WINTER 2017

RIKEN RESEARCH

SHOWCASING THE BEST OF JAPAN'S PREMIER RESEARCH ORGANIZATION

www.riken.jp/en/research/rikenresearch

JAPANESE RESEARCH IN CRISIS

RIKEN's three point plan for recovery

'EGGNESS' OFF SWITCH

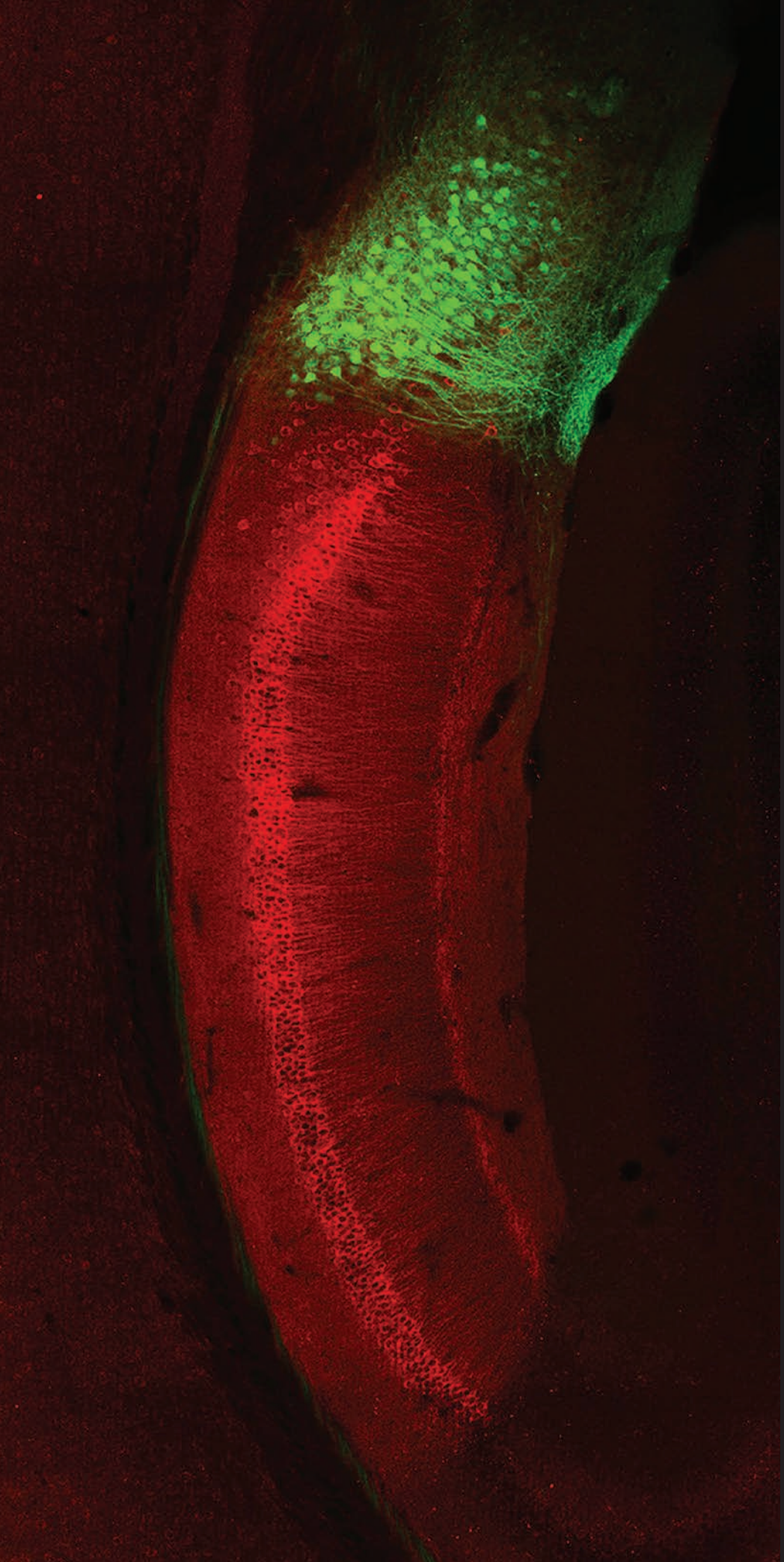
Insight into embryos and infertility

WASH AND WEAR

Solar power in your clothes

THE NEW GOLD STANDARD

A Midas touch for skin sensors



RIKEN–MIT Center for Neural Circuit Genetics (CNCG) Researchers have genetically expressed fluorescent proteins only in neurons in the subiculum and shown that in mice the subiculum is needed for memory retrieval, but not for memory formation.

RIKEN, Japan's flagship research institute, conducts basic and applied experimental research in a wide range of science and technology fields including physics, chemistry, medical science, biology and engineering.

Initially established as a private research foundation in Tokyo in 1917, RIKEN became a national research and development institute in 2015.

RIKEN Research is an online and print publication that highlights the best research published by RIKEN. This publication is a selection of the articles published by RIKEN at: www.riken.jp/en/research/rikenresearch
Please visit the website for recent updates and related articles. Articles showcase RIKEN's groundbreaking results and are written for a non-specialist audience.

For further information on the research presented in this publication or to arrange an interview with a researcher, please contact:

RIKEN International Affairs Division
2-1, Hirosawa, Wako, Saitama,
351-0198, Japan
Tel: +81 48 462 1225
Fax: +81 48 463 3687
E-mail: rikenresearch@riken.jp

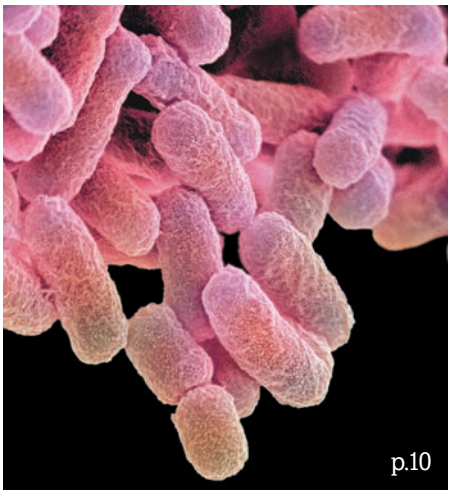
ISSN 1883-3519

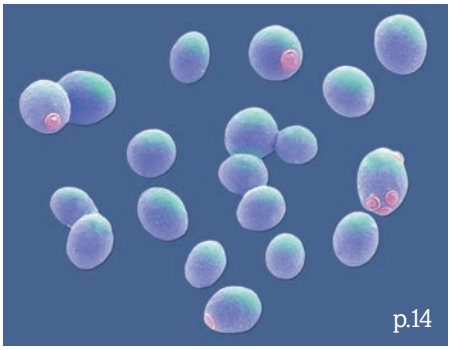
RIKEN Research is published by RIKEN in collaboration with the Partnership and Custom Media unit of Nature Research, a division of Nature Japan KK.

RIKEN
RESEARCH

RIKEN

www.riken.jp/en





Making sure Japanese science counts

Hiroshi Matsumoto
President, RIKEN

There has been a great deal of concern in Japan recently regarding the international competitiveness of the scientific research conducted in the country. As a result, at RIKEN, we are planning a series of reforms to address these problems, which I explain in detail on page 29. These reforms will become major parts of our next mid- to long-term plan, which we will embark on in April next year.

One of the key features of these changes will be to install systems that make sure that our discoveries at RIKEN are more effectively funneled into innovation pipelines and put into use by industry. The ultimate aim is both to raise the level of science and technology in Japan and to help us to better contribute to the creation of a more sustainable society. With regards to the latter, I would like to draw your attention to a report on the Sixth Global Summit of Research Institute Leaders, which you will find on page 9. This year, leaders of 20 institutions from 12 countries gathered in Kyoto to discuss how we can work together as global research institute leaders to further global sustainability goals.

Also, as an exciting example of work researchers at RIKEN have performed that could lead to a more energy efficient and healthy society, scientists from one of our laboratories at the Center for Emergent Matter Science have developed a stretchable photovoltaic cell that can be incorporated into clothing and can even be put through the wash. These solar cells could be used to power biosensors integrated into our clothing. The details of that work are on page 26 of this issue.

Cover story: A RIKEN-led team has developed a breathable sensor that has promising for applications in sport and health.
Page 15

Keep up to date

Online
www.riken.jp/en

Facebook
facebook.com/RIKEN.english

Twitter
twitter.com/RIKEN_en

LinkedIn
linkedin.com/company/riken

Engineering life

Miki Ebisuya

Unit Leader, Laboratory for Reconstitutive Developmental Biology

RIKEN Quantitative Biology Center

Please describe your role at RIKEN.
I lead and manage my laboratory, where we are seeking to reconstruct the basic developmental mechanisms of multicellular organisms.

Please briefly describe your current research? Why is it important?
My research is filed under synthetic biology—a young field, born in about 2000, that attempts to apply engineering principles to the design and construction of complex biological systems. But while most synthetic biologists use single-cell organisms such as *E. coli*, my research focuses on multicellular developmental mechanisms and so I call it synthetic developmental biology. By artificially recreating developmental processes, we're trying to better understand how our body is built. So far, my lab has reconstituted a mechanism for spontaneous cell differentiation—the diversification of cell types—by constructing a synthetic gene circuit that makes neighboring cells communicate with each other in a cell culture. We are now working on reconstructing the mechanisms for pattern formation and tissue deformation, both of which are fundamental to animal development.

What excites you the most about your current research?
Current knowledge and technology are still too immature to make or reconstitute biological phenomena at will. In fact, most of the reconstitution projects we've planned so far have yet to be realized. While this is frustrating, I feel that there are unlimited possibilities and enormous potential in this area.

How did you become interested in the field?
I've liked building things since I was a young child—my favorite toy used to be LEGO. I also like living creatures and used to observe insects in the garden for hours. So I figured that building biological phenomena was for me.

When and how did you join RIKEN?
As an undergraduate, I visited and greatly admired the RIKEN Center for Developmental Biology (CDB) and was very happy when I got a unit leader position in 2013 (in 2014, my lab moved to the RIKEN Quantitative Biology Center, QBiC).

What are some of the technologies that you use for your research?
RIKEN's Kobe campus has some state-of-the-art technologies, including an animal facility, an imaging facility and a genome analysis facility. We often consult with the staff of these facilities about experimental problems.

> *By artificially recreating developmental processes, we're trying to better understand how our body is built.*

What made you decide to become a scientist?
As a child, I thought that becoming a scientist and figuring out the secrets of this world was incredibly romantic. Then, as an undergraduate, I started to like the process of research itself—from making a hypothesis and planning an experiment, to carefully carrying out the experiment, admitting failures, revising hypotheses, repeating trials, and, once in a long while, discovering something new!

How has being at RIKEN helped your research?
Since my laboratory is affiliated with QBiC and located in the same building as the CDB, I have had the opportunity to learn advanced imaging and engineering at QBiC, as well as about animal development at the CDB.

Please tell us about your professional and personal goals.
I want to make artificially created biological phenomena seem as beautiful as other natural phenomena and to discover a new biological principle through synthetic reconstitution. ■

Dreams of exploding stars

Shigehiro Nagataki

Chief Scientist, Astrophysical Big Bang Laboratory

Chief Scientist Laboratories

Please describe your role at RIKEN.
As a principal investigator, I manage the Astrophysical Big Bang Lab. I also pursue my scientific goals as well as support lab members in realizing their research dreams.

Please briefly describe your current research? Why is it important?
My lab studies massive star explosions—astrophysical big bangs. Massive exploding stars synthesize heavy elements (that is, carbon and heavier elements). The Earth and our bodies are made of these heavy elements, including carbon, oxygen and iron. In other words, we were born from massive stars. We are studying how and why massive stars explode, as well as how and what kind of heavy elements these explosions produced.

What excites you the most about your current research?
Gamma-ray bursts are the most energetic explosions in the Universe and are sometimes the result of massive star explosions. We recently discovered evidence of why gamma-ray bursts occur by mathematically simulating the propagation of relativistic jets emitted from progenitor stars, calculating the radiation transfer of the jets, and estimating the resulting brightness and spectrum of the gamma-rays.

How and when did you join RIKEN?
I met Professor Emiko Hiyama at a meeting supported by the Ministry of Education, Culture, Sports, Science and Technology, and she invited me to give a talk at her laboratory at RIKEN. After that, I went for dinner with Professors Tetsuo Hatsuda and Hiyama, and I thought it would be really interesting to work with them. A few months later, I applied for RIKEN's Associate Chief Scientist Program.

How has being at RIKEN helped your research?
Among other things, the Associate Chief Scientist Program guaranteed a 100-million-yen start-up budget, with which I could hire top-level researchers.

What are some technologies you use to conduct your research?
The K computer and Hokusai supercomputers are very important to crunch the data needed for our research.

What is the best thing about working at RIKEN?
I think that the barrier between laboratories is lower at RIKEN than at Japanese universities. For example, my lab has a close relationship with the Interdisciplinary Theoretical and Mathematical Sciences Program—I'm a deputy director and all my lab members are associates—which facilitates interdisciplinary communication and collaboration with other labs.

What has been your most memorable experience at RIKEN?
I feel that the president is closer to us at RIKEN than at Japanese universities. When I was an associate chief scientist, I felt that the program was very good, but that some improvements were possible. So I proposed some improvements to President Hiroshi Matsumoto, together with all associate chief scientists, which were partially adopted. This interaction greatly enhanced the research environment I was working in.

Please tell us about your professional and personal goals.
I want to understand how the Universe was born by studying black holes, as they are also created as a result of massive star explosions or failures of massive stars to explode. ■

Careers at RIKEN

For further information, visit our Careers page:
Website: www.riken.jp/en/careers
E-mail: pr@riken.jp

Managing science: RIKEN and Max Planck Society cooperate

The first MPG–RIKEN Administrative Roundtable Meeting was held at the Max Planck Society Headquarters in Munich. The participants included RIKEN Executive Director Motoko Kotani and MPG Secretary General Rüdiger Willems.

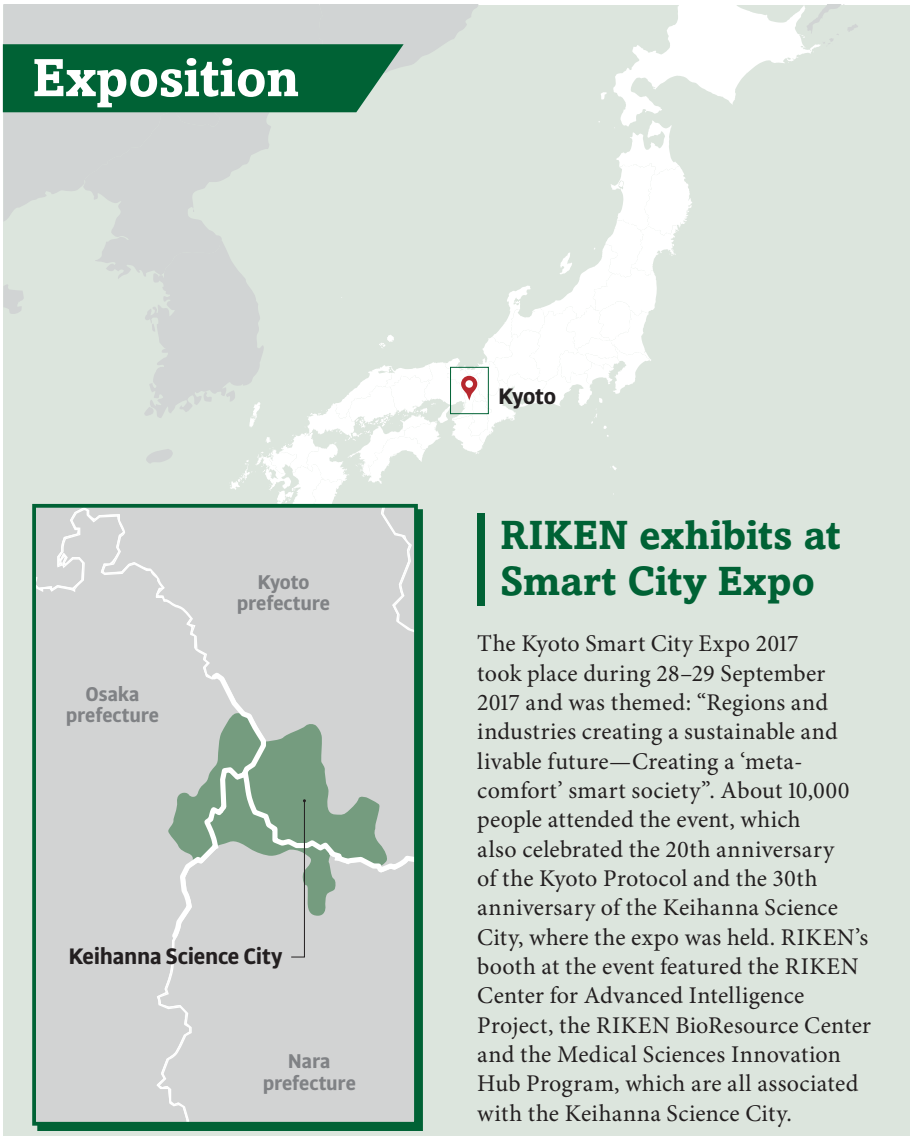
RIKEN and the Max Planck Society (MPG) have a long shared history—in fact the German scientific society, which was founded in 1911, was one of the inspirations for establishing RIKEN in 1917 and they have collaborated on research for some three decades. Although administrative work rarely reaches the headlines, it is crucial to the success of the two large, long-standing scientific organizations. So, they are now sharing their experiences in this important domain as well.

