FALL 2017

RIKEN RESEARCH

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SELF-HEALING PLASTICS
The incredible potential of hydrogels

RODENTS IN VR
Plugging mice into the matrix

JUPITER'S AURORAS
How moon volcanoes fire them up

SIMPLE SOLUTION
Vinegar makes common crops more resistant to drought

RIKEN Center for Emergent Matter Science (CEMS)
An elastic conductor unveiled in May was developed in collaboration with CEMS (see page 31) and the RIKEN Thin-Film Device Laboratory. It can be printed on textiles as stretchable wiring for wearable devices.

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.

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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:

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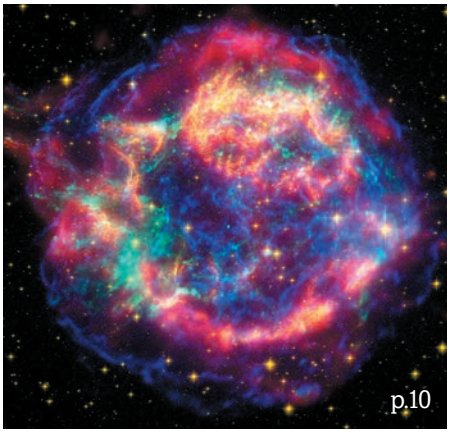

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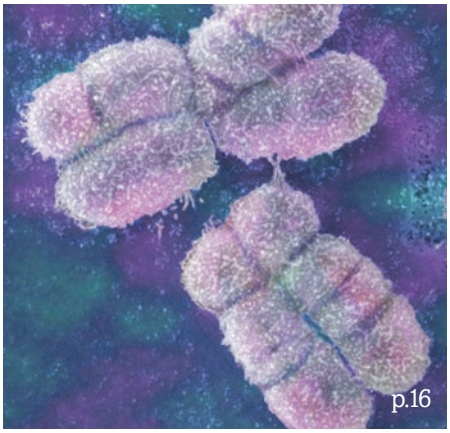

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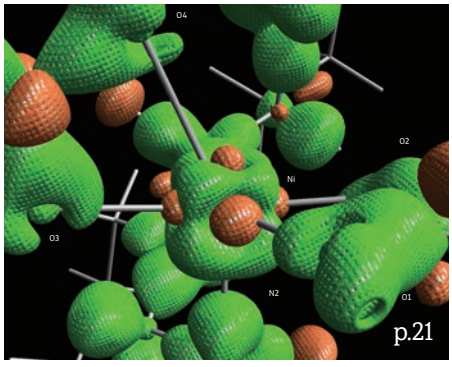

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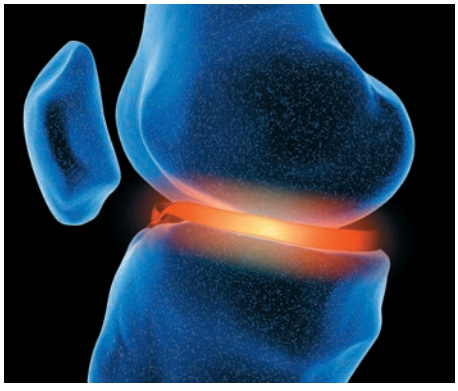

RIKEN's direction under the next mid- to long-term plan

Shuichiro Itakura
Executive Director, RIKEN

Since assuming my position as RIKEN's newest executive director in April this year, I have been focusing on the organization's management plan and general affairs. This year is a particularly important one for the institute since we will embark on a new seven-year plan next April and discussions regarding this matter are already underway.

One major topic in has been how we can strengthen our research in big data analysis and artificial intelligence in line with the goals of the government-led Science and Technology Basic Plan including to create a 'super smart society'—dubbed Society 5.0. Another key discussion point has been the need to reorganize our life science centers so that we can strategically tackle issues such as how to create a healthy society for the aged.

A major focus will be efforts to pioneer new areas of science by encouraging interdisciplinary research. And, of course, we will continue to maintain and improve our world-leading infrastructure centers including SPring-8, the K computer and the RI Beam Factory, which we make available to researchers around the world.

Of significance will also be the adoption of cutting-edge technology so that we can lead the way in all areas, as mandated by our new status as a Designated National Research and Development Institute.

For researchers, we will be working to provide increased career stability with the adoption of a system of indefinite-term employment. As always, we hope to continue to actively recruit young researchers from Japan and abroad, to develop RIKEN into a science-and-technology hub, and to strengthen our links with the private sector with these initiatives.

All of these efforts will go hand in hand with the current work that President Matsumoto announced under the RIKEN Initiative for Scientific Excellence. We will continue to flesh out our plan in anticipation of the first quarter of next year, when we will take our first steps into our second century of existence.

Cover story: Simply adding vinegar to the soil makes common crops such as maize, rice and wheat more drought resistant. **Page 22**

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Peering into blood vessel formation

Li-Kun Phng

Team Leader

Laboratory for Vascular Morphogenesis
RIKEN Center for Developmental Biology (CDB)

Please describe your role at RIKEN.
I joined CDB as a team leader in October 2016 and am still in the process of hiring scientists and setting up a zebrafish study facility for my research.

What is your current research focus?
I'm primarily interested in understanding how the cells that line blood vessels, known as endothelial cells, behave and how they coordinate to form new blood vessels. We employ genetics, pharmacology and advanced microscopy to investigate the fundamental principles of blood vessel formation using the zebrafish as our model organism. We use zebrafish because we can easily label their cellular and subcellular structures with fluorescent proteins and their embryos are optically transparent. These properties are useful as we use live imaging to help us visualize the dynamics of blood vessel formation.

What are the potential applications?
Excessive or abnormal blood vessel formation can cause diseases such as cancer metastasis, when cancer cells spread to different parts of the body through the vessels, and diabetic retinopathy, where excessive blood vessel formation in the retina can lead to blindness. I hope that my work on the basic mechanisms of vascular development will lead to a better understanding of vascular diseases, which will enhance treatments.

