka's study showed how a mutation in a viral receptor-encoding gene could turn it into virus transmissible though respiratory droplets. "This finding calls for the continued development and stock-piling of vaccines against highly pathogenic avian H5N1 influenza viruses and thus has major implications for pandemic preparedness planning," says Kawaoka.

The viral genomes are always changing, and even subtle changes can have a devastating outcome. Kawaoka's group demonstrated, for example, that the strain of H1N1 circulating in 2009 was more pathogenic than previously known H1N1 strains. In particular, their animal studies showed severe lesions in the lungs of mice, ferrets, and non-human primates. "These findings highlighted the potential threat to human health of new emerging influenza viruses," says Kawaoka.

Constant vigilance is necessary, and the University of Tokyo has made that possible. The biosafety-level 3 laboratory enables the team to study virulent pathogens. And, Kawaoka says, hard-working and creative students turn around experiments quickly. This next generation in the battle against a pandemic is receiving comprehensive training in various virology techniques, learning reverse genetics and the production of large virus mutant libraries, interacting with scientists from different backgrounds and institutions, and presenting findings at national and international scientific meetings.

These young researchers will be needed in the future. Thousands of influenza virus strains have been sequenced, and the basic functions of influenza virus proteins have been studied for several decades. Despite all these advances, "we still do not understand the key features that determine the severity of influenza virus infections in humans, and the transmissibility of influenza viruses among humans," says Kawaoka. The race to keep up with rapidly evolving viruses will continue.

Division of Virology, Department of Microbiology and Immunology, Institute of Medical Science
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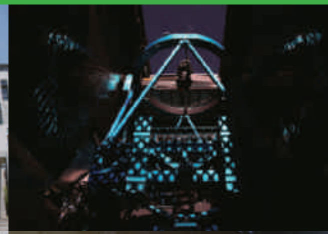

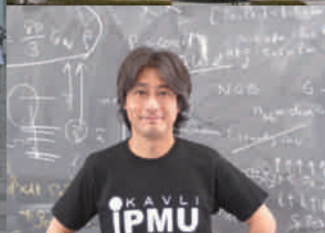

THE UNIVERSITY OF TOKYO

Deep and wide, SuMIRe surveys the cosmos

Last year, the Andromeda galaxy was captured as never before. By spreading across the sky with the area of ten full moons, the Subaru Telescope caught the entire galaxy in one shot. And the color image had such a high resolution—870 million pixels—that individual stars could be picked out and galaxies billions of light years away could be seen through the Andromeda galaxy's disk.

The image was made possible by the SuMIRe project, a collaboration led by the Kavli Institute for the Physics and Mathematics of the Universe at The University of Tokyo. Project scientists will combine imaging and spectroscopy to conduct a large-scale census of the universe with an ambitious mission: "The ultimate goal is to understand the origin and fate of the Universe," says Hitoshi Murayama, the institute's director.

The Subaru Telescope, built by the National Astronomical Observatory of Japan and one of the world's largest telescopes, can peer deep enough into space to pick up faint objects billions of light years away. At the same time, it boasts the biggest field of view, about 1,000 times that of the Hubble Space Telescope and 100 times that of other ground-based telescopes with similar apertures.

SuMIRe will enhance that power. The first phase of the project is an imaging survey using the Hyper Suprime-Cam (HSC), a new camera whose wide field of view enabled the capture of Andromeda and whose wide aperture allows it to go deeper than a competing project (the Dark Energy Survey in Chile). This phase is already approved to run for 300 nights on Subaru—what Murayama calls, "an unprecedented allocation on a shared community facility."

The second phase is a spectroscopic survey using a Prime Focus Spectrograph on Subaru. This spectrograph will catapult the sensitivity to levels that allow researchers to analyse the nature of dark energy, thereby uncovering the fate of the universe.

The project is led by Kavli IPMU, but many international collaborators play essential roles. Princeton University and Johns Hopkins University bring experience in large-scale census and camera design. The California Institute of Technology and the Jet Propulsion Laboratory use their expertise to build tiny robots that control optical fibers with tremendous accuracy. Researchers from Marseille contribute knowledge in design and optics. A Brazilian team proved very good at handling optical fibers. Taiwan's Academia Sinica Institute of Astronomy and Astrophysics build precision mechanical devices. Of course, bringing all that expertise together takes a toll: "Teleconferences that involve four continents are very difficult to schedule. Somebody gets sleep deprived," says Murayama. "But lacking any one of them, the project would not succeed."