The first MPG–RIKEN Administrative Roundtable Meeting was held from 16–18 October 2017 at the MPG Headquarters in Munich. The participants included MPG Secretary General Rüdiger Willems and RIKEN Executive Director Motoko Kotani, as well as administrative staff from both sides. Discussion focused on governance, research evaluation, human resources, international collaboration and communication. Of particular interest was the question of how to enhance relationships between headquarters and individual centers.

"The participants from both RIKEN and MPG, who share strong motivation and responsibility as staff of national flagship institutes in basic research, held enthusiastic discussions from the beginning," says Kotani. "They came to understand that they had common issues as administrative staff and that there were different working styles appropriate to each country."

A second roundtable meeting, to be held at RIKEN, is planned in the near future.

Exposition



RIKEN exhibits at Smart City Expo

The Kyoto Smart City Expo 2017 took place during 28–29 September 2017 and was themed: "Regions and industries creating a sustainable and livable future—Creating a 'meta-comfort' smart society". About 10,000 people attended the event, which also celebrated the 20th anniversary of the Kyoto Protocol and the 30th anniversary of the Keihanna Science City, where the expo was held. RIKEN's booth at the event featured the RIKEN Center for Advanced Intelligence Project, the RIKEN BioResource Center and the Medical Sciences Innovation Hub Program, which are all associated with the Keihanna Science City.

Summer school for young researchers

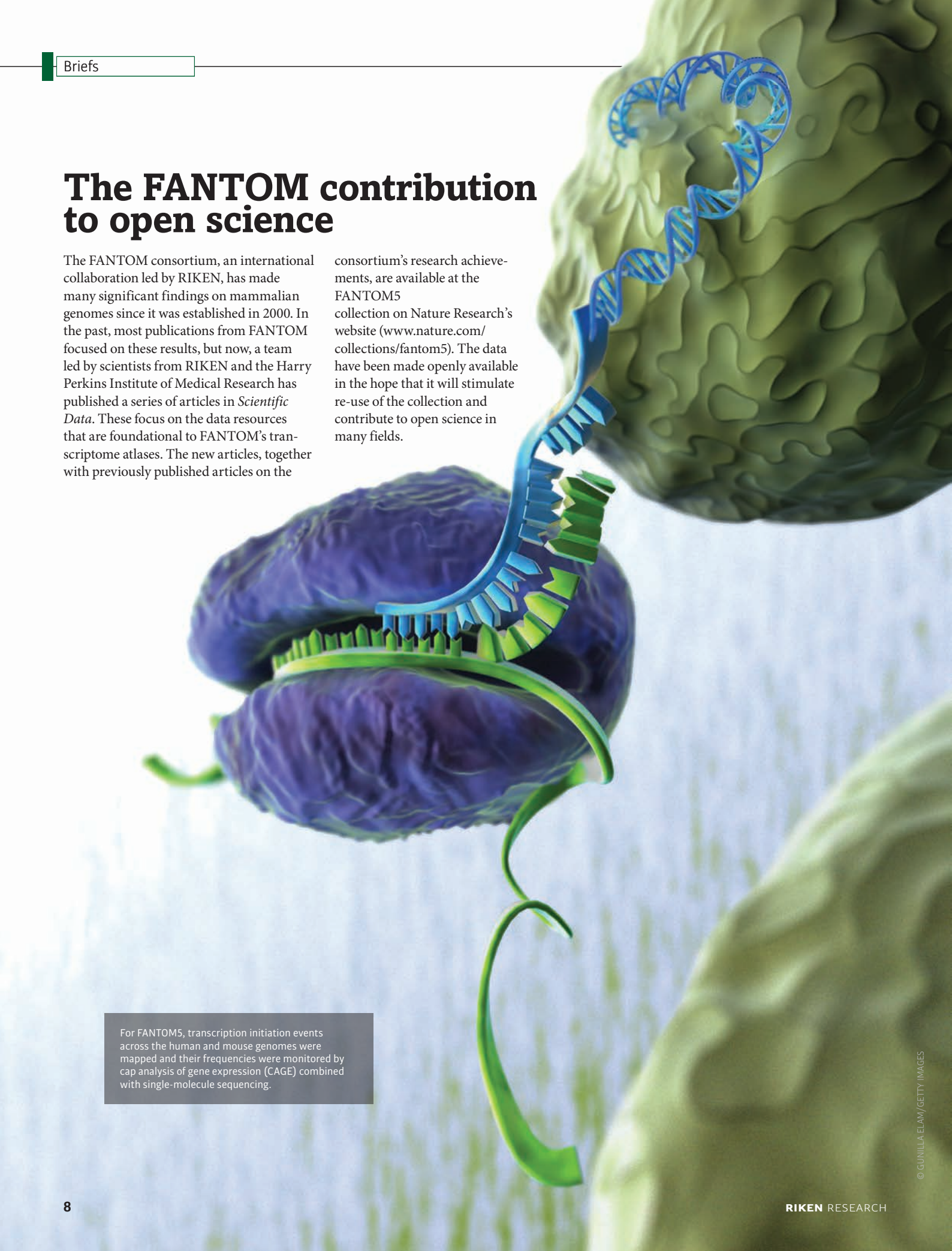
All 107 participants at the RIKEN Summer School gave poster presentations, which were evaluated by a team of experienced researchers.

The ninth annual RIKEN Summer School was held on 1–2 September 2017 at Kazusa Arc in Chiba prefecture. More than 100 students in the International Program Associate and Junior Research Associate Programs attended and gave poster presentations. Masatoshi Takeichi from the RIKEN Center for Developmental Biology gave the keynote speech on choosing research subjects and working within a global community. Takeichi is known for the seminal discovery of the cell adhesion molecule cadherin. Three principal investigators also talked about their fascinating paths to discovery. Kazuyo Moro talked about group 2 innate lymphoid cells (ILC2), which she discovered in 2010. Miki Ebisuya explained her journey from gene transcription to synthetic biology. And Kouji Morimoto spoke about the unusual path that led him to help discover the element nihonium. The best poster prize went to Takeshi Tsusaka, a junior research associate at the Cellular Memory Laboratory, who recently discovered methylation's unexpected role in recruiting the protein UHRF1 to replicating sites and maintaining DNA methylation for a 'histone-mimic'.

http://www.riken.jp/summerschool/index.html

The FANTOM contribution to open science

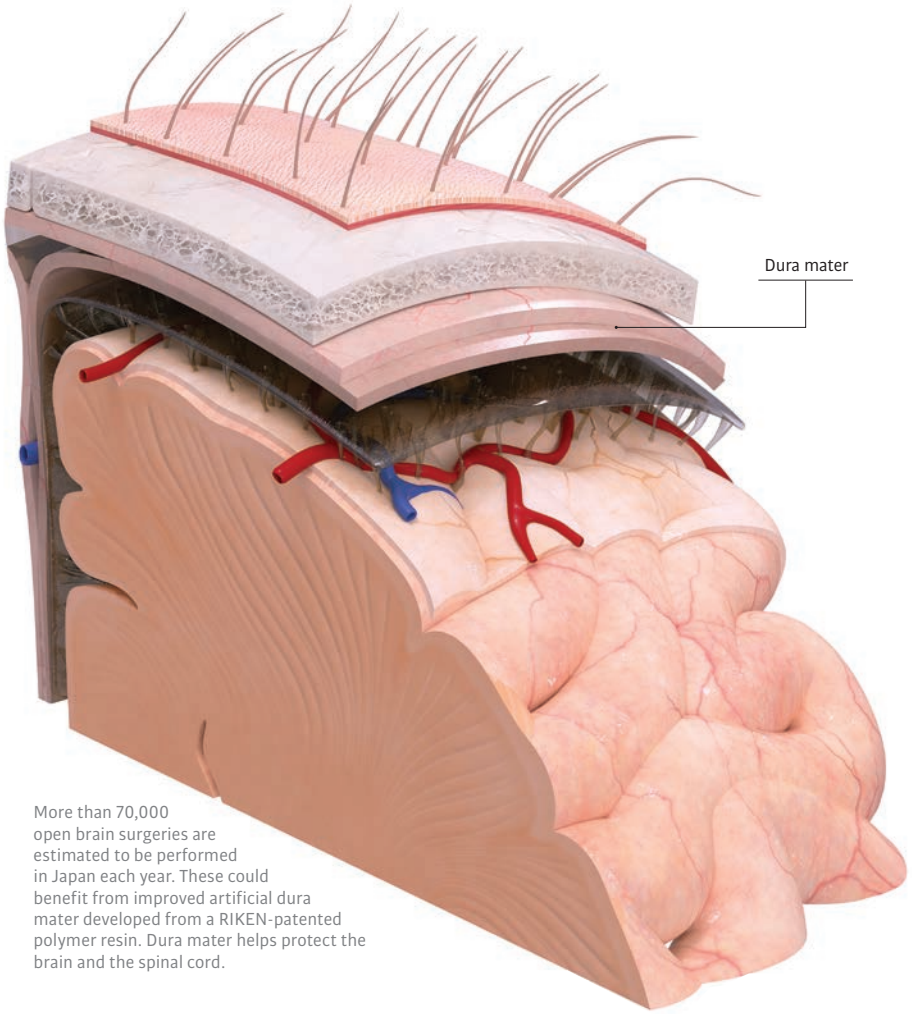
The FANTOM consortium, an international collaboration led by RIKEN, has made many significant findings on mammalian genomes since it was established in 2000. In the past, most publications from FANTOM focused on these results, but now, a team led by scientists from RIKEN and the Harry Perkins Institute of Medical Research has published a series of articles in *Scientific Data*. These focus on the data resources that are foundational to FANTOM's transcriptome atlases. The new articles, together with previously published articles on the consortium's research achievements, are available at the FANTOM5 collection on Nature Research's website (www.nature.com/collections/fantom5). The data have been made openly available in the hope that it will stimulate re-use of the collection and contribute to open science in many fields.



For FANTOM5, transcription initiation events across the human and mouse genomes were mapped and their frequencies were monitored by cap analysis of gene expression (CAGE) combined with single-molecule sequencing.

Life-saving surgery material

An artificial material that could be useful in synthetic dura mater for cranial surgery, cardiovascular repair patches, trigeminal neuralgia treatment devices and artificial heart valves has been approved for production and distribution in Japan. It is produced using a polymer resin developed and patented by RIKEN scientists. Currently, artificial dura mater is widely used in dura mater reconstruction in cases involving brain tumors or trauma surgery, and particularly to prevent cerebrospinal fluid leakage. But there have been problems with post-surgery infections and adhesion. DuraBeam™, developed by TamaBio, is designed using RIKEN's resin to overcome these issues and is expected to offer higher biocompatibility, shortened surgery times and lower infection risk. Produced in surgical sheets, it means surgeons do not need to attach it using minute stitches, which dramatically reduces both operation time and risk of infection. "The research for this product's technology began 20 years ago at RIKEN," said TamaBio's chief executive officer, Makoto Sawada. "I am convinced that it holds the key to saving millions of patient lives across the globe."

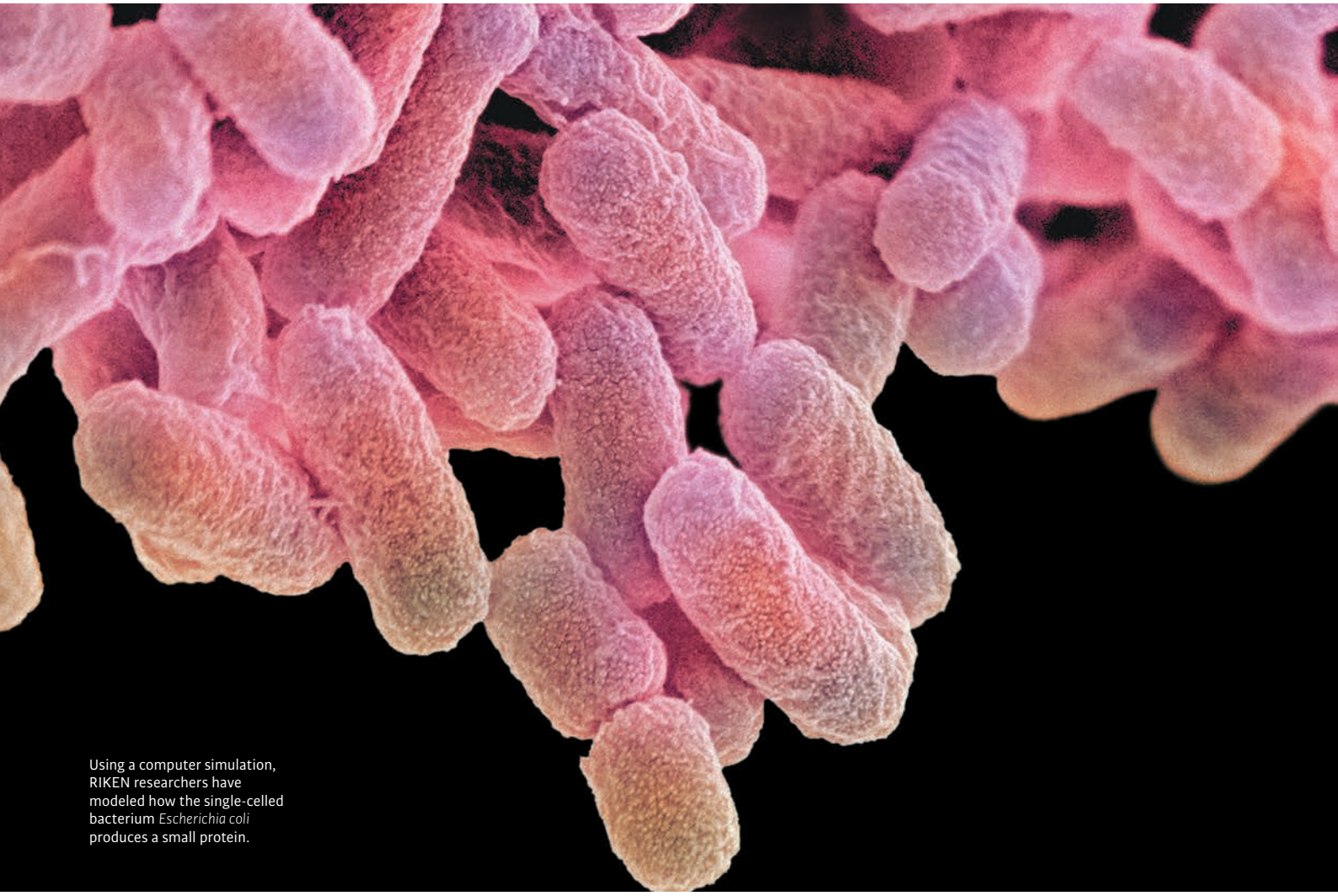


More than 70,000 open brain surgeries are estimated to be performed in Japan each year. These could benefit from improved artificial dura mater developed from a RIKEN-patented polymer resin. Dura mater helps protect the brain and the spinal cord.

Summit on sustainable societies

On 30 September 2017, leaders representing 20 national research institutes from 12 countries attended the sixth Global Summit of Research Institute Leaders in Kyoto, jointly organized by RIKEN and the National Institute of Advanced Industrial Science and Technology. Representatives focused on how to create sustainable societies. In a joint statement, the attendees declared that "research for the benefit of sustainable development will require large-scale efforts that go beyond the abilities of any single institution or nation", and pledged to engage with these challenges.

BOTTOM: 2017 RIKEN; TOP: CLAUS LUNAU/SCIENCE PHOTO LIBRARY



Using a computer simulation, RIKEN researchers have modeled how the single-celled bacterium *Escherichia coli* produces a small protein.

BIOLOGY

Complexity in the simplest of processes

The incredible complexity of a single-celled organism is revealed by a computer model of protein production

Creating a small protein in a simple organism is a breathtakingly complex undertaking, new computer modeling has revealed. RIKEN scientists have mapped how the concentrations of more than 240 compounds vary with time when the tiny single-celled bacterium *Escherichia coli* makes a small protein[1]. They found that while all the concentrations eventually plateau, they do not reach those plateaus in a smooth, linear fashion; rather, they exhibit temporary periods of stability—known as quasi-stationary states—followed by periods of sudden change. This finding could provide a powerful way to explore the dynamics of complex systems.