What excites you the most about your current research?
My research entails a substantial amount of live imaging and it's very exciting to be able to observe the dynamics of cellular processes first-hand, particularly when we observe new behaviors and phenomenon.

What do you think has been the most interesting discovery in your field in the last few years? How has it influenced your research?
There is a growing body of evidence on the importance of hemodynamic forces (i.e. blood flow and pressure) in regulating endothelial cell behavior and blood vessel formation. I was part of a recent discovery published in *Nature Cell Biology* that identified a new type of membrane protrusion—called inverse blebbing—at the apical membrane of endothelial cells. These inverse blebs drive the expansion of the lumen, which is a structure that allows blood to flow through the vessels. This process is therefore important in the formation of functional blood vessels.

> *I hope that my work on the basic mechanisms of vascular development will lead to a better understanding of vascular diseases.*

How has being at RIKEN helped your research?
I've had a lot of support from CDB to set up my lab. I am also glad that there is child support to help working parents—particularly the nearby affiliated childcare center where I send my daughter when I'm at work.

Please tell us about your professional and personal goals.
My long-term goal is to understand how upstream signals and hemodynamic forces regulate endothelial cell behavior to shape blood vessel architecture. To achieve this, I believe that interdisciplinary approaches are required, and I would like to forge collaborations with scientists from different backgrounds—such as physics and engineering—to understand the mechanics behind building blood vessels. ●

Home to nuclear families

Marco Rosenbusch

RIKEN Special Postdoctoral Researcher

SLOWRI team
Nishina Center for Accelerator-Based Science, Radioactive-Isotope Beam Factory

Please describe your role at RIKEN.
I experimentally study the physics of atomic nuclei. I mainly focus on very precisely measuring the masses of new short-lived isotopes and developing fresh ways to do this through high-precision mass spectrometry. Short-lived isotopes exist briefly after supernovae or other types of stellar explosions. They provide vital clues into how stellar explosions generated the elements found on Earth and other planets, among other things.

What is your current research focus?
The SLOW Radioactive Isotope (SLOWRI) team is developing a new facility at RIKEN. It will allow us to perform cutting-edge experiments on short-lived nuclei at low particle energies using RIKEN's Superconducting Ring Cyclotron in the Radioactive Isotope Beam Factory. Essentially, we're looking for ways to efficiently slow down charged ions so we can do high-precision experiments on them.

Why is your current research important?
There are still many surprises coming from short-lived nuclei, and understanding them adds to theoretical disciplines like nuclear astrophysics, particle physics, and the physics of fundamental interactions and natural constants. But pharmacy, cancer therapy and tumor tracing, and precision age verification, all benefit as well from ongoing developments.

How did you become interested in your current field of research?
While studying in Germany, I became interested in the physics of ion traps and started working with a group of experts in this field. I was then offered a master thesis placement at the ISOLDE Radioactive Ion Beam facility (located at the accelerator complex at CERN in Geneva) studying short-lived isotopes using precision mass measurements. What young physicist on the planet would decline such an offer? I spent the next six years there, during which I finished my PhD.

RIKEN is one of the best equipped science institutes in the world.

When did you join RIKEN and what did you first work on?
I joined RIKEN in May last year. The start was actually very tough, as the group was in the middle of a long series of experiments when I joined. We did many long shifts, but it was worth it because our results were fantastic, including the first direct mass measurements of synthetic mendelevium isotopes.

What has been your most interesting discovery in the last few years?
I'm excited by the fact that our experimental precision at RIKEN is fine enough to see if an atomic nucleus is in an excited quantum state or not. It was also amazing to be part of the first use of multi-reflection time-of-flight mass spectrometers for short-lived nuclei, which helps us to study isotopes with previously unreached lifetimes.

What are some technologies you use for your research?
RIKEN is one of the best equipped science institutes in the world. Most important for my work are fast oscilloscopes and frequency generators as well as access to precision machining and fast-ion detectors.

What is the best thing about working at RIKEN?
One of the best things about RIKEN is life on campus. The meals are very reasonably priced and provide important recovery time with colleagues, enabling fruitful discussions about work and on new ideas. ●

Careers at RIKEN

For further information, visit our Careers page:
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Nowcasting accurate downpour warnings

New forecasting technology known as three-dimensional nowcasting could provide very precise advanced warning of dangerous rainfall up to 10 minutes before it occurs. Leading the team that developed the new system is Takemasa Miyoshi of the RIKEN Advanced Institute for Computational Science, who says that this technology could save lives. "Torrential rains can have tragic consequences, as they lead to flash floods or dangerous landslides in a matter of minutes."

Today, nowcasting—short-term weather forecasting done in real time—is usually conducted using dish-like parabolic radar antennas. These take 5–10 minutes to scan about 15 layers of the entire sky. If rain is detected in one part of the sky, later showers are predicted based on current weather conditions. The new system, which is part of an international effort, uses more complex phased-array radar, coupled with forecasting algorithms that were originally developed using the powerful K computer. These radars can scan the entire sky in 10–30 seconds, looking at about 100 angles with a range of 60 kilometers. Phased-array radars are currently being operated by the National Institute of Information and Communications Technology (NICT), Tokyo Metropolitan University and Osaka University.

To make this information widely available, the researchers are collaborating with a smartphone app designer. Currently, three-dimensional nowcasting forecasts covering Japan's Kansai area (Osaka, Kyoto and Kobe) are available online at **www.aics.riken.jp/en/topics/170324.html**, and the group hopes to expand this area in the future as more phased-array systems and computer resources become available.