These international partnerships helped SuMIRe 'rise from the ashes' after one of its Japanese grants was slashed. The project still faces a challenge—namely a $20 million shortfall—but Murayama hopes the Japanese government will come through. There's too much to lose, especially for the country's reputation in hosting international partners. "Once the survey starts this year, our young scientists will have an ample opportunity to exploit the power of the beautiful data set," says Murayama.

Those data hold an unprecedented range of astronomical possibilities. These include studies of the tiny variations in density created when the entire universe was smaller than an atomic nucleus and inferences about the distribution of dark matter that formed stars and galaxies. In addition, researchers will be able to measure the universe's expansion with such precision that they will be able to calculate whether it will expand for ever or reach an end.

KAVLI IPMU INSTITUTE FOR THE PHYSICS AND MATHEMATICS OF THE UNIVERSE

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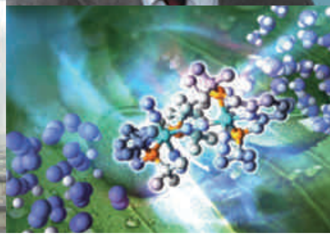


THE UNIVERSITY OF TOKYO

Ammonia revolution

The Haber-Bosch process, which converts atmospheric nitrogen to ammonia, revolutionized agriculture in the early twentieth century. As the crucial industrial process in the production of fertilizer, this process accounts for about half of the nitrogen that is contained in our DNA and proteins. “It’s no exaggeration to say that half of our bodies are made in the factory through the Haber-Bosch process,” says Yoshiaki Nishibayashi.

But Nishibayashi wants to do away with it.

At his laboratory in the University of Tokyo’s Institute of Engineering Innovation, Nishibayashi is taking on the challenge of finding a substitute process. The problem with the Haber Bosch process is that it requires a huge amount of energy.

“One of the most important challenges facing chemists is to find a way to fix nitrogen that doesn’t use fossil fuels and that is energy efficient,” says Nishibayashi. “It’s our ultimate goal.”

His team has succeeded in creating ammonia from nitrogen at room temperature and standard pressure using a molybdenum complex as a catalyst. While he admits that there are still many problems to be worked out, he is confident that this discovery will lead to a next-generation nitrogen fixing process.

Using a simple iron complex as a catalyst, he has also synthesized silylamine, which can be readily turned into ammonium by adding water. This was the first time anyone had synthesized ammonia from nitrogen gas at ambient pressure and temperature using anything but molybdenum.

Now, the challenge is to make the process sufficiently efficient. The molybdenum catalytic reaction that is currently used in Nishibayashi’s laboratory is six times more efficient than the first successful conversion using molybdenum in 2003, but it is still not feasible.

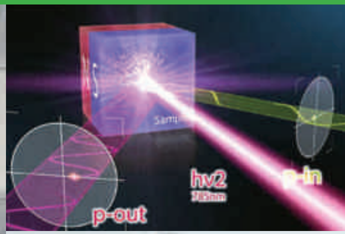
Nishibayashi is now pursuing techniques to increase that efficiency by improving the catalytic activation. Another problem is that the process requires costly hydrogen and reducing agents. “We need to find a cheaper way to make this reaction work,” he says. His team is currently analyzing the structure of the reaction to find solutions to these problems. His next target is to develop a catalytic reaction to synthesize ammonia from nitrogen gas and hydrogen gas, something he thinks possible based on his success in doing the same using a stoichiometric reaction 15 years ago. His ultimate goal, however, is to develop a process for the catalytic formation of ammonia from dinitrogen, water and sunlight.

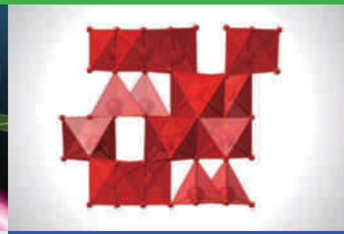
The challenges are many, but the School of Engineering has provided significant support in overcoming them. Starting in 2005, for example, Nishibayashi was selected for a Young Leaders Cultivation Program. These grants aim to raise the next generation of scientists and engineers: “they have given me the chance to supervise the laboratory and focus on science at the same time. This research wouldn’t have been possible otherwise,” says Nishibayashi.