The process of producing the tripeptide Met–Gly–Gly, a protein made up of just three amino acids, uses 27 starting chemicals that make 241 products and intermediate compounds through a staggering 968 reactions. Determining how the concentrations of these 241 compounds vary with time would seem to be a hopelessly complex task, but that is what Yoshihiro Shimizu at the RIKEN Quantitative Biology Center and co-workers have succeeded in doing.

The team constructed a large-scale model of the protein synthesis in *E. coli*. To do this, they scoured the literature for experimental

reaction rates of the reactions involved in the synthesis. They then made a simulation of the first 15 minutes of the process, which accurately reproduced the kinetics of the tripeptide synthesis.

The results yielded two surprises. The first was that the synthesis rate of the tripeptide was remarkably robust against changes in the parameters used in the model. "When we varied the kinetic parameters in the simulation, we found that many changes in the parameters do not affect the synthesis rate of the tripeptide," says Shimizu. "This suggests that only a few parameters determine the synthesis rate of the product, even in such a large-scale reaction network."

> **"Their concentrations would reach stable values for a while, only to later change dramatically."**

The second unexpected finding was that although the synthesis of the tripeptide increased linearly over the 15-minute period, this masked surprising fluctuations in the concentrations of many of the other compounds. In particular, their concentrations would reach stable values for a while, only to later change dramatically.

"The process involved collapse and regrowth of clusters of compounds in a quasi-stationary state," explains Shimizu. "Network collapse occurred at two time points as a result of changes in the supply of recyclable substrates and the presence of a reaction cascade bottleneck." This finding suggests that focusing on these quasi-stationary states might be a helpful way to analyze complex reaction dynamics.

The team now intends to obtain experimental data to both confirm the accuracy of their simulation and to improve it. ●

Reference

1. Matsuura, T., Tanimura, N., Hosoda, K., Yomo, T. & Shimizu, Y. Reaction dynamics analysis of a reconstituted *Escherichia coli* protein translation system by computational modeling. *Proceedings of the National Academy of Sciences USA* **114,** E1336–E1344 (2017).

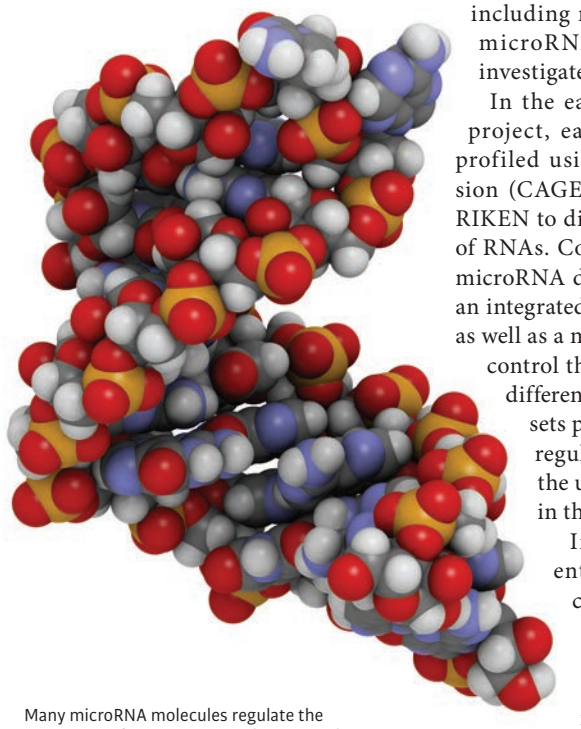
BIOLOGY

Mapping microRNA expression in human cells

An atlas of microRNA in human primary cells is a vital resource for understanding microRNA regulation and its role in human disease

FANTOM, an international scientific consortium led by RIKEN, has created the first extensive atlas of microRNA expression in human primary cells[1].

The human body consists of hundreds of different cell types that have very different functions and behaviors, and yet almost all the cells of an individual person have identical genome sequences. The variation in functional roles of cells is accomplished by an intricate regulatory network consisting of regulatory proteins as well as regulatory RNAs, such as microRNAs. Dysregulation of such networks plays a major role in the development of various diseases, particularly cancer. It is thus important to characterize the expression profiles of microRNAs across cell types and tissues in order to understand the functions of microRNAs and their roles in health and disease.



Many microRNA molecules regulate the expression of genes. FANTOM has created the first extensive atlas of microRNA expression in human primary cells.

Leveraging the collection of RNA samples from humans and mice established as part of the fifth edition of FANTOM, the FANTOM team has sequenced microRNA libraries of hundreds of human samples, including many cell types for which the microRNA presence had never been investigated before.

In the earlier stages of the FANTOM project, each of the samples had been profiled using cap analysis gene expression (CAGE), a technology developed at RIKEN to discover the precise starting site of RNAs. Combining the CAGE data with microRNA data allowed the team to create an integrated atlas of microRNA expression as well as a map of the genomic regions that control the expression of microRNAs in different cell types. Together, these data sets provide a first view of how these regulators contribute to establishing the unique identity of each cell type in the human body.

In the present study, the scientists found that the genomic control regions of microRNAs identified in this study were highly conserved in evolution, underlining their importance in cellular regulation. They also found thousands of new genomic loci

producing short RNAs, which may prove to constitute a novel class of regulatory short RNAs.

The study provides a broad atlas of microRNA expression and promoters in primary mammalian cells and hence establishes a platform for further detailed analysis of microRNA expression patterns and transcriptional control regions.

"We have made the expression atlas available online and expect to have thousands of users all around the world," says Michiel de Hoon of the RIKEN Center for Life Science Technologies. "We believe it will be an essential resource for understanding microRNA regulation and its role in human disease," he adds. The atlas is available online at: **http://fantom.gsc.riken.jp/5/suppl/De_Rie_et_al_2017/**

Reference

1. de Rie, D., Abugessaisa, I., Alam, T., Arner, E., Arner, P., Ashoor, H., Åström, G., Babina, M., Bertin, N., Burroughs, A. M. *et al*. An integrated expression atlas of miRNAs and their promoters in human and mouse. *Nature Biotechnology* **35,** 872–878 (2017).

BIOLOGY

How diet during pregnancy could lead to schizophrenia

Study shows how depriving pregnant mice of two fatty acids during pregnancy could result in schizophrenic-like symptoms in their adult offspring

RIKEN researchers have discovered how nutritional changes during early mouse pregnancy can lead to offspring developing schizophrenic-like symptoms as adults[1].

Detrimental conditions during pregnancy affect the health of offspring, even in adulthood. This explains why schizophrenia rates sometimes double after famines.

To develop schizophrenia treatments, Takeo Yoshikawa's team at the RIKEN Brain Science Institute is researching how malnutrition during early development changes the brain.

They first determined the most likely nutrients whose deficiency is related to schizophrenia. The team studied two polyunsaturated fatty acids—the omega-3 fatty acid DHA and the omega-6 fatty acid AA—because they are abundant in the brain and are related to brain development. When they deprived pregnant mice of DHA and AA, they found that their adult offspring shared similar characteristics to those exhibited by people with early stage schizophrenia.

A lack of omega-3 fatty acid DHA, found in oily fish, during pregnancy might increase an offspring's risk of schizophrenia.

As dysfunction in the prefrontal cortex is a hallmark of schizophrenia, the researchers looked at how DHA/AA deprivation affects gene expression in that brain region. Among the hundreds of affected genes, they found a group of genes downregulated in both people with schizophrenia and in the affected mice. These genes are related to oligodendrocytes—cells that surround neurons and help signal transmission. Additionally, expression of genes affecting the GABA neurotransmitter system was altered in ways that mimicked findings from the postmortem brains of people with schizophrenia.

Gene expression can be controlled by a class of proteins called nuclear receptors

that attach to DNA and initiate the transcription process. When the team further analyzed the fatty-acid-deprived mice, they found that several nuclear receptor genes related to fatty acids had been downregulated. The abnormal expression of oligodendrocyte-related genes was related to the low expression of these nuclear receptors, which in turn was due to higher levels of DNA methylation, a common way to regulate gene expression. In this way, the altered diet created long-lasting changes in gene expression.

> **“This was evidence that drugs acting on nuclear receptors can be a new therapy for schizophrenia.”**

The team considered how to reverse the process. When they gave mice a drug that acted on RXR nuclear receptors, oligodendrocyte- and GABA-related genes were upregulated and some of the abnormal motor behavior was reduced. “This was evidence that drugs acting on nuclear receptors can be a new therapy for schizophrenia,” says first author Motoko Maekawa.

Furthermore, hair follicles from two populations of human patients with schizophrenia were found to exhibit reduced expression of the same nuclear receptor genes.

“The next step is to test the effectiveness of drugs that target these nuclear receptors in patients with schizophrenia and to investigate how nuclear receptors regulate the function of oligodendrocytes and GABAergic neurons to prevent the development of schizophrenic pathophysiology,” says Maekawa. ●

Reference

1. Maekawa, M., Watanabe, A., Iwayama, Y., Kimura, T., Hamazaki, K., Balan, S., Ohba, H., Hisano, Y., Nozaki, Y., Ohnishi, T. *et al.* Polyunsaturated fatty acid deficiency during neurodevelopment in mice models the prodromal state of schizophrenia through epigenetic changes in nuclear receptor genes. *Translational Psychiatry* **7,** e1229 (2017).

PHYSICS/ASTRONOMY

An uneven resistance

Superconducting molybdenum disulfide exhibits a huge enhancement in the variability of resistance with magnetic field direction

In certain materials, a magnetic field can be used to control electrical resistance. RIKEN researchers have now found that this effect is dramatically enhanced when such materials enter a superconducting state[1]. This discovery could help to develop superconducting diodes—devices that allow current to flow without resistance in one direction only.

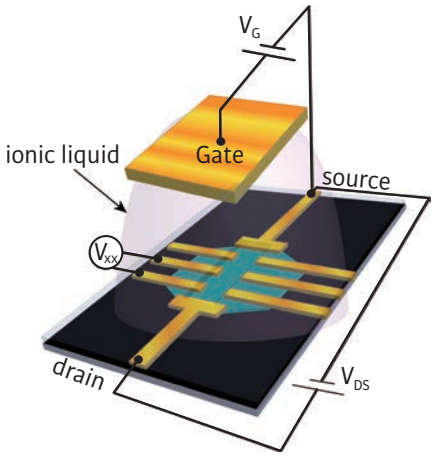
In conventional metals, electrical current flows equally in any direction. But when a magnetic field is applied to materials with a particular type of asymmetry in their crystal structure, their electrical resistance depends on the strength and direction of both the magnetic field and the current. This phenomenon is called magnetochiral anisotropy.

Naoto Nagaosa of the RIKEN Center for Emergent Matter Science and colleagues have now studied magnetochiral anisotropy in flakes of molybdenum disulphide, which are composed of many atom-thin layers. Each layer contains a repeating pattern of atoms, with every molybdenum atom sandwiched between two sulfur atoms. This pattern cannot be superimposed on its mirror image—just as a left hand cannot be superimposed on a right hand—giving it a form of asymmetry called chirality. But when many of these layers stack up, each rotated 180 degrees relative to the one below it, the structure they create is no longer chiral.

The researchers used a 20-nanometer-thick, multilayer flake of molybdenum disulphide in a device called an electric double-layer transistor, which allowed them to monitor the material’s resistance when exposed to an electric field and a magnetic field (Fig. 1).

The electric field changed the material’s energy levels so that its electrons localized within each layer. Under these conditions, the material behaved as if it was a single, chiral monolayer of molybdenum disulfide.

Adding a magnetic field initially caused no discernible difference to the material’s resistance. But when the researchers cooled the molybdenum disulphide to just below −264 degrees Celsius, it became superconducting.



A flake of molybdenum disulfide (central blue channel) connected to electrodes (gold) in an electric double-layer transistor can exhibit a huge magnetochiral anisotropy effect in its superconducting state.

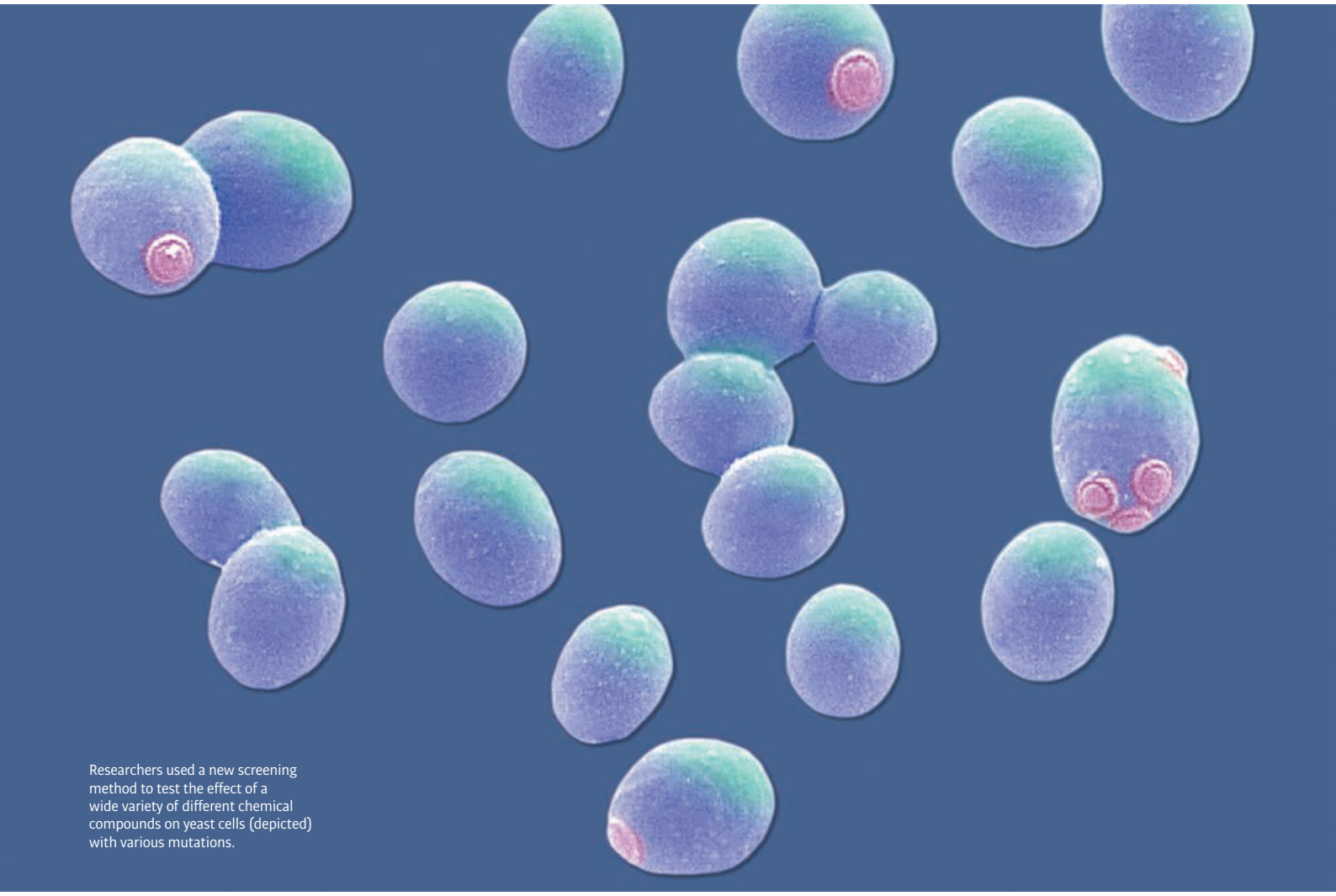
At this point, they observed huge variations in resistance that depended on the current and the magnetic field. This magnetochiral anisotropy effect was hundreds of thousands of times larger than in conventional materials.

Superconducting currents flow when electrons form pairs, and the team proposes that this pairing up increases the electrons’ sensitivity to the asymmetry of a molybdenum disulphide monolayer. “We’ve concluded that magnetochiral anisotropy is significantly enhanced in the superconducting state,” says Nagaosa.

The same effect could be seen in other chiral superconductors, and the researchers hope to apply their discovery to create superconducting nanoelectronic devices. ●

Reference

1. Wakatsuki, R., Saito, Y., Hoshino, S., Itahashi, Y. M., Ideue, T., Ezawa, M., Iwasa, Y. & Nagaosa, N. Nonreciprocal charge transport in noncentrosymmetric superconductors. *Science Advances* **3,** e1602390 (2017).



Researchers used a new screening method to test the effect of a wide variety of different chemical compounds on yeast cells (depicted) with various mutations.