Aging Research Project: brain and nerve aging

In April 2016, a research project to examine aging phenomena in terms of "the brain and nerves", "homeostasis via immune and other systems" and "metabolism", was started. In June, the annual meeting of this Aging Research Project, which is headed by Tadafumi Kato of the Brain Science Institute (BSI), was held at the Wako campus. It involved the project's 25 teams, hailing from 7 centers and institute laboratories. At the meeting, Aki Minoda from the Center for Life Science Technology (CLST) talked about single-cell transcriptome analysis of aged mice and human super-centenarians. Eiki Takahashi (BSI) and Shigeharu Wakana of the BioResource Center described managing aged-mice breeding environments and their comprehensive phenotyping system for their rodents. Yoshio Hirabayashi (BSI) introduced technology developments around new lipidomics. Shintaro Iwasaki of the RNA Systems Biochemistry Laboratory discussed single-cell ribosome profiling. In addition, a new joint research program on age-dependent mouse maternal factors and aging regulation in Drosophila was introduced by Hiroshi Hamada of the Center for Developmental Biology and Sa Kan Yoo from the Physiological Genetics Laboratory, respectively. Tadafumi Kato and Sidonia Fagarasan of the Center for Integrative Medical Sciences and Minoru Yoshida at the Center for Sustainable Resource Science head up three of the project's four overarching groups. In April, Piero Carninci (CLST) formed a fourth group focused on developing resources and technology.

www.riken.jp/en/research/labs/super_aging/

Street to commemorate nihonium's discovery

A new street is being created in Wako to commemorate the discovery of element 113 (nihonium) by Kosuke Morita's team at the RIKEN Nishina Center for Accelerator-Based Science. It will be a 1.1 kilometer path from the south exit of Wakoshi station to RIKEN's west gate, featuring plaques illustrating the elements from 1 (hydrogen) to 113.

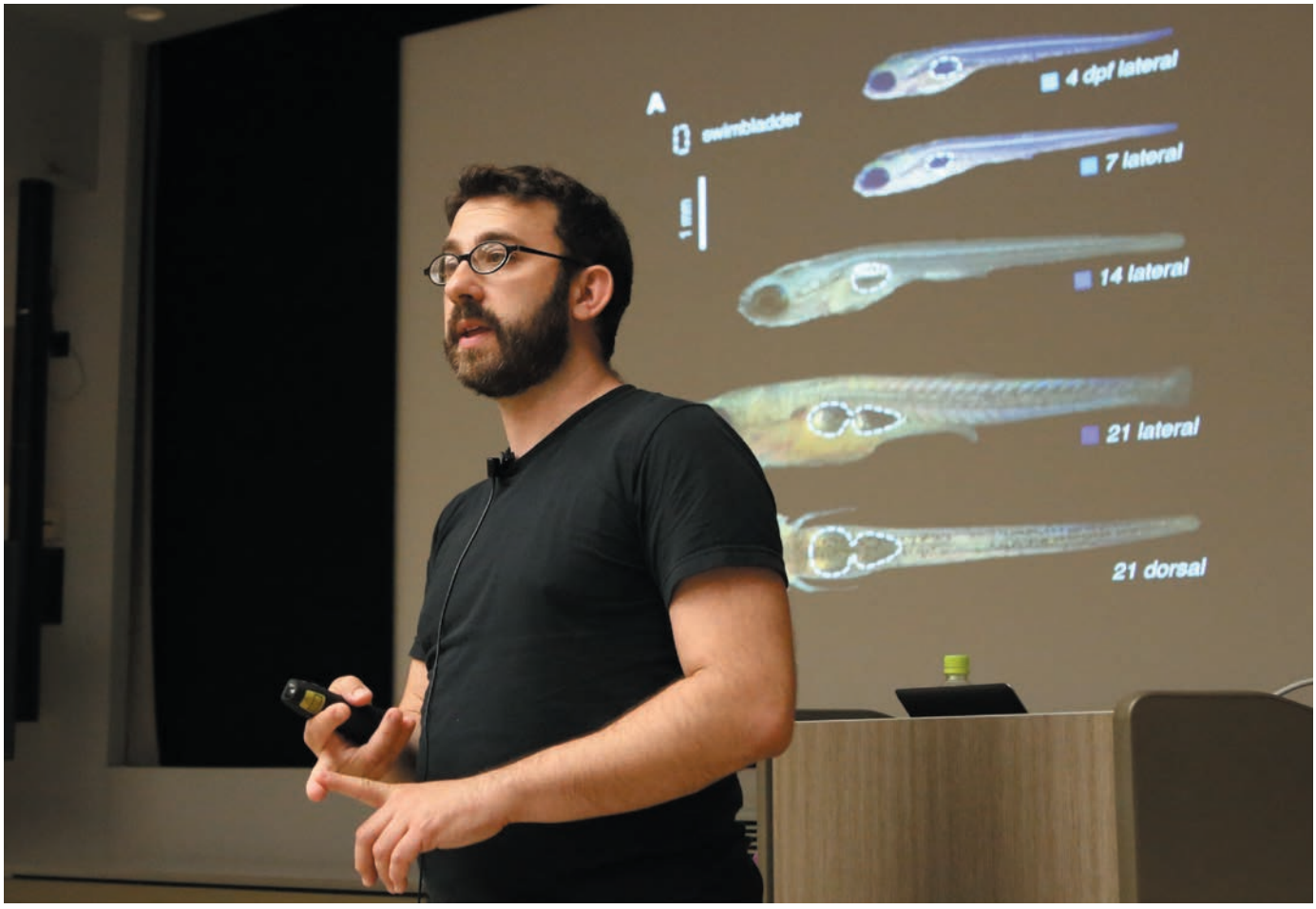
http://itaintmagic.riken.jp/whats-up-with-us/nihonium-street/

K computer tops HPCG benchmark

In June, the K computer took first place for the second consecutive time in the High Performance Conjugate Gradient (HPCG) benchmark—a new index developed to measure a supercomputer's ability to solve problems typically encountered in actual engineering and industrial applications. "The HPCG benchmark is very demanding," said the developer of the HPCG benchmark, Mike Heroux of Sandia National Laboratories. "A good score requires strong and versatile memory system performance, excellent interconnect network performance at scale and an overall balanced system." All 82,944 of the K computer's nodes were used in testing, achieving the world's top performance at roughly 603 teraflops (read more on the K computer on page 32).

www.riken.jp/en/pr/topics/2017/20170620_1/

Summer program attracts the best emerging minds in neuroscience



David Schoppik talks at the Brain Science Institute summer program about the spatiotemporal development of interneurons and motoneurons. He now leads a lab at New York University and was a participant of the program in 2003.