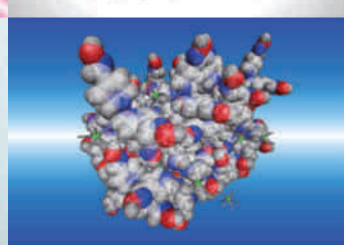
Success in these endeavours will have many great and unpredictable implications. Ammonia effectively stores and transports hydrogen, so a cheap and sustainably produced source could be a boon for a hydrogen-fuelled society. Researchers are now investigating its potential use in fuel cell batteries. Japan is just starting a national project to develop these ideas. Of course the most important and most urgent application is to save the earth from the environmental menace resulting menace resulting from the the Haber-Bosch process. “For the future development of mankind, it’s something we must do,” says Nishibayashi.

Institute of Engineering Innovation, School of Engineering

http://sogo.t.u-tokyo.ac.jp/english/







THE UNIVERSITY OF TOKYO

Making the most of magnetic materials

Magnetic recording media that possess unprecedented reliability, hybrid motors that do not depend on rare earth elements, next-generation wireless communications that ensure stable and secure transmission, and paint that can protect signals coming from a sensitive surgical device from interference or block unwanted phone calls in a movie theatre.

These are just some of the vast array of applications of magnetic chemistry being developed by researchers at Shin-ichi Ohkoshi's laboratory at The University of Tokyo.

Most recently, the team developed a magnet that could switch the polarization plane of light by 90 degrees. This discovery, which could be used in optical switching or optical memory for computers, resulted from an investigation into the relationship between the crystal structure of Prussian blue materials and their magnetic and optical properties. The discovery built on earlier work in which the properties of Prussian blue were used to make magnets that were sensitive to humidity and non-magnets that could be turned into magnets when they were irradiated with light.

The group has also given new life to iron oxides, which are safe and cheap but whose use in magnets has been limited because of their small coercive force. The ε-iron oxides synthesized in Ohkoshi's laboratory have, even at room temperature, a coercive field greater than any seen in ferrite magnets—useful features for manufacturers of hybrid motors and magnetic recording media.

Titanium oxide, which is often used in cosmetics and white pigments, also got a makeover. The λ-titanium oxide developed by Ohkoshi's group is the first example of a metal oxide exhibiting light-induced phase transition at room temperature. Using this λ-titanium oxide could produce much optical recording media with higher density than conventional germanium-antimony-tellurium optical discs. Moreover, because of the low pressure of its phase transition, "λ-Ti_3O_5 has the possibility as a solar heat storage material in which solar heat is stored and energy is released by pressure," says Ohkoshi.

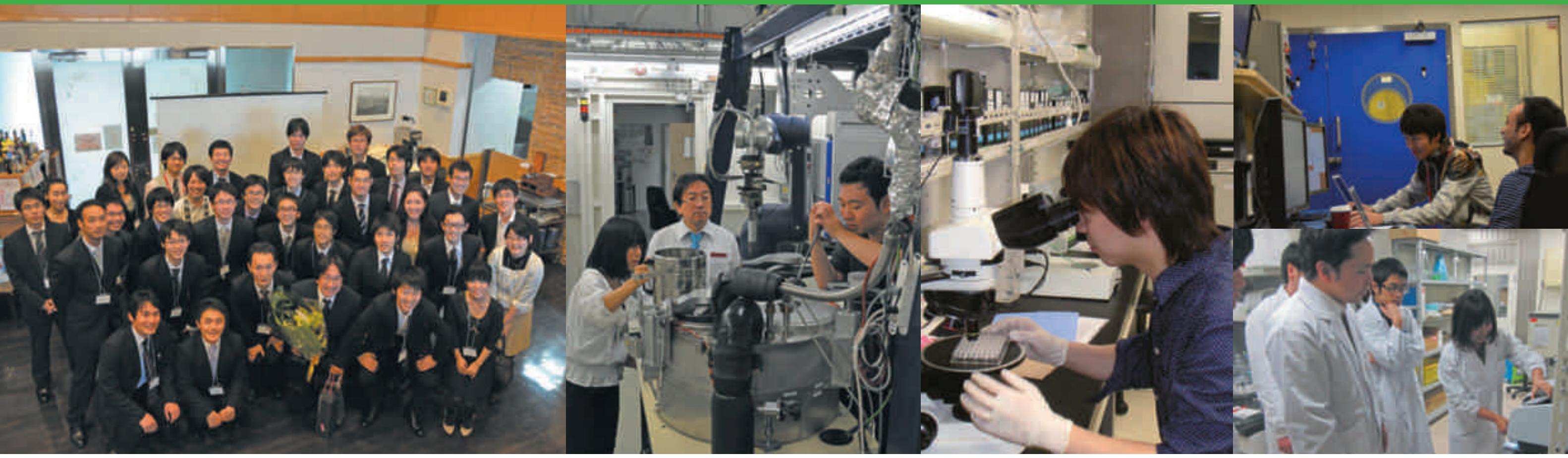
These exciting developments have been a boon for up-and-coming researchers. Members of Ohkoshi's laboratory have received over 20 awards, including poster presentation awards at international conferences, The University of Tokyo President Prize, and the Dean of School of Science Prize. "I push my staff members or students to present at conferences," says Ohkoshi.