BIOLOGY

A smarter way to screen molecular libraries

Large-scale screening of mutant yeast strains allows researchers to home in on and assign functions to biologically active chemical compounds

A powerful screening strategy devised by RIKEN researchers will make it easier for scientists to assign likely biological functions to different molecules, facilitating the development of safe and effective drugs[1].

The scientific community is sitting atop vast mountains of genetic data as well as enormous collections of chemicals that might serve as the foundation for potential drugs. But it is notoriously difficult to figure out which genetic pathways these chemicals affect.

The new technique promises to facilitate finding these connections. It is based on two strategies developed in the 1990s, the first of which was led by Stanford University biologist Ronald Davis, who built a vast collection of yeast strains that carried different gene deletions.

"Davis wisely included a specific 'DNA barcode' in the genome of each strain," says Charles Boone of the RIKEN Center for Sustainable Resource Science. "This means we can pool hundreds of mutants in a single test tube and follow their growth

by simply monitoring the abundance of their barcodes."

Around the same time, Boone's group developed a strategy for identifying genes that collaborate in the same biological pathway by creating massive collections of double mutants and mapping genetic networks. "We scored 'synthetic lethality', which occurs when two single mutants are viable but the double mutant is lethal," says Boone.

The team's newly developed chemical screening strategy operates on a similar principle. Barcode-labeled yeast strains with various mutations are treated with a wide variety of chemical compounds. If a given gene mutation makes a cell more susceptible to the toxic effects of a particular compound, the abundance of its DNA barcode will drop. By integrating this chemical–genetic data with their genetic network data, the researchers can determine the biochemical effects of a compound, identifying which biological pathways it affects.

Boone's group used this methodology to screen about 13,500 compounds from 7 libraries. From these compounds, they determined how about 1,500 chemicals influenced 17 essential cellular functions, including some agents that affected multiple pathways.

"Our results show that you can functionally annotate a large compound library in an efficient, systematic and unbiased manner," comments Boone.

His team is working on a second-generation screen that will make it possible to pinpoint even more precisely the individual genes and biochemical processes affected by a compound. They are also developing a version of the assay that might prove more effective at identifying agents with clinical potential. "We really think we can take everything we've developed in yeast over the last 20 years and transfer it to a human cell system," Boone says. "That's one of the next important challenges." ●

Reference

1. Piotrowski, J. S., Li, S. C., Deshpande, R., Simpkins, S. W., Nelson, J., Yashiroda, Y., Barber, J. M., Safizadeh, H., Wilson, E., Okada, H. *et al.* Functional annotation of chemical libraries across diverse biological processes. *Nature Chemical Biology* **13,** 982–993 (2017).

ENGINEERING

Electronics that feel like a second skin

Sensors made from stretchable nanomeshes allow patients' skin to breathe naturally while continuously monitoring their health

Gold meshes developed by a RIKEN-led team can be attached to the skin for several days without triggering dermatitis[1]. These devices promise to boost both patient comfort as well as the accuracy of clinical diagnostics.

Replacing the clunky cables associated with conventional electronic medical devices with wearable, wireless-enabled patches is a long-standing goal in medical diagnostics. To realize this, on-skin electronics capable of conforming to the body's curved surfaces under a range of motions while remaining conductive need to be developed. Most demonstrations of this technology have used soft, stretchy silicone or organic polymers as substrates, but these kinds of films have tightly knit chemical structures that can trap humidity and microorganisms beneath them.

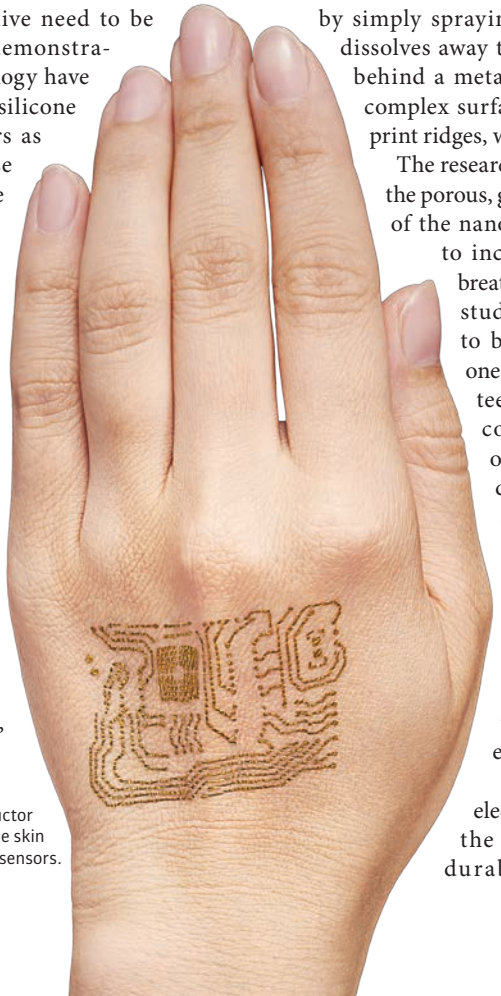
Takao Someya from the Thin-Film Device Laboratory and the RIKEN Center for Emergent Matter Science is well aware of the challenges of integrating electronics with human bodies. In 2013, he and his colleagues developed an ultra-lightweight, nearly unbreakable wearable plastic that could be imprinted with organic transistors. "However, this sensor blocked airflow around the skin and caused irritation during long-term use due to its lack of breathability," Someya recalls.

To solve this problem, Someya and co-workers decided to eliminate the backing substrate. They spun a polymer made from biocompatible polyvinyl alcohol into nanometer-thin, spaghetti-like strands and overlaid them in a mesh pattern. The team then deposited a thin gold coating onto the nanomesh plastic.

The device can be applied to the skin by simply spraying with water. This dissolves away the polymer, leaving behind a metal pattern that coats complex surfaces, such as fingerprint ridges, with ease.

The researchers anticipated that the porous, gas-permeable nature of the nanomeshes would lead to increased airflow and breathability, and clinical studies confirmed this to be the case. After a one-week study of volunteers wearing flexible conductive patches on their forearms, a dermatologist found significantly less skin inflammation with the laminated metal than conventional polymers, and participants reported forgetting the sensors were even attached.

Mechanical and electrical tests revealed the nanomeshes were durable enough for ↗



A flexible, breathable conductor can be applied directly to the skin to power up wireless touch sensors.

> **“This sensor makes it possible to measure biological information.”**

use as wireless touch sensors, even after hundreds of bending cycles. Their setup, which places the mesh conductor onto the fingertips and runs conductive patterns back to a wrist-held wireless module, uses changes in electrical resistance to spot when the skin touches an object. The researchers applied the same principle to produce temperature and pressure sensors and to fabricate electrodes for electromyography diagnostics.

“This sensor makes it possible to measure biological information without stress or discomfort, which may make it useful in fields from sports to medical care,” says Someya.

Reference
1. Miyamoto, A., Lee, S., Cooray, N. F., Lee, S., Mori, M., Matsuhisa, N., Jin, H., Yoda, L., Yokota, T., Itoh, A. *et al.* Inflammation-free, gas-permeable, lightweight, stretchable on-skin electronics with nanomeshes. *Nature Nanotechnology* **12,** 907–913 (2017).

BIOLOGY

Learning and unlearning fear

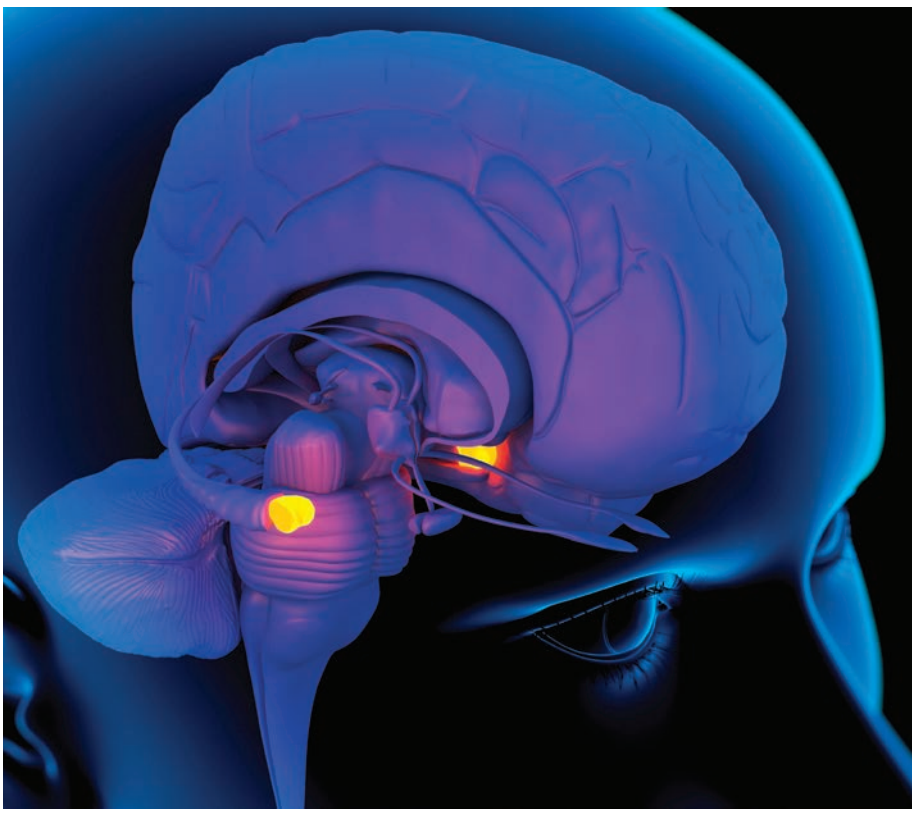
The neurotransmitter noradrenaline plays a vital role in both learning and forgetting fear

Emotional and flexible learning relies on an important division of labor in the brain, find RIKEN researchers[1].

Noradrenaline, a hormone and neurotransmitter, is important for arousal as well as many other sensory, psychological and visceral functions. Although scientists have long thought that all noradrenergic neurons in the locus coeruleus, located in the brain stem, send the same signals to the rest of the brain through a single, homogenous population of cells, researchers at the RIKEN Brain Science Institute suspected otherwise.

“The locus coeruleus functions in many behaviors, including emotional learning and cognitive and behavioral flexibility,” explains team leader Joshua Johansen. “We wondered how a homogeneous system could regulate these seemingly opposing aspects of behavior. Surprisingly, the answer was that the system is not homogenous.”

The team examined two types of learning: fear learning (where an animal learns to associate a sound with a fearful event) and fear extinction (where the association between the sound and the event is unlearned by repeating the sound without the fearful event). Fear learning involves noradrenaline increases in a brain region called the amygdala, whereas fear extinction involves noradrenaline increases in the medial prefrontal cortex.



The amygdalae are almond-shaped groups of nuclei located deep within the medial temporal lobes of the brain, and they are involved the learning of fear.

Experiments showed that during fear learning, most noradrenergic neurons were activated by the intense aversive situation. As fear responses changed during extinction, one group of locus coeruleus neurons that was active early in the fear-learning process, when fear reactions were still high, gave way to another group that began to respond as the

association was unlearned and emotional reactions were suppressed.

Further experiments revealed that the noradrenergic cell group active during fearful states sent projections to the amygdala, while the group active during extinction projected to the medial prefrontal cortex.

“Inhibiting the projection to the amygdala during fear learning prevented animals from associating the sound with the fearful event.”

The functions of these two projections became clear when the team used optogenetics to inhibit one or the other during the different learning states. Inhibiting the projection to the amygdala during fear learning prevented animals from associating the sound with the fearful event, while inhibiting it during extinction facilitated a return to normal, flexible behavior. In contrast, inhibiting the prefrontal projection had no effect on fear learning, but reduced extinction learning.

Because drugs that target the noradrenaline system are currently being developed for treating anxiety disorders, these findings could impact future drug discovery.

“Our study suggests that noradrenaline-based treatment approaches would benefit from more specific targeting and differential regulation of these pro-fear and anti-fear populations of noradrenergic cells,” says Johansen.

The team is currently examining the molecular differences between these different cell populations in the hope of developing better drug treatments for anxiety disorders. ●

Reference

1. Uematsu, A., Tan, B. Z., Ycu, E. A., Cuevas, J. S., Koivumaa, J., Junyent, F., Kremer, E. J., Witten, I. B., Deisseroth, K. & Johansen, J. P. Modular organization of the brainstem noradrenaline system coordinates opposing learning states. *Nature Neuroscience* **20,** 1602–1611 (2017).

PHYSICS/ASTRONOMY

Protons are lighter than expected

The most accurate measurements of proton mass performed to date reveal that the proton is lighter than previously believed

By performing precise measurements on a single proton, an international collaboration, including members from RIKEN’s Ulmer Fundamental Symmetries Laboratory, has improved threefold the accuracy of measuring the proton’s mass, finding that it is significantly lighter than previously thought[1].

The proton is one of the basic building blocks of atomic nuclei. Its mass is an important parameter in atomic physics since it affects electron motion around the atomic nucleus, which in turn affects the colors, or wavelengths, at which atoms absorb and emit light. Comparison of these wavelengths with theoretical predictions enables fundamental physical theories to be tested. Furthermore, precise comparisons of the proton and antiproton masses may aid the search for the crucial difference between matter and antimatter.

The team employed a sophisticated Penning trap for their measurements, which uses electric and magnetic fields to confine a charged particle such as a proton nearly indefinitely. A particle in the trap performs periodic motion at a certain frequency, which can be measured and used to calculate the particle’s mass.

The carbon isotope ^{12}C, with a mass of 12 atomic mass units, is the mass standard for atoms. “We directly used it for comparison,” says Sven Sturm of the Max Planck Institute for Nuclear Physics in Germany (see image). “We stored one proton and one carbon ion each in separate compartments of our Penning trap apparatus. We then transported each of the two ions into the central measurement compartment and measured its motion.” From the ratio of the two measured values, the group obtained the proton’s mass directly in terms of atomic units.

To reach the target precision, an elaborate measurement technique was required. The purpose-built electronics in the measurement compartment allowed the researchers to measure the proton under identical conditions as the carbon ion, despite its approximately 12-fold lower mass and 6-fold smaller charge, explains Andreas Mooser of the RIKEN Ulmer Fundamental Symmetries Laboratory.

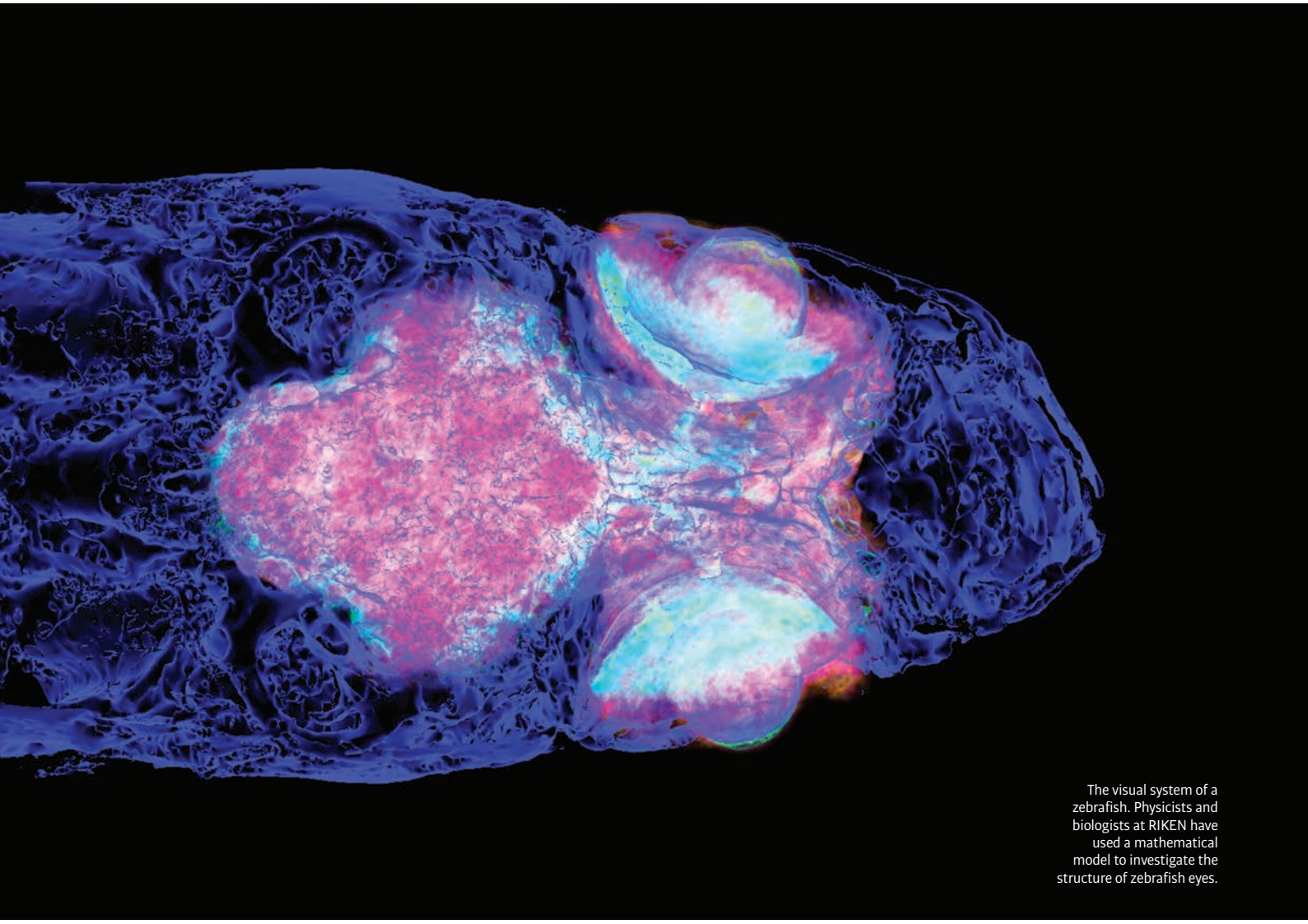
By directly comparing the mass of a proton with that of carbon isotope ^{12}C, researchers have measured the proton mass more accurately than ever before.