Some of the world's leading neuroscientists have helped their careers along by taking part in the RIKEN Brain Science Institute (BSI) summer program. These include one of this year's guest lecturers, David Schoppik of New York University—a participant in 2003. Schoppik's lab looks into how developing brains learn to balance. He gave a talk on the spatiotemporal development of interneurons and motoneurons. The program, which had 50 participants this year, offers the choice of a two-month internship at a BSI laboratory or an intensive one-week lecture course featuring distinguished international faculty.

Several current laboratory heads at BSI, including Tom McHugh and Josh Johansen, initially came into contact with the BSI through the summer program.

www.brain.riken.jp/en/summer/stories.html

Developments in lightweight kits for infectious diseases

In 2016, RIKEN signed a joint research agreement aimed at commercializing cutting-edge portable technology for diagnosing infectious diseases with a Russian manufacturer of medical devices, Eidos-Medicine, and a RIKEN venture company, DNAFORM. Eidos-Medicine is known for its production of educational medical simulators, which use virtual reality to teach practitioners. In April 2017, the parties agreed to accelerate technological development and formalized an agreement at Pashkov House in Moscow as part of the document exchange ceremony for the Japan–Russia Economic Cooperation.

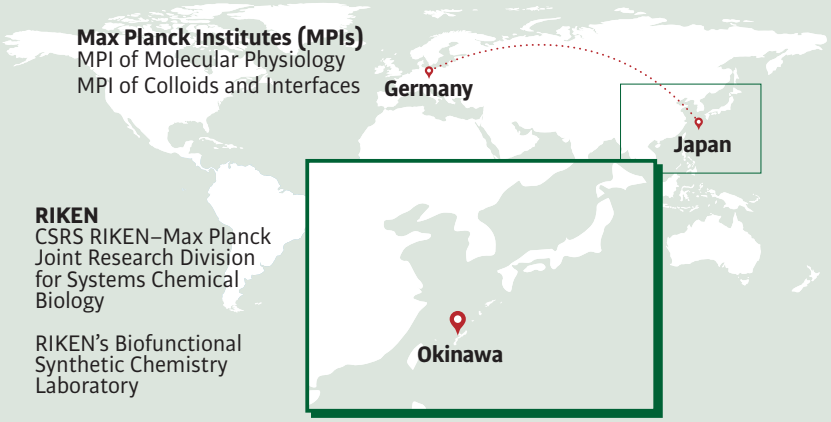
www.riken.jp/en/pr/topics/2017/20170602_1/

Ties tighten with national universities

RIKEN President Hiroshi Matsumoto signs an agreement with President Seiichi Matsuo of Nagoya University.

RIKEN President Hiroshi Matsumoto is strengthening RIKEN's ties with national universities. With this, he is reviving one of RIKEN's early mandates, which was to strengthen scientific research at Japan's universities. In March 2015, Matsumoto began by signing a collaboration agreement with Kyushu University. The agreement was designed to enhance innovation work between the two institutions. Kosuke Morita, whose team at RIKEN discovered element 113 last year, works across both institutions. In June 2016, Matsumoto also signed an agreement between RIKEN and Kyoto University to build more widely on existing joint work in fields such as iPS cells, glycobiology, drug discovery, photonics and plant science. Their collaboration on iPS cells resulted in the historic world-first eye transplant surgery using iPS (adult derived) stem cells earlier this year. In June this year, a comprehensive agreement was signed between RIKEN and Nagoya University promoting collaborations in basic plant science, crop science, natural compound science, synthetic chemistry and in basic infrastructures for manufacturing informatics. Many early RIKEN researchers held joint appointments and President Matsumoto bolstering this collaborative culture. In addition, in July, RIKEN signed a joint research agreement with the Japan Fisheries Research and Education Agency aimed at improving fishery technology and contributing to the United Nation's Sustainable Development Goals.