Ohkoshi's team now sits in a dense web of international collaborations in which it provides samples or carries out joint measurements with some 20 research groups in Europe, the USA, China, and elsewhere. Ohkoshi has worked with a UK research group through a Japan-UK exchanging program, served as an invited professor at Durham University in the UK, the University of Pierre and Marie Curie and the University of Bordeaux in France, and, most recently, Palacký University in the Czech Republic as part of a European Union project. In Tokyo, he also hosts professors, researchers, and students from universities around the world.

Efforts by The University of Tokyo's Technology Licensing Organization and the Division of University Corporate Relations to exploit the research have paid off with 115 patent applications and 46 registered patents. Unsurprisingly, the unique and powerful technology is luring in industry: Ohkoshi collaborates with more than 20 companies, and another 60 parties from within Japan and outside have expressed interest. "I strive to make a harmonious research environment that can contribute to society," he says. ■

Department of Chemistry

www.chem.s.u-tokyo.ac.jp/en/



THE UNIVERSITY OF TOKYO

Opening up channels

Membrane channels that allow proteins, ions and other molecules to pass in and out of cells and the membrane transporters that drive this process carry out a bewildering range of subtle functions, including ensuring that the appropriate molecules pass through membranes at the correct times. A basic understanding of these mechanisms could be applied to the development of more effective drugs for cancer, better antibiotics, and new methods for studying and treating mental disorders, but the key molecules involved are difficult to isolate and characterize.

The University of Tokyo's Osamu Nureki is not fazed. He brings a powerful array of analytic techniques, including x-ray crystallography, x-ray free electron laser imaging, molecular kinetic simulations, genetic and patch clamp analyses, and spectroscopic assays, to bear on these tiny but critical players.

His goal is practical and conceptual. "Using these tools, I want to understand the various molecular mechanisms of different membrane channels and membrane transporters. Based on that, I want to find a common principle working in the diverse mechanisms," says Nureki.

For example, a recent study used high resolution imaging to show how membrane channels called channelrhodopsins open when activated by light. Many researchers now manipulate channelrhodopsins with light to study single neurons even in live, moving animals, and others are investigating whether this effect can be used to treat patients with psychiatric diseases. Nureki's study offers the potential to design new forms of channelrhodopsins. "We should be able to make new tools that can be used in basic neuroscience and contribute to the development of new treatments for mental health problems," says Nureki.

Another transporter named MATE, which is very active in the liver and kidney, helps to expel drugs and other foreign chemical compounds from cells. Nureki produced high-resolution, three-dimensional images of MATE alone and when binding antibiotics. The images showed MATE to be composed of two lobes of six membrane-penetrating helices that, depending on pH levels, take on one of two formations — one straight and one bent. The analysis shows how a drug is recognized and, when MATE is in the bent form, expelled from the cell.

The results of the MATE study also suggested clinical applications. Expression of MATE in pathogens can make them resistant to antibiotics, and expression in cancer cells can make the cells resistant to chemotherapy. In such cases, inhibiting MATE would help to improve the effectiveness of these drugs. Nureki screened peptides that bind with MATE and found inhibitory proteins that penetrate bacterial membranes and disable MATE. "Since any drugs are usually expelled from the cell, until now it's been impossible to make an inhibitory protein to MATE. We've opened the path to doing just that."

Nureki wants to continue the work, focusing on the relationship between the dynamics of the membrane channels and higher order processes such as pathogenesis and aging. He also wants to map out the range of impacts that other physical factors—light, temperature, pressure, electric field variation—have on the channels and the related proteins. Eventually he wants to link these high-resolution structural analyses to drug development, and he already collaborates with Japan's big drug makers.

Nureki credits access to the world's most powerful synchrotron light at SPring-8 and outstanding graduate students at The University of Tokyo with the series of successes. "Being able to get great students on consistent basis was the biggest support," he says.

Department of Biophysics and Biochemistry, Graduate School of Science

www.nurekilab.net/index.php/en