The measurement of the proton mass is three times more precise than the presently accepted value. Intriguingly, the measured mass was significantly smaller than the current standard value. Previous measurements by other researchers had yielded discrepancies. “Our result contributes to solving this puzzle, since it corrects the proton’s mass in the proper direction,” says Klaus Blaum of the Max Planck Institute for Nuclear Physics.

In future experiments, the team intends to store a third ion in the trap tower. “By simultaneously measuring the motion of this reference ion, we will be able to eliminate the uncertainty originating from fluctuations of the magnetic field,” explains Florian Köhler-Langes of the Max Planck Institute for Nuclear Physics. ●

Reference

1. Heiße, F., Köhler-Langes, F., Rau, S., Hou, J., Junck, S., Kracke, A., Mooser, A., Quint, W., Ulmer, S., Werth, G. *et al.* High-precision measurement of the proton’s atomic mass. *Physical Review Letters* **119,** 033001 (2017).



The visual system of a zebrafish. Physicists and biologists at RIKEN have used a mathematical model to investigate the structure of zebrafish eyes.

BIOLOGY

Patterns within fish eyes explained

A mathematical model reveals why the cone cells in zebrafish eyes arrange themselves in a certain pattern

In fish and other animals, the color-detecting cone cells in the retina are arranged in specific patterns, and this is believed to be important for allowing animals to properly sense their surroundings. Now, an interdisciplinary group of physicists and biologists at RIKEN have used a mathematical model to determine how the cone cells in zebrafish are arranged in a specific pattern in all individuals[1]. They found that small defects in the patterns lead the cells to arrange themselves into only one of two possible patterns.

Zebrafish eyes have four types of cone cells, which sense blue, ultraviolet, and a combination of red and green. The 'double cone' cells that sense red and green can be arranged in different orientations, so different patterns of ultraviolet, blue and red/green cells can form. As the fish eyes develop, these cells originate from an area called the ciliary marginal zone, differentiate into the different cone cells, and arrange themselves randomly. However, they eventually rearrange themselves into

a definite pattern. One hypothesis is that the patterns emerge from the different adhesion forces between the cells in various orientations. Essentially, they end up in the pattern that has the lowest energy level.

"While this is well known, there is an unexplained problem," explains Noriaki Ogawa of the RIKEN Interdisciplinary Theoretical Science Research Group. "There are two patterns with the same lowest energy level, one parallel to the growth of the retina and the other perpendicular to it, so that they are simply the same pattern but rotated 90 degrees. In real fish, however, only one of these two patterns is actually found."

"This is an important finding because it could have implications for the development of other structures in many organisms."

The researchers realized there must be some mechanism leading to that pattern. They found that though the two patterns were equivalent in a static model, they were not so in a dynamic setting. Using a mathematical model of dynamic pattern selection, the researchers discovered that small flaws in the pattern can disrupt it and drive it to rearrange itself in a way that always leads to the pattern found in real fish.

"This is an important finding because it could have implications for the development of other structures in many organisms," explains Ogawa. "There is much work to be done to fully explain the situation. For example, we know that there are other mechanisms that direct the development process and the polarities of cells. To fully understand how these patterns emerge in real organisms, we also need to understand the relationship between these mechanisms." ●

Reference

1. Ogawa, N., Hatsuda, T., Mochizuki, A. & Tachikawa, M. Dynamical pattern selection of growing cellular mosaic in fish retina. *Physical Review E* **96,** 032416 (2017).

BIOLOGY

Visualizing cancer spread at the single-cell level

By using transparent mice and sophisticated statistical processing, a new imaging method can spot the spread of single cancer cells

A method that can visualize cancer metastasis in whole organs at the single-cell level has been developed by RIKEN researchers[1]. By combining transparent mice with statistical analysis, it creates three-dimensional maps of cancer cells throughout the body and organs.

Recent research in optical clearing methods has made it possible to create transparent bodies and organs of experimental animals. This has led to a new wave of anatomical studies that combine tissue transparency with sophisticated cell-labeling techniques and light microscopy.

The team, led by Hiroki Ueda at the RIKEN Quantitative Biology Center and Kohei Miyazono at the University of Tokyo, has focused on visualizing and profiling cancer metastasis throughout the body.

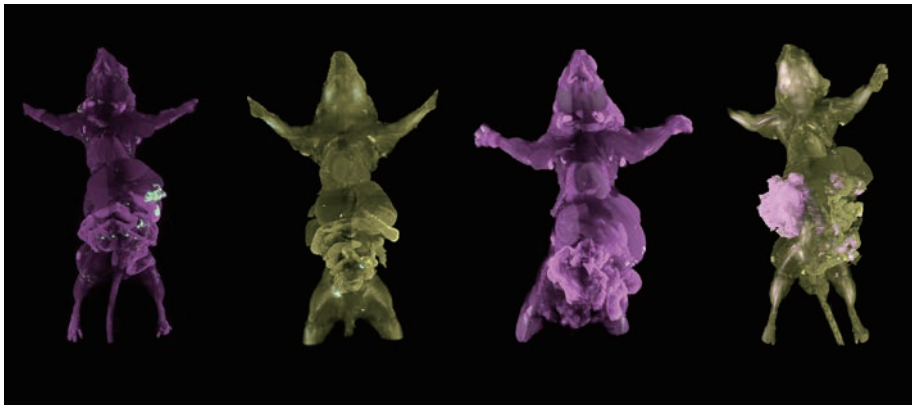
"One of the biggest difficulties in studying cancer is that tumor metastasis is started by just a few metastasized cells," explains Ueda. "Our new method makes it possible to image the whole body down to the individual cell level, and therefore we can detect cancer at spatial resolutions beyond what is possible using other current imaging techniques."

The team first determined the optimal refractive index—a number that describes how much light is bent as it moves through an object and which can affect the quality of light microscopy images—for their clearing agent, CUBIC.

When the researchers used the CUBIC method with this refractive index and combined it with different kinds of microscopies, they were able to detect metastasis of single cells throughout the body and organs of the mouse specimens.

Miyazono notes that this method is a bridge between conventional histology and *in vivo* imaging of live animals. "Although we cannot apply our new CUBIC-cancer analysis to live animals, we were able to quantify metastatic cells very early in their formation," he says. "This will be a very powerful tool for evaluating the effectiveness of anti-cancer drugs."

To demonstrate the potential of their



A new imaging method has been used to image the spread of single cancer cells in mice.

technique for assessing drugs, the team treated mice with anti-cancer drugs and used CUBIC-cancer analysis to profile their effectiveness. They were able to detect differences in the total volume and number of cancer colonies throughout the lungs of the mice.

The technique was even able to detect individual cancer cells. "This is very promising because these cells might be dormant or resistant to anti-cancer drugs," co-first authors Shimpei Kubota and Kei Takahashi explain. "As just one surviving cancer cell can lead to tumor metastasis, being able to use CUBIC-cancer analysis to evaluate drug effectiveness at this level is going to be a very useful and practical application." ●

Reference
1. Kubota, S. I., Takahashi, K., Nishida, J., Morishita, Y., Ehata, S., Tainaka, K., Miyazono, K. & Ueda, H. R. Whole-body profiling of cancer metastasis with single-cell resolution. *Cell Reports* **20,** 236–250 (2017).

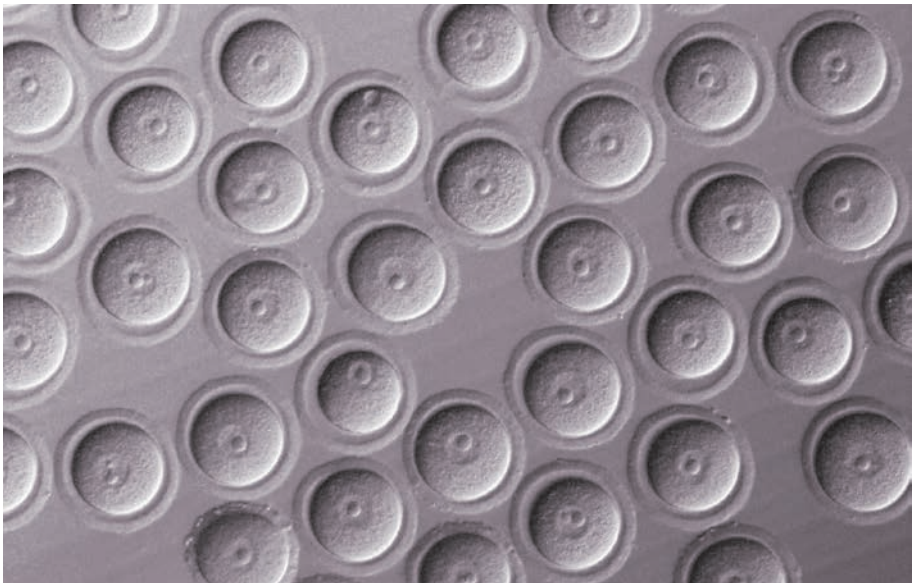
BIOLOGY

The bigger they are, the more mistakes they make

The large size of mouse oocytes is shown to create errors when chromosomes divide between daughter cells

During the first meiotic cell division, in which a parent cell containing two sets of chromosomes produces two daughter cells that each have a single set of chromosomes, immature egg cells known as oocytes make many more mistakes than any other cell type. Such errors can give rise to miscarriages and birth defects. Two RIKEN researchers have now shown experimentally in mice that this propensity to make errors is related to the large size of oocytes[1].

"It has long been speculated that the large size of the oocyte is one reason why they are so error prone," says Tomoya Kitajima from the RIKEN Center for Developmental Biology. "But I wasn't sure if this could be experimentally tested." However, when Kitajima saw the excellent micromanipulation skills of co-worker Hirohisa Kyogoku, he was convinced that Kyogoku would be able to test this point.



Scanning electron micrograph of mouse oocytes that clearly shows their nuclei (larger circles inside the cells).

Kyogoku created oocytes that had either half or double the cytoplasm of normal oocytes, by removing half of the cytoplasmic material with a micropipette or fusing two oocytes after removing the nucleus from one of them. The pair then imaged the cells as they underwent cell division to determine whether the volume of cytoplasm affected the accuracy of chromosome segregation.

Cell division is a tightly controlled process. Microtubules emanating from spindle poles attach to condensed chromosomes and align them along a plane at the equator of the spindle. Proteins that are part of a checkpoint ensure that this alignment is done correctly. If the alignment is not done, division is delayed until correction has taken place.

Kitajima and Kyogoku found that doubled oocytes displayed a variety of defects. In particular, the structure of spindle poles was deformed and thus chromosome alignment at the equator of the spindle was substantially delayed compared to halved and normal oocytes.

In addition to carrying genetic material from the mother, oocytes contain many factors in their cytoplasm that are important for the early development of the embryo after fertilization. The researchers conjecture

that factors needed for checking the proper spindle attachment to the chromosomes were diluted by the large cytoplasm. Consequently, the stringency of the checkpoint was compromised and the larger oocytes produced more daughter cells with abnormal distributions of chromosomes.

"We're now interested in the mechanisms behind this deformation," says Kitajima. "If we could identify molecules and mechanisms for how the cytoplasm size affects the chromosome segregation machinery, we may find a strategy to make it less error prone." ●

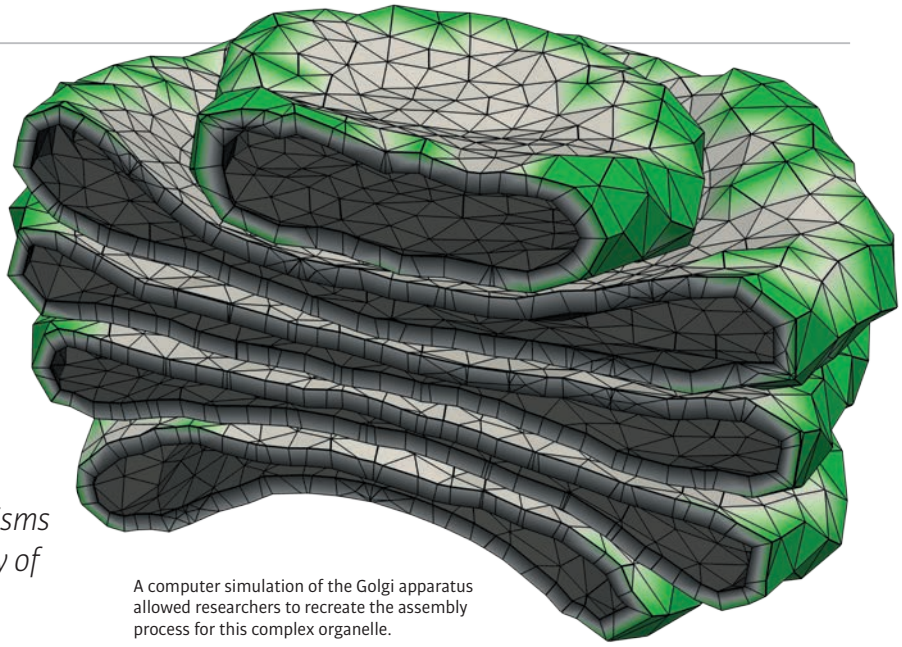
Reference

1. Kyogoku, H. & Kitajima, T. S. Large cytoplasm is linked to the error-prone nature of oocytes. *Developmental Cell* **41,** 287–298.e4 (2017).

BIOLOGY

Building a virtual organelle

Computer simulations expose the mechanisms underlying the disassembly and reassembly of a complex cellular organelle



A computer simulation of the Golgi apparatus allowed researchers to recreate the assembly process for this complex organelle.

Every time a mammalian cell divides, it must deconstruct and then rebuild the complex protein-processing machinery of the Golgi apparatus. Computational simulations have allowed two RIKEN scientists to identify critical factors that govern this process[1].

The Golgi consists of a stack of interconnected membrane-bound structures, which act as an assembly line that uses enzymes to convert newly made proteins into their fully functional, mature forms. Scientists have struggled to understand both how this organelle breaks down during cell division and how it re-forms in the resulting daughter cells.

Masashi Tachikawa, a researcher in Atsushi Mochizuki's Theoretical Biology Laboratory, found this a daunting question to tackle. "It seemed too complicated to simulate," he recalls.

But the researchers learned of experimental findings suggesting that this process is primarily self-governed by physical forces, rather than actively stage-managed by the cell. This meant the process could realistically be modeled if one could identify the essential 'rules'.

Tachikawa developed a simulation that accounted for the physical and thermodynamic features of the Golgi membrane, as well as the effects of proteins that bind to and reshape the membrane. The calculations were computationally demanding, requiring a week to complete a full simulation, but they were ultimately successful.

"We first constructed a physical model of the Golgi based on its stationary state (see image), before cell division," says Tachikawa. "This model also reproduced the highly dynamic reassembly process of the mitotic Golgi—no additional assumptions were necessary."

Through their simulation, the pair could home in on physical factors that determine whether the fragmented vesicles of the disassembled Golgi form a properly organized structure or give rise to warped and distorted structures.