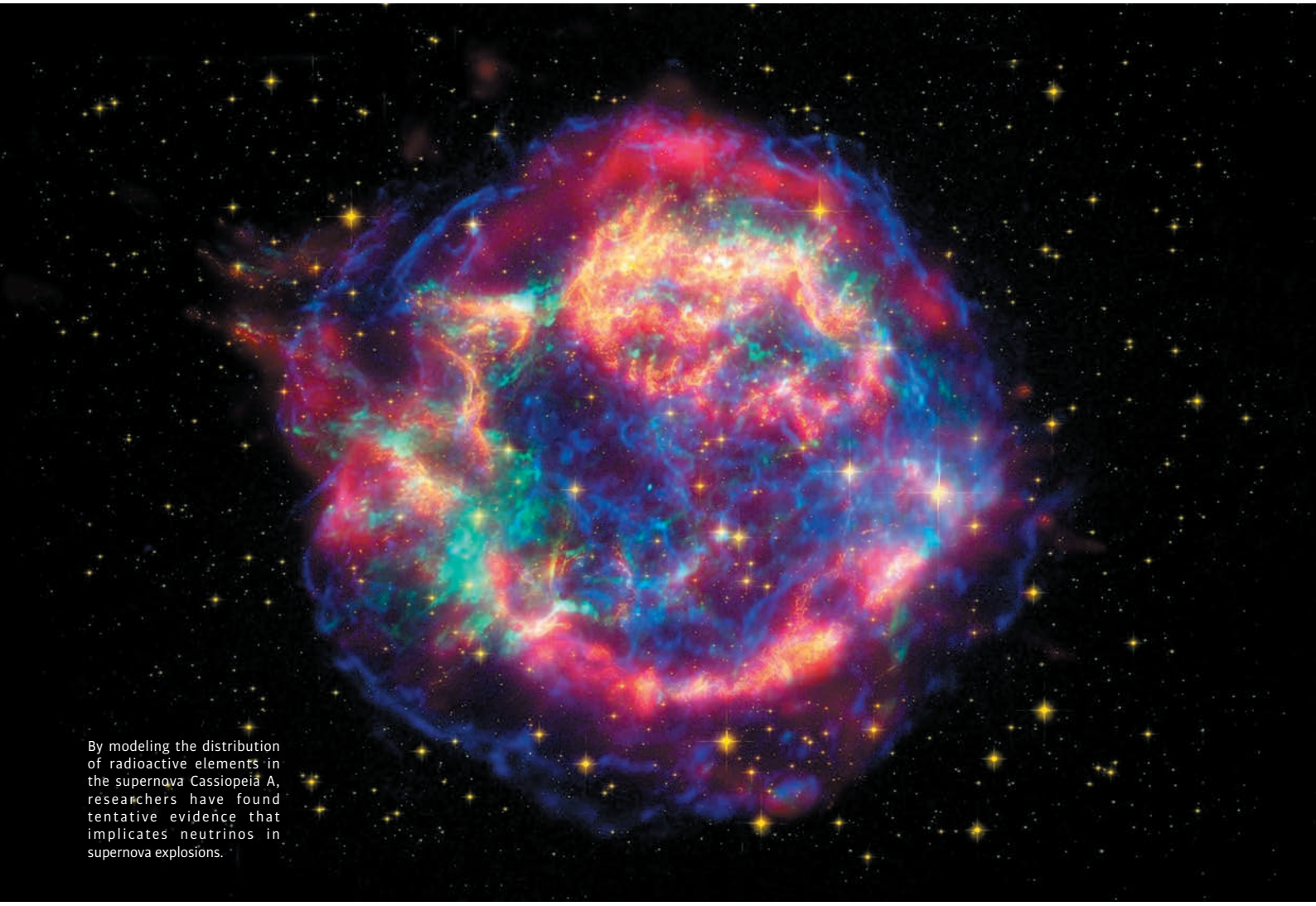
Symposium



Discussing new active ingredients

In 2011, the RIKEN–Max Planck Joint Research Center for Systems Chemical Biology was established to identify and study new active ingredients—for example, plants that could contribute to antimalarial drugs—and how these ingredients affect proteins. In April, roughly 50 scientists, including 15 from Germany, attended the sixth symposium of the group in Okinawa. At the symposium, Nobel laureate Tim Hunt discussed recent, groundbreaking results on the mechanisms of cell cycle regulation. The center has already attracted an impressive team of leaders who are driving its work. They include Director Herbert Waldmann of the Max Planck Institute for Molecular Physiology, Director Peter Seeberger of the Max Planck Institute for Colloids and Interfaces, Director Hiroyuki Osada of the RIKEN–Max Planck Joint Research Division for Systems Chemical Biology and RIKEN Chief Scientist Katsunori Tanaka.

www.riken.jp/en/pr/topics/2017/20170531_1/



By modeling the distribution of radioactive elements in the supernova Cassiopeia A, researchers have found tentative evidence that implicates neutrinos in supernova explosions.

PHYSICS

Neutrino clues hiding in Cassiopeia supernova

Tentative evidence indicates that supernova explosions are caused by neutrinos

Tackling a 50-year-old puzzle, astronomers have uncovered clues as to what causes a star to explode as a supernova by modeling the distribution of radioactive elements in Cassiopeia A (see image), a roughly 340-year-old gas remnant of a nearby supernova[1].

Over its multi-million-year life span, a star builds up a heavy central core of fused elements. When the core reaches about 1.5 times the mass of our Sun, it collapses under its own gravity and forms a neutron star. Enormous amounts of energy are released in the process, mostly in the form of neutrinos.

One hypothesis for what turns a star into a supernova involves massless neutrinos. According to the idea, a small fraction of the ejected neutrinos are absorbed in the surrounding gas causing violent motion, similar to a pot of boiling water on a stove. When the bubbling of the gas becomes sufficiently powerful, a supernova explosion is the metaphorical lid blowing off the pot. The outer layers of the dying star are expelled into space and new elements are created in the hot ejecta, among them radioactive species of titanium and nickel.

Because of the wild boiling of the neutrino-heated gas, the blast wave starts out non-spherical and imprints a large-scale asymmetry on the ejected stellar matter and the supernova as a whole. According to the theory, the production of heavy elements (including ^{44}Ti, ^{56}Ni and its decay product, iron) should be more efficient in directions where the explosion is stronger and where more matter is heated to high temperatures.

"This ability to reproduce the basic properties of the observations impressively confirms that Cassiopeia A may be the remnant of a neutrino-driven supernova."

Using elaborate computer simulations, a team of researchers from RIKEN in Japan and the Max Planck Institute for Astrophysics modeled expected spatial distributions of radioactive ^{44}Ti and ^{56}Ni in Cassiopeia A.

The computer simulation, viewed from a suitably chosen direction, exhibits a striking similarity to a recent observational image. Not only do the spatial distributions of titanium and iron resemble those in Cassiopeia A, the total amounts of these elements, their expansion velocities, and the velocity of the neutron star are in amazing agreement too. "This ability to reproduce the basic properties of the observations impressively confirms that Cassiopeia A may be the remnant of a neutrino-driven supernova with its violent gas motions around the nascent neutron star," concludes Hans-Thomas Janka from Max–Planck.

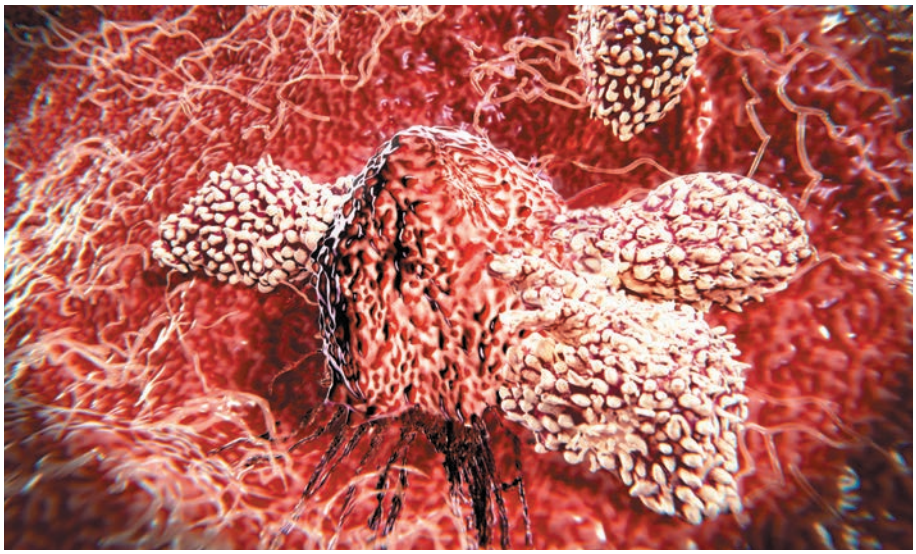
The team has now joined a bigger collaboration to test the theoretical predictions for neutrino-driven explosions by a close analysis of a larger sample of young supernova remnants. ●