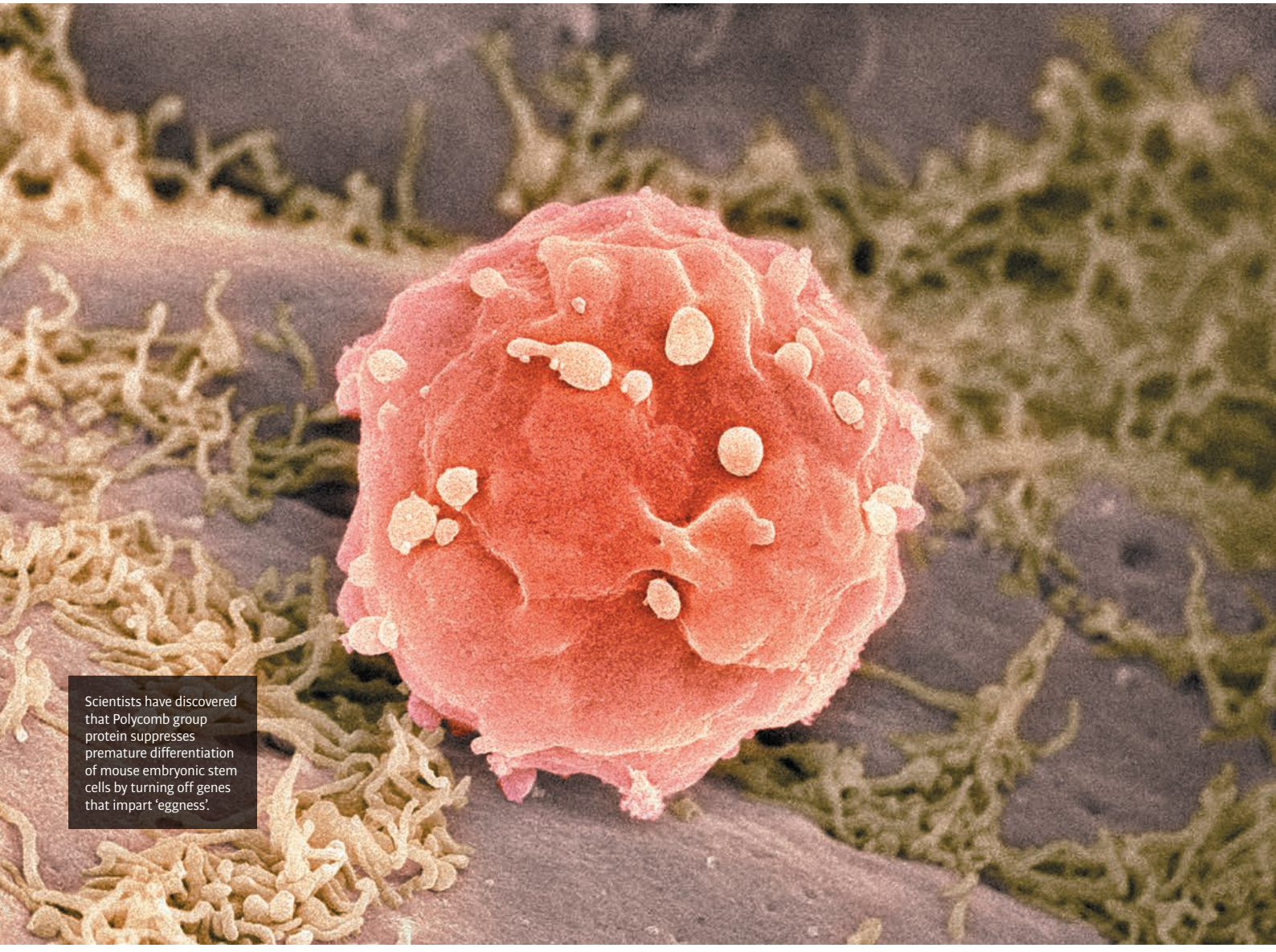
Their results provide strong additional support for the self-assembly model of Golgi organization. They also demonstrate the power of using models to recreate dynamic biological processes that occur at a scale too tiny to observe with standard microscopes.

"Our simulation visualized membrane dynamics based on physical laws, helping us to image the details of the process and test hypothetical mechanisms," says Tachikawa. He and Mochizuki are now collaborating with cell biologists to conduct experiments that could validate their computational model.

Tachikawa also hopes to extend such modeling approaches to even more complex cellular systems, through collaborations with RIKEN's Interdisciplinary Theoretical Science and Interdisciplinary Theoretical and Mathematical Science programs. "We think there are lots of possibilities of updating cell biology using physical, mathematical and theoretical sciences," he says. ●

Reference

1. Tachikawa, M. & Mochizuki, A. Golgi apparatus self-organizes into the characteristic shape via postmitotic reassembly dynamics. *Proceedings of the National Academy of Sciences USA* **114,** 5177–5182 (2017).



Scientists have discovered that Polycomb group protein suppresses premature differentiation of mouse embryonic stem cells by turning off genes that impart 'eggness'.

BIOLOGY

How embryos stop being eggs

'Eggness' genes get switched off in early development

Egg cells are remarkably malleable on a molecular level. But after an egg is fertilized and becomes a single-celled zygote, its 'eggness' is nullified, as the genes that make an egg an egg are suddenly switched off. These genes only turn on again at a later gestation stage, when the embryo is ready to make its own primordial egg or sperm cells (collectively known as germ cells).

The molecular determinants of this on-again, off-again regulation of germ cell development have long befuddled biologists. Now, however, a team led by researchers at the RIKEN Center for Integrative Medical Sciences has identified the repressor of germ cell genes in mouse embryonic stem cells[1].

The same suppressing pathway is likely to be at play in early embryo development as well. As well as offering a crucial missing piece of the early development puzzle, the results have potential clinical applications. "The findings could contribute to a better understanding of the mechanisms underlying infertility, which may lead to new kinds of treatments," says Haruhiko Koseki, who led the research.

Koseki did not set out to investigate the regulation of germ cell genes. He was studying a

type of developmental gene silencer known as a Polycomb group protein, when he noticed that one such protein—PCGF6—and its associated complex bound to the gene-activating promoter region of germ cell-related genes in mouse embryonic stem cells, turning them off. In stem cells that lacked a working version of PCGF6, however, no such dialing down of gene expression occurred.

“Some women may have trouble conceiving because their egg cells fail to stop expressing their germ cell genes after fertilization.”

Koseki and his colleagues then worked out how this PCGF6-associated complex recruits another factor called RING1B to alter the way the DNA is coiled at these bound sites, which helps to explain why the genes were silenced.

While Polycomb-related complexes usually recognize their target genes in a fairly generic fashion, Koseki’s team documented how PCGF6 is specifically recruited to the germ cell genes by a pair of guide proteins that recognize particular stretches of DNA.

“This suggests Polycomb proteins may use several mechanisms to bind their targets,” says Koseki. If correct, that leaves much uncharted biology to explore.

Although the study was in mouse cells, Koseki suspects similar processes are at play in human embryonic stem cells and in human early embryos as well. Thus, some women may have trouble conceiving because their egg cells fail to stop expressing their germ cell genes after fertilization. ●

Reference

1. Endoh, M., Endo, T. A., Shinga, J., Hayashi, K., Farcas, A., Ma, K. W., Ito, S., Sharif, J., Endoh, T., Onaga, N. *et al.* PCGF6-PRC1 suppresses premature differentiation of mouse embryonic stem cells by regulating germ cell-related genes. *eLife* **6,** e21064 (2017).

BIOLOGY

No direct flights for memory retrieval

Retrieval of memories in mice requires making a ‘stopover’ at a brain region known as the subiculum

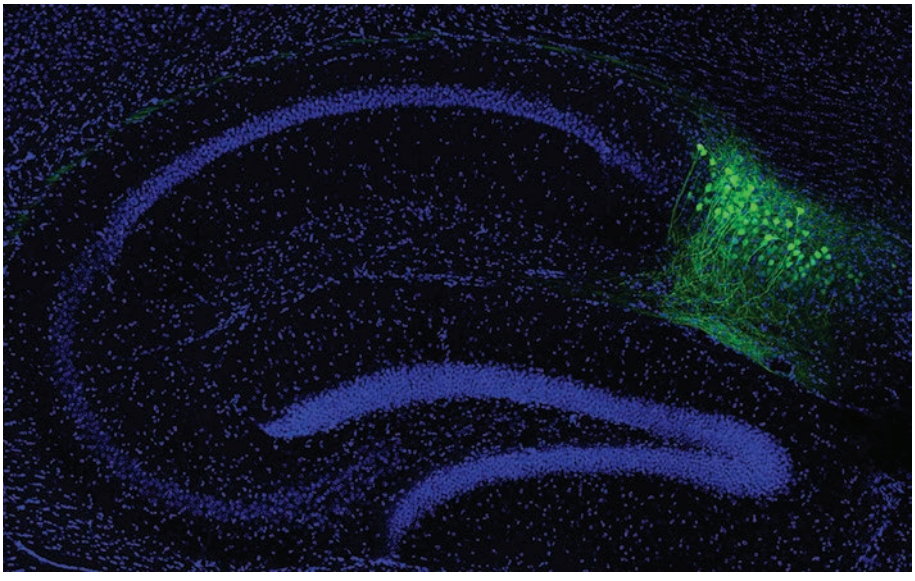
Experiencing something and remembering it later is not a neural ‘direct flight’, researchers at RIKEN have shown[1].

Memory formation in mammals appears to loop around the hippocampus, mirroring its physical structure: neural signaling from the entorhinal cortex proceeds through the central hippocampus to an area called CA1. From there, signals either take a direct flight to the deep entorhinal cortex or make a stopover at a region called the subiculum before proceeding to the entorhinal cortex or other brain regions. Until now, the exact function of the subiculum has been unclear.

A team of researchers led by Susumu Tonegawa, the director of the RIKEN–MIT Center for Neural Circuit Genetics (CNCG), has now investigated the role of the subiculum in mouse memory by genetically expressing fluorescent proteins only in these neurons (see image). They could then selectively turn the neurons on or off with optogenetics—targeted bursts of light that activate or deactivate tagged brain cells.

Turning the subiculum off during training had no effect on later recall. In contrast, mice that had learned to associate an environment with footshocks no longer froze when the subiculum cells were silenced during subsequent recall tests. These results indicate that the subiculum is essential for retrieving memories, but not for forming them.

Activating the subiculum during the memory test also affected memory recall—it seemed to enhance the fearful memory and cause mice to freeze more often. This newly discovered function contrasts with the direct connection from CA1 to



By genetically expressing fluorescent proteins only in neurons in the subiculum, researchers at the RIKEN–MIT Center for Neural Circuit Genetics have found that in mice the subiculum is needed for retrieving memories, but not for forming them.

the deep layers of the entorhinal cortex, which is essential for memory formation, but not retrieval.

Why are there separate pathways for forming and recalling memories? "Recall through the subiculum detour may allow memories that are important for triggering instinctual behaviors to be rapidly updated," says Dheeraj Roy, a post-doctoral associate at the CNCG. Although the two hippocampal pathways are largely subserved by the same neurons, only inhibiting the subiculum circuit before testing affected memory recall in the mice. Coordinated fear behaviors like freezing and increases in blood stress hormones may prepare animals to effectively encounter and respond to dangers.

"The subiculum is unique in that it has a bidirectional effect on memory recall, enhancing recall when activated and impairing recall when inhibited," notes Tonegawa.

This region of the brain sends outputs to many cortical and subcortical brain regions, and it is widely believed to be one of the areas earliest affected by Alzheimer's disease, making the subiculum an exciting target for memory research. ●

Reference

1. Roy, D. S., Kitamura, T., Okuyama, T., Ogawa, S. K., Sun, C., Obata, Y., Yoshiki, A. & Tonegawa, S. Distinct neural circuits for the formation and retrieval of episodic memories. *Cell* **170,** 1000–1012.e19 (2017).

MEDICINE

Making a mark on tumor cells

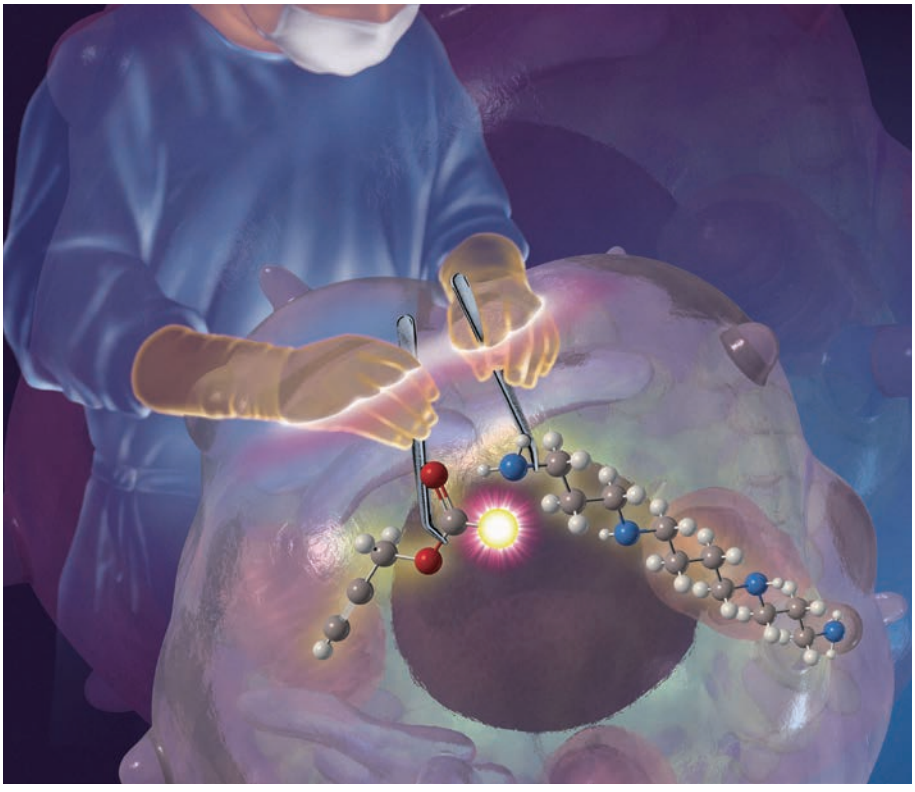
A selective chemical reaction that tags cancer cells could also facilitate precisely targeted treatments

One of the key challenges in fighting cancer is finding agents that attack tumor cells without causing collateral damage to adjacent healthy tissue. By building on a chemical strategy that labels a family of molecules involved in cell proliferation, RIKEN researchers have found a way to tag—and potentially kill—cells engaged in cancerous growth[1].

While studying a class of compounds called propargyl esters, Katsunori Tanaka, head of the RIKEN Biofunctional Synthetic Chemistry Laboratory, found that they exhibited a surprisingly strong propensity to attach to cellular biomolecules known as polyamines. Scientists are interested in polyamines because they appear to play a prominent role in driving cell division, although their specific mode of action is poorly understood.

"Polyamines are present in higher concentrations near tumors," explains Tanaka. "Furthermore, previous studies have shown that cancer cell growth can be arrested by knocking out the genes responsible for the biosynthesis of polyamines."

Tanaka, Kenward Vong and colleagues investigated whether the reaction between propargyl esters and polyamines could be exploited to detect cancer cells. In



The ability to label propargyl esters with fluorescently tagged propargyl ester probes opens up new possibilities of imaging cancer cells. Researchers demonstrated this potential using breast cancer cells.

preliminary tests, they demonstrated that a fluorescently tagged version of their propargyl ester probe efficiently attached itself to various polyamines, achieving maximum labeling within a couple of hours. Importantly, the probe did not label other biomolecules containing similar chemical groups, such as the amino acid lysine—a critical feature for avoiding false-positive signals from healthy cells. "This degree of selectivity has never been seen in the literature before," notes Tanaka.

Next, the researchers engineered their fluorescent propargyl ester probe to make it both soluble in water and able to penetrate cell membranes. This probe consistently produced strong fluorescent signals in three different breast cancer cell lines, whereas no such labeling occurred in healthy breast and non-breast-derived cells. This is both in keeping with previous findings that breast cancer cells contain sharply elevated levels of polyamine compounds and it confirms that chemically related molecules remain unmodified in noncancerous cells.

> **"This degree of selectivity has never been seen in the literature before."**

This highly selective labeling could be useful both for research and diagnosis, and Tanaka and colleagues are now testing to see whether their probes work equally well in other cancers. If they do, he envisions powerful therapeutic possibilities for compounds based on propargyl ester. "There are possibilities to develop anticancer therapies that rely, for example, on sequestering polyamines," says Tanaka. "Due to the importance of polyamines in cancer cell growth and proliferation, there should be many avenues for our group to explore." ●

Reference

1. Vong, K. K. H., Tsubokura, K., Nakao, Y., Tanei, T., Noguchi, S., Kitazume, S., Taniguchi, N. & Tanaka, K. Cancer cell targeting driven by selective polyamine reactivity with glycine propargyl esters. *Chemical Communications* **53,** 8403–8406 (2017).

BIOLOGY

Navigating on the fly

Using a specially designed flight simulator, researchers have found that flies use two separate neural pathways when they navigate while flying

Two independent pathways in the fly brain that are integrated to allow successful navigation during flight have been identified by two RIKEN researchers[1].