Reference:
1. Wongwathanarat, A., Janka, H.-T., Müller, E., Pllumbi, E. & Wanajo, S. Production and distribution of ^{44}Ti and ^{56}Ni in a three-dimensional supernova model resembling Cassiopeia A. *The Astrophysical Journal* **842,** 13 (2017).

BIOLOGY

Natural born cancer killers

A better understanding of how natural killer T cells, which prevent tumors, develop could lead to more effective treatment



An artist's depiction of cytotoxic T-lymphocytes attacking a cancer cell.

New insights into the development of a group of immune cells that help defend the body against cancer have been gained by a RIKEN team[1]. The findings could pave the way for developing and improving therapies for fighting cancer that harness the body's immune system, known as immunotherapies.

Natural killer T (NKT) cells play important roles in a range of immune responses. A subset of these called invariant NKT (iNKT) cells is involved in tumor surveillance as well as in fighting allergy, asthma, autoimmune diseases and infectious diseases.

Immunologists subdivide iNKT cells into two populations according to the molecules they express on their surfaces: CD4$^+$ iNKT cells and CD4$^-$CD8$^-$ (or double-negative) iNKT cells. Previous studies in both mice and humans have shown that, unlike those that express CD4, double-negative iNKTs are important in combating pathogens and cancers. However, the drivers behind the functional differences between the two cell types have remained unclear.

T cells generally go through three steps as they differentiate into their subtypes in the thymus. As immature precursor cells they do not express CD4 or CD8 surface molecules or markers. As they develop, they express both surface markers before finally maturing into either CD4$^+$ or CD8$^+$ T cells. These three stages of T cell development are known as the double-negative, double-positive and single-positive stages.

Nyambayar Dashtsoodol, Masaru Taniguchi and colleagues at the RIKEN Center for Integrative Medical Sciences explored iNKT development using a technique called genetic fate mapping. To do this, they employed transgenic mice with a gene that expresses a yellow fluorescent protein when turned on during the double-positive stage.

While CD4$^+$ and CD8$^+$ T cells from the mice expressed the fluorescent protein, some mature double-negative iNKT cells did not, indicating that they developed without passing through the double-positive stage. The

CONTINUED ON PAGE 12

researchers confirmed this result by showing that double-negative iNKT cells could still develop even when the *Rag2* gene was knocked out during the double-positive stage.

"Our findings demonstrate that some NKT cells can bypass the double-positive stage," says Dashtsoodol. "This alternative development pathway could help to explain the uniqueness of a subset of NKT cells that have strong anti-tumor properties."

The team believes that the early expression of the T-cell receptor before the double-positive stage could play a key role in determining their later properties and functions.

Scientists are seeking to use the properties of NKT cells to develop cancer immunotherapies. Dashtsoodol and his colleagues anticipate that their findings will help the development of more effective therapies.

Reference

1. Dashtsoodol, N., Shigeura, T., Aihara, M., Ozawa, R., Kojo, S., Harada, M., Endo, T. A., Watanabe, T., Ohara, O. & Taniguchi, M. Alternative pathway for the development of $V_{\alpha}14^{+}$ NKT cells directly from $CD4^{-}CD8^{-}$ thymocytes that bypasses the $CD4^{+}CD8^{+}$ stage. *Nature Immunology* **18,** 274–282 (2017).

BIOLOGY

Stopping the brain's memory circuits from overheating

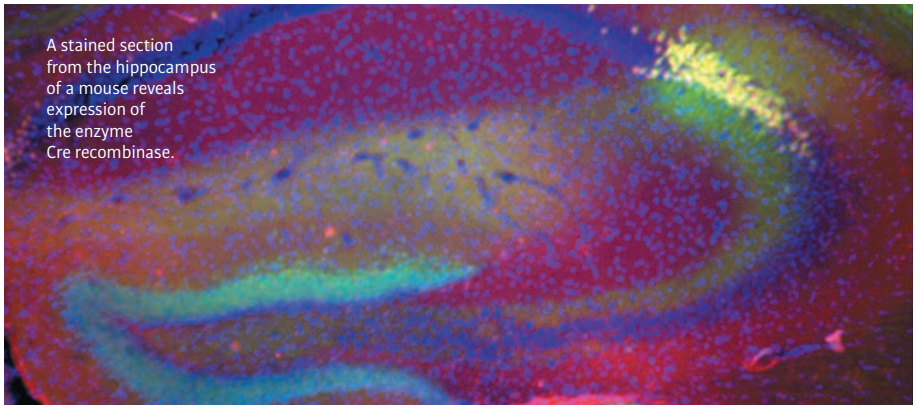
A region within the hippocampus is found to be critical in preventing overexcitation in the brain

The highly interconnected zones of the brain's hippocampus mediate spatial and episodic memory, but to keep memories organized they need the right balance of exciting and calming input. RIKEN researchers have found that a region of the hippocampus called CA2 is responsible for this regulation and that it prevents local brain circuits from becoming hyperactive[1]. In the absence of CA2 activity, mice exhibited epileptic-like brain activity, a sign that this area is essential for regulating the balance of excitation and inhibition in the brain. A silenced CA2 region has broader implications for information processing in hippocampal circuits.

Thomas McHugh at the RIKEN Brain Science Institute and colleagues studied mice that had temporary or permanent CA2 impairment and found that CA2 is responsible for maintaining inhibition throughout its connected network.