Most animals rely on navigation to find food, shelter and mates. It often requires combining many types of information. "Animals can save time when searching for food if they keep track of their location using cues such as landmarks and heading directions," explains Hokto Kazama of the RIKEN Brain Science Institute.

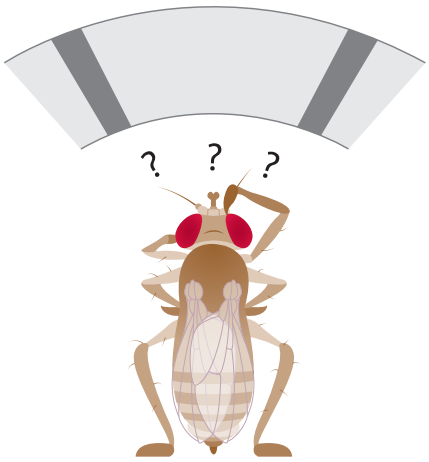
Kazama and co-worker Hiroshi Shiozaki want to know how this ability is accomplished in the brain. While past research has focused on mammals, the pair opted to work with the common fruit fly because, despite having a much simpler brain, it can zero in on fruit and avoid being squashed by irritated picnickers.

But how can fly brains be studied as flies navigate? "The big problem was that we needed to record brain activity in flies as they engaged in navigation," Shiozaki explains. "But this requires a head that is fixed in space, which obviously prevents natural navigation."

The pair designed a specialized flight simulator in which a fly watches a scene with its head fixed in place. When it flaps its wings, the scene rotates accordingly, allowing the fly to navigate through a virtual space. In this setup, flies exhibited cue combination—a hallmark of navigation in which animals decide where to orient themselves by combining information about visual landmarks with memories of landmarks present a few moments earlier.

The pair used two-photon calcium imaging to study the active brain as flies navigated in the flight simulator. This technique permits activity to be recorded from small individual compartments in the brain. It showed that the part of the fly brain called the bulb carried multiple types of information relevant for navigation.

Close examination revealed that within the bulb, different types of information were physically separated from each other. For example, one group of bulb neurons carried memories of landmark locations, while another carried information about the fly's ongoing steering maneuvers. "To our knowledge, this is the first example of neural activity reflecting a type of visual short-term memory that lasts for seconds in insects," notes Shiozaki.



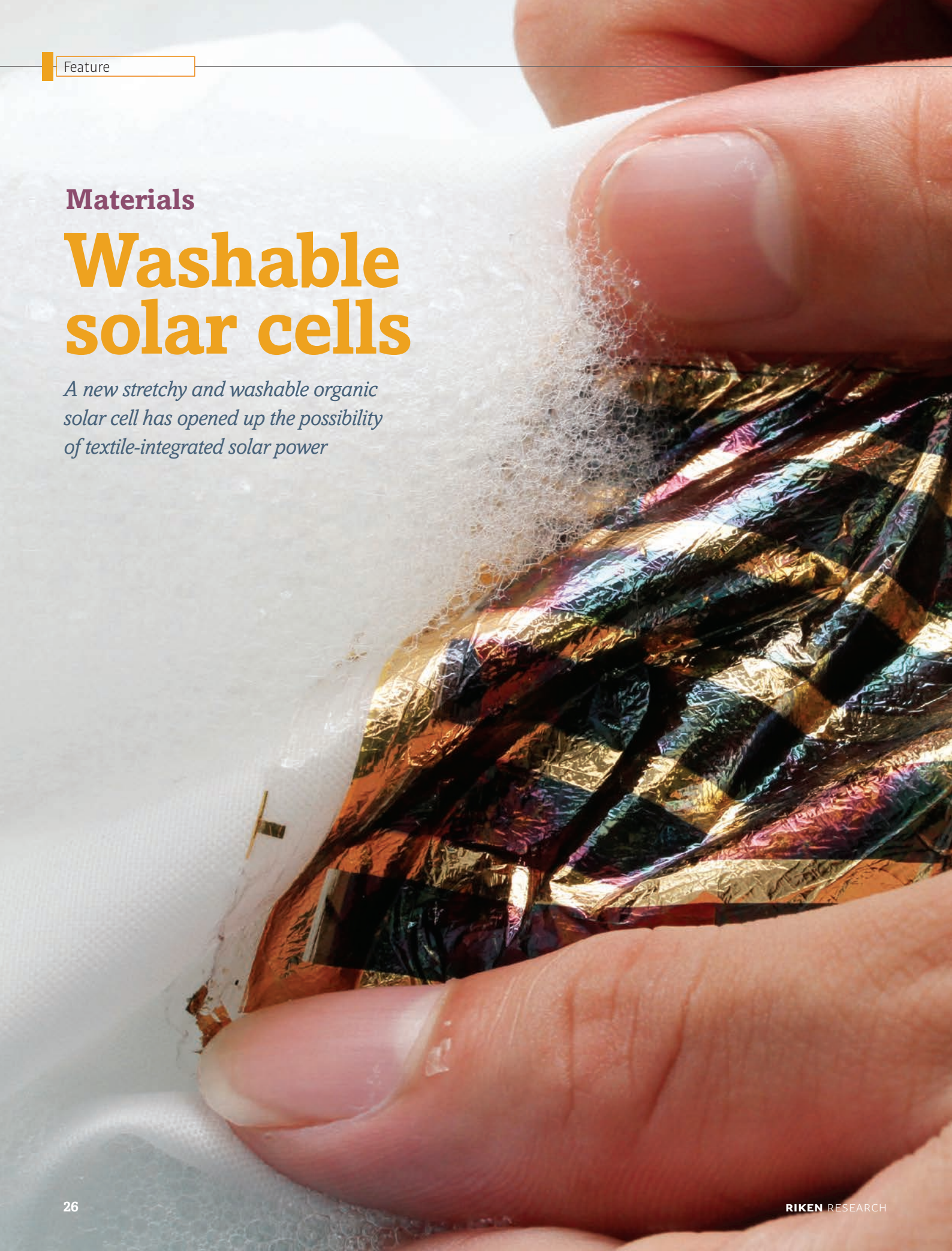
Using a specially designed flight simulator, RIKEN researchers investigated how flies navigate while flying.

The separate bulb regions are a part of two separate pathways that form independent neural circuits. This organization may ensure that many types of information can flow without interference, while minimizing space.

"Insects navigate the environment efficiently with economical brains," explains Shiozaki. "Understanding these biological principles will be useful not only for neuroscientists, but also for engineers and roboticists who are developing small navigating robots." ●

Reference

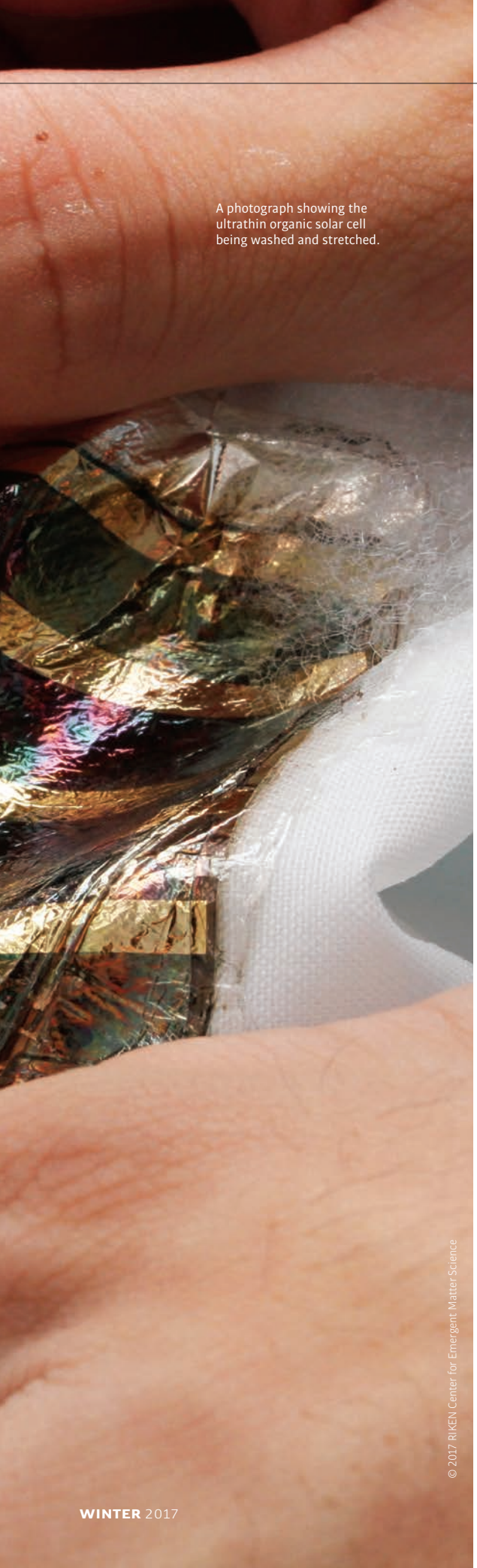
1. Shiozaki, H. M. & Kazama, H. Parallel encoding of recent visual experience and self-motion during navigation in *Drosophila*. *Nature Neuroscience* **20,** 1395–1403 (2017).



Materials

Washable solar cells

A new stretchy and washable organic solar cell has opened up the possibility of textile-integrated solar power



A photograph showing the ultrathin organic solar cell being washed and stretched.

Hard, flat solar panels are hardly something most people want to wear against their skin. However, flexible, washable solar cells are on the horizon thanks to a recent breakthrough by a team at RIKEN led by Takao Someya. The new organic, ultrathin photovoltaic cells can be stretched by half their length and withstand 20 simulated washing cycles. The possibilities are tantalizing. These properties mean the cells could, for example, be incorporated into textiles and Internet-of-Things devices (networked devices that can 'talk' to each other) to create electricity-generating clothing; power personal health monitors; and recharge mobile devices on the go.

An accordion in an elastomer sandwich

This is the first time that a single solar cell has combined a high energy efficiency, stretchability, and stability in air and water, explains lead researcher Kenjiro Fukuda from the Thin-Film Device Laboratory (Chief Scientist Laboratory) and the RIKEN Center for Emergent Matter Science (CEMS).

The work began, he says, when Kazuo Takimiya's group at CEMS developed the solar cell's ultrathin organic active layer, an organic photovoltaic (OPV). The layer converts sunlight into electricity at an efficiency of nearly 8 per cent, while also being very stable in air and water. Thicker OPVs can claim a peak conversion of 10 per cent—but for a photovoltaic material that is only 1 micrometer thick, 8 per cent is very high. And since the active material is very thin and based on an organic material, it can flex without breaking.

But the first solar cells produced with this active layer were not stretchable and were easily scratched. Fukuda's group solved these issues by placing stretched rubber-like elastomer films over the outside. "First, we pre-stretch the elastomer and fix the ultrathin solar cells gently," says Fukuda. "Next, the second elastomer is pre-stretched and attached, and we achieve this kind of sandwich structure." When the elastomer films were allowed to relax, the embedded solar cell folded itself into an accordion-like structure with troughs and peaks.

This folded structure gives the cell its stretchability—when it is pulled, the folds flatten out, meaning the device can be extended up to half its length without damage.

The elastomer films also somewhat waterproofed the cells making them washable—something that the researchers tested by subjecting the cells to 20 cycles of mechanical compression while exposing them to water for one hour and 40 minutes. The cell's efficiency dropped by only 20 per cent after this process.

This feature looks at the work of Kenjiro Fukuda

Kenjiro Fukuda received his PhD from the Department of Applied Physics at the University of Tokyo in 2011. From 2011 to 2015, he worked at Yamagata University as an assistant professor before joining RIKEN, where he is a research scientist in the Thin-film Device Laboratory and Emergent Soft System Research Team at the Center for Emergent Matter Science. Since 2014, he has also been a PRESTO researcher of the Japan Science and Technology Agency. His research interests include organic transistor, and flexible and printed electronics.

> By combining these technologies with our solar cells, we could achieve some very smart sensor clothes systems.

Stretchy batteries needed

The hope is that these solar cells could power electronic devices such as sensors to measure a wearer's heart rate, body temperature, blood pressure and other important medical parameters. They could also allow doctors to more easily monitor an out-patient's condition as well as enable athletes to continually measure their performance. "Recently, smart sensors that monitor the heartbeat, pressure or electrodermal activity, have been attracting attention," says Fukuda. "So there are now a lot of textiles with sensors embedded. By combining these technologies with our solar cells, we could achieve some very smart sensor clothes systems."

In the future, if sufficiently high voltages and currents can be realized, solar cells in clothing could also be used to recharge mobile devices and may even be able to supply household electricity, meaning things like OPV awnings could be used in, for example, developing regions.

And if the solar cells could be combined with thin, lightweight batteries, their usefulness could be enhanced even further. "We need a very thin or stretchable battery system, but this very difficult to realize," says Fukuda. "Batteries need some thickness to store a lot of power." But he adds: "If we can find a suitable collaborator, we could realize good synergy between our team and a battery research group."

Commercializing the technology

Currently, OPV models cannot compete against traditional inorganic solar cells for longevity and therefore price. Rooftop models target lifetimes of 20 years, while organic photovoltaic cells are targeting lifetimes of less than 10 years for glass-based products and less than five years for flexible products. German researchers Ning Li and Christoph J. Brabec noted this in a commentary piece on RIKEN's OPVs for *Nature Energy*.

But Brabec, who is from the Department of Material Science at Germany's Friedrich-Alexander University Erlangen-Nürnberg, says: "We got excited about [Someya and Fukuda's] work as it fits excellently into what we suggest as the roadmap for OPVs….[We] believe that OPVs should concentrate on integrated applications."

"Integration into bags, glasses, etc. has been around for quite some time, but integration into textiles hasn't been possible because OPVs couldn't be washed."

Fukuda says that real-world practical applications are probably three to five years down the track, but already there has been interest from companies in commercializing the technology.

The two main hurdles that will need to be overcome are the cost and size of the solar cells. The cells are currently limited to 10 centimeters by 10 centimeters and are fairly expensive to fabricate. But this is mostly down to the cost of the active layer, says Fukuda. The film coating, he says, is actually very thin and will ultimately reduce costs. "If companies commercialize this technology, they could develop a way to mass-produce the active layer material and reduce the cost."

"Many companies are interested in our technology and have contacted us recently," he says. "Collaborating with a company will accelerate commercialization."

Fukuda and his team are currently working on improving the cells' stability in air and stretchability.

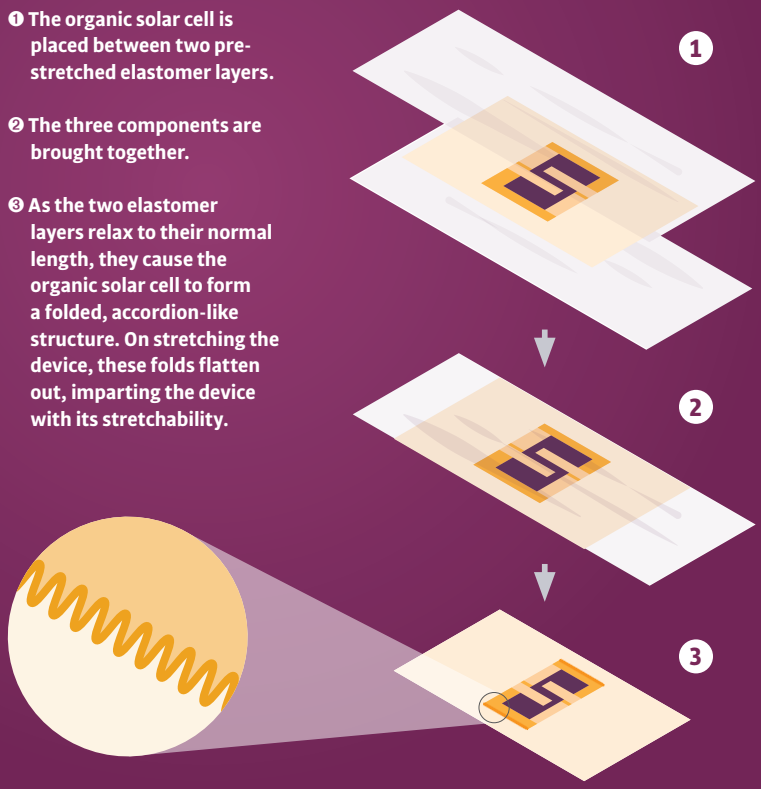
Making a solar cell stretchable

The secret to the solar cell's stretchability lies in its structure

❶ The organic solar cell is placed between two pre-stretched elastomer layers.

❷ The three components are brought together.

❸ As the two elastomer layers relax to their normal length, they cause the organic solar cell to form a folded, accordion-like structure. On stretching the device, these folds flatten out, imparting the device with its stretchability.