Investigating the connections from CA2 to its hippocampal neighbors CA1 and CA3, the researchers found that optogenetic stimulation there suppressed signaling in the network, especially in CA3. They further probed this inhibition by using a nerve toxin to shut down signaling from CA2, which resulted in a 'hyperexcitable' network state within CA3.

These observations were made in brain slices (see image), but the team reproduced and extended them in mice. While exploring open areas and tracks, mice with silenced CA2 activity had higher local field potentials—the summed electric current from a larger group of neurons in the hippocampus.



A stained section from the hippocampus of a mouse reveals expression of the enzyme Cre recombinase.

> **"In resting or immobile mice, however, the researchers observed something quite different—short, frequent, large-amplitude voltage spikes, which were reminiscent of epileptic brain activity."**

McHugh's group had previously reported how this kind of brain wave activity organizes spatial coding in the hippocampus. This time they discovered that large increases in the power of slow-wave activity of 4–12 hertz, dubbed the theta band, along with bursts of high-frequency oscillations, were spatially triggered. "These episodes of hyperexcitability lasted one or two seconds and were tied to specific locations visited by the mice," says McHugh.

In resting or immobile mice, however, the researchers observed something quite different—short, frequent, large-amplitude voltage spikes, which were reminiscent of epileptic brain activity.

CA2 thus appears to be a vital part of controlling the spread of excitatory neural activity in the hippocampus, potentially preventing it from entering a state of pathological spiking. Further study is needed to determine how this affects navigation and memory in mice, however.

"The hippocampus encodes place, and we saw a subtle shift in the spatial organization of pyramidal cells spiking in the face of CA2 inhibition," explains McHugh. "We still need to explore how timing and strength of inputs in this degraded network manifests in these interesting changes." ●

Reference

1. Boehringer, R., Polygalov, D., Huang, A. J. Y., Middleton, S. J., Robert, V., Wintzer, M. E., Piskorowski, R. A., Chevaleyre, V. & McHugh, T. J. Chronic loss of CA2 transmission leads to hippocampal hyperexcitability. *Neuron* **94,** 642–655 (2017).

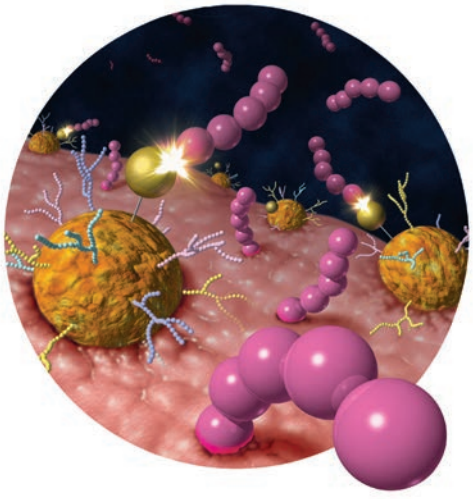
BIOLOGY

A golden opportunity for drug targeting

Tissue-targeting gold complexes could be used to activate drugs only at specific sites in the body

Gold complexes can be delivered to target organs in living mice, where they can speed chemical reactions for diagnostic or therapeutic purposes, show RIKEN researchers[1]. This paves the way for future clinical applications in humans.

"Our method enables various therapeutic molecules to be synthesized directly at the target organs in living organisms," says Katsunori Tanaka, chief scientist of the RIKEN Biofunctional Synthetic Chemistry Laboratory. This ability to synthesize diagnostic or therapeutic molecules exactly where they are needed can reduce the amount of compound needed and the risk of side effects.



Gold complexes can speed chemical reactions at targeted sites in the body.

Most previous demonstrations of metal-mediated reactions in biological systems involved human cells in a dish, while a few studies have been done in bacteria or developing fish embryos. But for the method to be developed for therapy, it is vital to show that it works with tissue specificity in mature mammals.

To achieve this, Tanaka's team linked a gold-ion catalyst via an intermediate locking system to a protein called albumin, which can be tagged with sugar molecules known as glycans. These sugary markers determine where the complex will go when it is injected into the body—attach one kind of glycan, and the complex will go to the liver; attach another, and it will head to the intestine.

The team injected their gold complexes into mice and then injected an imaging agent. The agent fluoresces only when gold complexes catalyze the formation of amide bonds between the imaging agent and proteins on the surface of organs. By imaging where the mice glowed, the researchers showed that their gold complexes arrived at the target organ, the liver or intestine, within just a couple of hours after injection. The same basic idea, Tanaka explains, could work with a drug instead of an imaging probe.

The researchers have also recently developed a way of engineering glycan complexes that include more than one type of sugar molecule[2]. This increased the precision of tissue targeting, explains Tanaka. "We can even target specific tumor cells out of many other tumor cells, which cannot be realized by other methods," he says.

Pharmaceutical companies have abandoned many once-promising drug candidates either because they showed toxic side effects in off-target tissues or because the drugs were too unstable be delivered intact to the desired organ. Using gold to activate drugs at their desired site "could re-optimize molecules that have been dropped during drug development," Tanaka says.

Tanaka's team is now trying to adapt the technique for use in rabbits and monkeys—and, soon, he hopes, in humans too. ●

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After a battery of tests, baby Grace was diagnosed with NGLY1 deficiency.

BIOLOGY

Serendipity helps in the fight against a genetic disorder

A surprise discovery has led to the development of a mouse model that can help scientists find treatments for human patients

A promising mouse model for a newly discovered genetic disorder known as *NGLY1* deficiency has been developed by RIKEN researchers[1]. These mice could be useful for testing potential therapies for people suffering from the debilitating condition.

NGLY1 deficiency was first identified in 2012 as a result of extensive tests conducted on two American patients including a baby called Grace (see image). It is characterized by severe symptoms including delayed development, disordered movement, low muscle tone and strength, and an inability to produce tears. Understanding how the lack of *NGLY1* leads to these symptoms is critical when considering targets for therapeutic interventions. It is thus vital to create useful animal models of the disease.