Reference

Jinno, H., Fukuda, K., Xu, X., Park, S., Suzuki, Y., Koizumi, M., Yokota, T., Osaka, I., Takimiya, K. & Someya, T. Stretchable and waterproof elastomer-coated organic photovoltaics for washable electronic textile applications. *Nature Energy* **2,** 780–785 (2017).

Reforms to confront a national crisis

RIKEN President Hiroshi Matsumoto has a plan to inject fresh life into Japanese science and technology.

Hiroshi Matsumoto, RIKEN President
Hiroshi Matsumoto has been president of RIKEN since 2015. He has a doctorate in engineering. His research centered on plasma in the geomagnetosphere and cosmosphere. He is an Honorary Officer of the Most Excellent Order of the British Empire (OBE) and a Chevalier in the French Legion of Honor and has twice been part of a group effort that received a NASA Group Achievement Award.

In March 2017, *Nature* published a Nature Index supplement focused on Japan. The front cover depicted a Japanese scientist in a dark room, with the headline 'Bright sparks needed'. The broad message of the supplement, which was widely covered in the news, was stark: Japanese science and technology, though still in the world's top tier, is slipping.

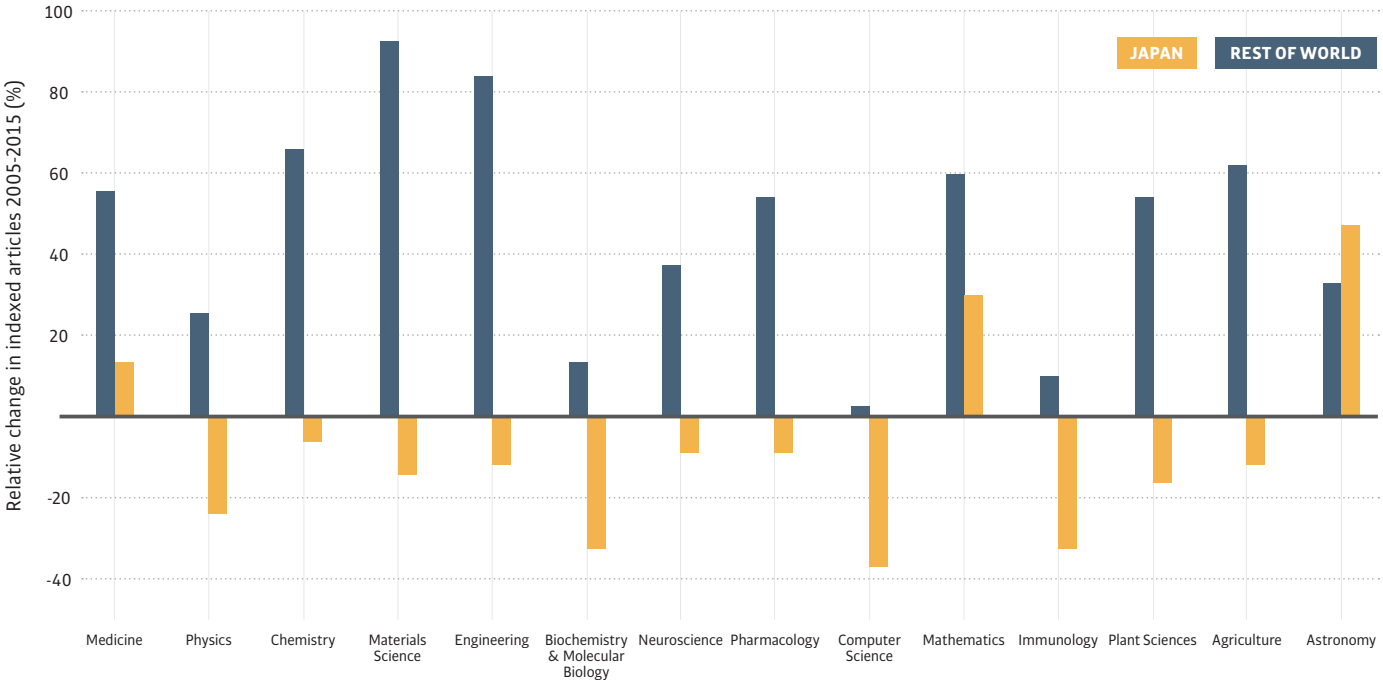
For RIKEN, this news comes at an opportune moment. We are preparing our next mid- to long-term plan, for the years 2018 to 2025, and this gives us a chance to put in place reforms that will allow us to play a pivotal role in overcoming this important crisis. I believe the key will be improving the quality of research in Japan, as well as the quality of Japanese researchers. To accomplish this, our reforms will be based around three major objectives.

The first is to develop RIKEN into a science and technology hub. Science in Japan is certainly not in a very robust position today. RIKEN is quite strong academically, with 28 per cent of our papers falling on the top 10 per cent most cited papers in their fields, but across Japan this number is only 8 per cent and that number is falling. While most universities do have individual academic stars, this low average across Japan is troubling. As RIKEN has outperformed the rest of Japan in this respect, it makes sense for us to take the lead in improving scientific research for everyone.

A successful hub will be able to help raise the overall standard of scientific research in Japan. While RIKEN cannot magically make all science in Japan strong again, we can act as a catalyst. At our Science and Technology Hub, for example, RIKEN will act as a focal point for research and will be able to help support

JAPAN VS THE WORLD

In 2017, *Nature Index* noted that while the number of publications indexed in the Web of Science has increased in all fields between 2005 and 2015, Japan has not kept pace with the rest of the world. In most fields, Japan produced fewer articles in 2015 than in 2005.



collaborations between universities and private companies. We hope that the collaborations established by the hub will lead funds to be funneled to top researchers across Japan, allowing them to make pioneering leaps in knowledge and innovation.

We already have a proven track record with this model. Within RIKEN itself, the main Wako campus has, in effect, functioned as the hub for a number of RIKEN's satellite sites around Japan. This has been quite successful, and we can use our experience to contribute to technological and scientific advances on a national level.

The second objective of our reform program is to develop what we call innovation designers. Typically, scientists focus their energy on the scientific tasks that interest them and are often not aware of all the applications that their work might have for society. I personally believe that scientists should be philosophers as well as researchers, and should always have a vision of the future that they wish to create as they carry out their research. So, of course, I encourage our researchers to have their own dreams and vision. But I also think it is important to have people within an organization like RIKEN who can re-examine the work of individual scientists and look for ways to harness useful advances.

> **"We want to hire exceptionally bright and creative individuals ... and offer them the chance to excel in scientific research."**

Translating our basic research into innovation is a key to improving our country's research trajectory. Although the Cluster for Industrial Partnerships at RIKEN works to commercialize our discoveries, its staff are very busy with existing partnerships. As a result, even though many companies know of RIKEN, most do not know how they can work with us.

Currently, we are planning to set up a company that will manage our intellectual property, similar to what has been established at other global research institutions such as Oxford, Cambridge and the Max Planck Society. Eventually, I hope we can re-visit some of the innovation strengths of the RIKEN Konzern—the highly successful network of research and subsidiary companies set up in the early 20th century, which at its peak generated more than half of RIKEN's income.

Our third objective is to reform the personnel system, which should help improve the quality of our research and of our researchers. At present, RIKEN's research personnel are mainly divided into two groups—those working in individual research centers and those working in laboratories run by our chief scientists. The chief-scientist system is unique to RIKEN; it allows laboratories to conduct pioneering research outside the confines of our mission-driven centers.

But there is also a large cultural

Source: Web of Science

difference between the two, in that many scientists in chief-scientist laboratories are tenured, while those at the mission-driven centers tend to be on 5- to 10-year fixed-term contracts. For young researchers in particular, this system creates a lack of stability that may hinder their ability to focus on research and deter international researchers from feeling able to take up positions at RIKEN. It is also a terrible waste in that good researchers often leave RIKEN when a center is abolished because they are not tenured. The rise in fixed-term contracts is often discussed as a broad issue hindering Japan's science and technology research communities, so this problem is not limited to RIKEN.

To redress this, we are now implementing a system under which researchers who have been at RIKEN for some time will be able to apply for tenure, regardless of whether they are at a center or an independent laboratory. Under the new system, someone with this status will be a type of RIKEN employee that has to accept an assignment given to them even if it is in a field of research different from their initial area of study or a position such as a research administrator. In this way, we will set up a system that can hold on to high-quality scientists as the organization changes. One of our presidents, Minoru Oda, compared RIKEN to an amoeba, which could expand amorphously to incorporate new fields. I think this is an interesting idea, but this is only possible when we have outstanding scientists who are able to adapt.

We have also launched a new program for young researchers, called the Hakubi program. A concept taken from China's Three Kingdoms period (220–280 CE), *hakubi* refers to an excellent person. The program is about taking risks. We want to hire exceptionally bright and creative individuals in science-related fields and offer them the chance to excel in scientific research. In particular, we want to give strong consideration to people who can bridge the gap between the natural sciences and the humanities.

We are also planning the launch of a new engineering network. Although RIKEN was once heavily devoted to engineering, these days the field only finds a place in a few laboratories. But engineering is very important. The world economy has shifted toward areas such as information technology and finance, where Japan is relatively weak. We need to take the time to rebuild our manufacturing power. So we will bring the remnants of our engineering division together as a network, and once again do research to bolster this area.

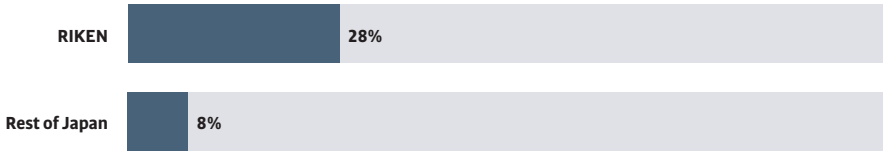
Another major change in our next mid-term period involves shifts to adjust to our new status as a Designated National Research and Development Institute. This will mean that RIKEN's plans and projects will mostly run for seven-year periods rather than five. We will be reorganizing some of our centers under the new plan. We will keep *RIKEN Research* readers up to date when more information becomes available. ●

PLANS TO WORK CLOSELY WITH INDUSTRY

Academically, RIKEN is still well placed to act as a catalyst to raise the standard of research across Japan. RIKEN also has a long history of working with industry to generate funds. Part of RIKEN's plan between 2018 and 2025 is to revive the spirit that saw industry funds help shape RIKEN, and to act as a hub for industry collaborations with Japanese universities.

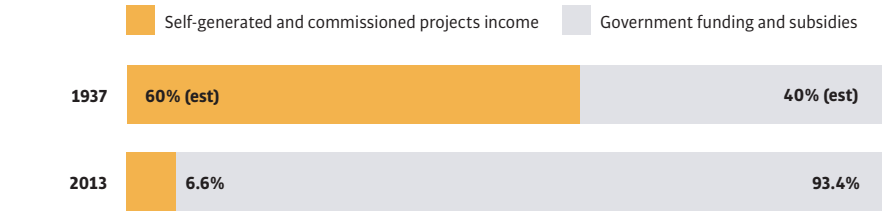
ACADEMIC STRENGTH

RIKEN's proportion of the world's most commonly cited papers remains strong



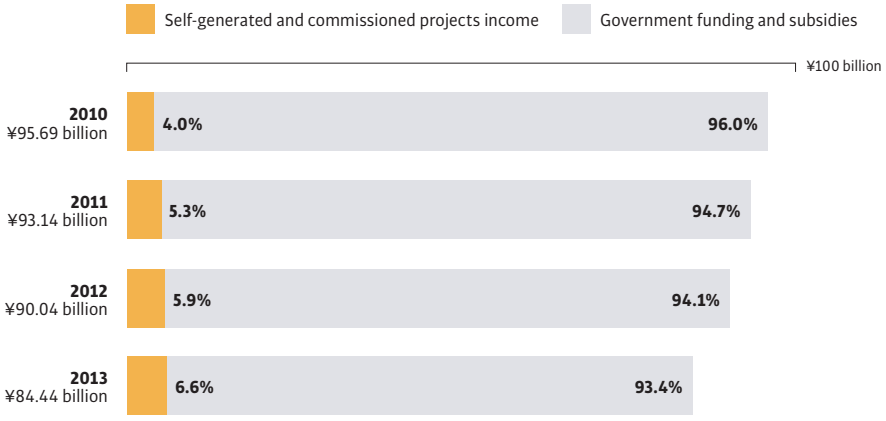
NON-GOVERNMENT INCOME – THEN AND NOW

RIKEN has a history of generating significant non-government funds



NON-GOVERNMENT FUNDS BOLSTERING RIKEN'S INCOME

As government funds have declined RIKEN's industry income has proportionally increased



Source: RIKEN Annual Reports 2009-2014

Programs for young scientists

RIKEN provides exciting opportunities for young scientists from all over the world during the crucial early years of their careers. The Special Postdoctoral Researcher Program offers young scientists funding for an autonomous research project under the direction of a RIKEN laboratory head. RIKEN also accepts non-Japanese PhD candidates as International Program Associates through collaborations with partner universities.

International Program Associate (IPA)

QUALIFICATIONS: Non-Japanese doctoral students enrolled at universities that have (or are expected to have) a Joint Graduate Program agreement with RIKEN.

FIELDS: All areas related to research being done at RIKEN in mathematical science, physics, chemistry, biology, medical science and engineering.

SUPPORT: Living allowance: ¥5,200/day; free on-campus housing or housing allowance of up to ¥70,000/month for off-campus housing; and one round-trip travel fare to and from RIKEN.

DURATION: IPAs are hosted at RIKEN for 1–3 years. The duration for each IPA is decided between the candidate, RIKEN and the university supervisors. IPA status is similar to that of internship students, but IPAs are not employed by RIKEN.

APPLICATIONS: Internal calls for applications are made in spring and autumn, which is when a RIKEN researcher can apply to host a student. Students should start by contacting the RIKEN researcher they would like to work with.

DETAILS: Contact *ipa-info@riken.jp* or go to *http://www.riken.jp/careers/programs/ipa/*

Special Postdoctoral Researcher (SPDR)

QUALIFICATIONS: Applicants must have been awarded a PhD within five years of application, or expect to be awarded a PhD by the date of hire.

FIELDS: All areas related to research being done at RIKEN in mathematical science, physics, chemistry, biology, medical science and engineering.

FUNDS, SALARY AND BENEFITS: Annual research budget: ¥1,000,000; Monthly salary: ¥487,000; and a commuting and housing allowance.

DURATION: The contract can be renewed annually up to 3 years from the date of hire.

APPLICATIONS: Calls for applications begin each February. All candidates will go through an application and interview process and be assessed by scientists working in relevant fields.

DETAILS: Contact *wakate@riken.jp* or go to *http://www.riken.jp/en/careers/programs/spdr*

RIKEN'S CENTERS AND FACILITIES

across Japan and around the world

Established in 1967
WAKO
(RIKEN Headquarters)
Center for Emergent Matter Science
Center for Advanced Photonics
Center for Sustainable Resource Science
Brain Science Institute
Nishina Center for Accelerator-Based Science
Advanced Center for Computing and Communication
Cluster for Industry Partnerships
Cluster for Science and Technology Hub
Chief Scientist Laboratories*
Research Groups
Global Research Cluster
Interdisciplinary Theoretical and Mathematical Sciences Program
*Chief Scientist Laboratories are located throughout Japan

Established in 1984
TSUKUBA
BioResource Center

SENDAI
Center for Advanced Photonics

Established in 2000
YOKOHAMA
Center for Sustainable Resource Science
Center for Integrative Medical Sciences
Center for Life Science Technologies
Distinguished Senior Scientist Laboratory

TOKYO
Tokyo Liaison Office
Center for Advanced Intelligence Project

NAGOYA

Established in 2002
KOBE
Center for Developmental Biology
Center for Life Science Technologies
Advanced Institute for Computational Science
Quantitative Biology Center

OSAKA
Quantitative Biology Center

Established in 1997
HARIMA
SPring-8 Center

Since relocating its original campus from central Tokyo to Wako on the city's outskirts in 1967, RIKEN has rapidly expanded its domestic and international network. RIKEN now supports five main research campuses in Japan and has set up a number of research facilities overseas. In addition to its facilities in the United States and the United Kingdom, RIKEN has joint research centers or laboratories in Germany, Russia, China, South Korea, India and Malaysia. To expand our network, RIKEN works closely with researchers who have returned to their home countries or moved to another institute, with help from RIKEN's liaison offices in Singapore and Beijing.

For more information, please visit:
www.riken.jp/en/research/labs/
www.riken.jp/en/outreach/research/

RIKEN
RESEARCH

www.riken.jp/en/research/rikenresearch

itaintmagic.riken.jp

www.facebook.com/RIKEN.english

www.riken.jp/en

@riken_en

www.twitter.com/riken_en

LinkedIn

www.linkedin.com/company/riken

RIKEN 2017-022