Led by Tadashi Suzuki from the RIKEN Global Research Cluster, the researchers examined the effects of knocking out *Ngly1* in mice. They found that mice lacking both *Ngly1* genes—one from each parent—always died just before birth.

However, knocking out both *Ngly1* and another gene called *Engase* resulted in mice that survived birth, although not for very long.

This positive result was unexpected. "We thought that ENGase acted further downstream to Ngly1," notes Suzuki. "We were surprised when the double knockout was able to suppress the lethality of *Ngly1*-knockout mice. If ENGase was merely an enzyme downstream of Ngly1, nothing should have happened. This was truly a case of serendipity."

Although the double-knockout mice survived, they shared some symptoms similar to those of people with *NGLY1* deficiency. As they aged, the mice developed characteristics such as bent spines, trembling, and limb clasping and shaking. Also, only 60 per cent of them survived to 45 weeks of age. These mice could thus be useful models to develop treatments for *NGLY1* deficiency in people.

The genetic background of the mice, namely the genotypes of all genes related to *Ngly1* and *Engase*, was also found to affect survival and symptoms. When mice were crossed with an outbred strain, the single *Ngly1* knockout was less lethal and the double knockout was even more helpful. This indicates that quite complex biological processes are involved. Despite this, however, it is clear that preventing ENGase activity can alleviate symptoms of *Ngly1* deficiency in mice.

"The next step will be to isolate an *in vivo* inhibitor for ENGase and determine whether it can improve the symptoms related to *NGLY1* deficiency," explains Suzuki. "As we do not know much about the pathophysiology of the disorder, this might help us find potential targets for therapy. It might also lead to a better understanding of other diseases. Such chains of unexpected results are the beauty of basic science!"

This study was partially supported by Hiroshi Mikitani, who is the CEO of the Japanese internet company Rakuten, and the Grace Science Foundation, which was established by Grace's parents, Matt and Kristen Wilsey.

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BIOLOGY

Antidepressants help autism mice

A common antidepressant administered to baby mice with autism-like symptoms improved their social interaction

A deficiency of the neurotransmitter serotonin in early development has been linked to several symptoms that occur in autism spectrum disorder (ASD) by RIKEN researchers[1]. They found that increasing serotonin activity in the brain during early development led to more balanced brain activity and improved the abnormal sociability of these mice.

"Although abnormalities in the serotonin system have been thought to be part of the pathophysiology in patents with ASD, the functional impact of serotonin deficiency in ASD was totally unknown," Toru Takumi of the RIKEN Brain Science Institute explains. "Our work shows that early serotonergic intervention rescues regional excitatory–inhibitory abnormalities in the brain as well as behavioral abnormalities."

Previously, Takumi's group had generated a mouse model of ASD by duplicating one of the most frequent genetic variations found in people with ASD. These mice show poor social interaction and low behavioral flexibility. The model mice also have reduced levels of serotonin in the brain during development, a symptom that has been found in human ASD patients.

Patients with ASD also often exhibit abnormal responses in sensory regions of the brain, and the RIKEN scientists found similar abnormalities in the brain region of the model mice that detects whisker movement. Although specific whisker movements are normally tightly mapped across this brain region, calcium imaging showed that a given whisker movement activated a much larger region of sensory cortex in the ASD model mice. Normally inactive neurons were somehow active, which pointed to reduced inhibitory activity.

To reduce the cortical excitatory–inhibitory balance, the researchers tried giving infant mice serotonin. Specifically, they administered a common class of antidepressants known as selective serotonin reuptake inhibitors (SSRI) to mice during the first three weeks after birth. Sensory neurons in the model mice treated with the inhibitors showed more normal inhibitory responses, which improved the excitatory–inhibitory balance.

The researchers also found this intervention improved the social behavior of the model mice in adulthood.

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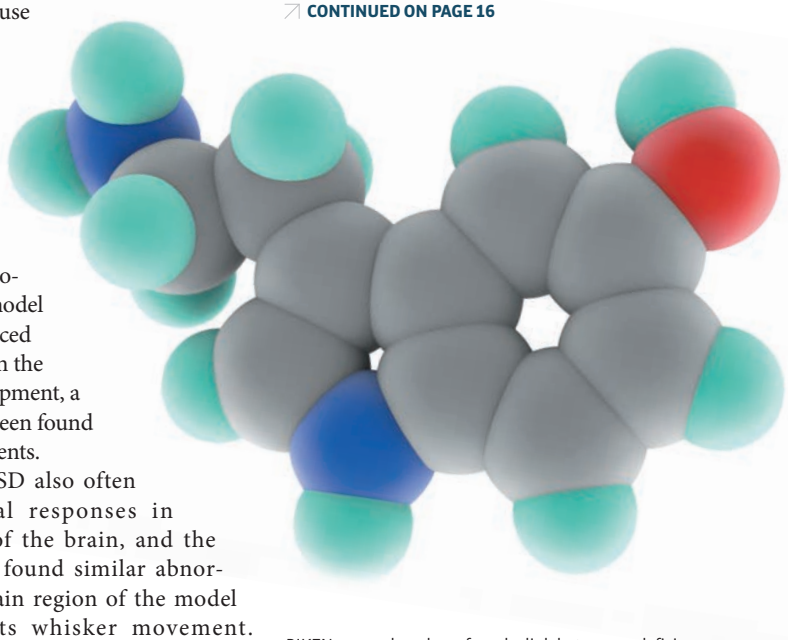

RIKEN researchers have found a link between a deficiency of the neurotransmitter serotonin in early development and several symptoms of autism.

Mice were exposed to a cage with an unknown mouse or an empty cage. Normal mice spent more time near the cage with the unknown mouse, whereas the ASD model mice preferred the empty cage. After SSRI treatment, ASD model mice spent more time around the cage with the unknown mouse, indicating more normal social behavior.

Another improvement was seen in the communication behavior of the ASD mouse pups. While ASD pups displayed anxiety through producing more vocalizations than normal, this behavior was rescued by the SSRI treatment.

These findings suggest that serotonin may be potentially therapeutic for discrete ASD symptoms. ●

Reference

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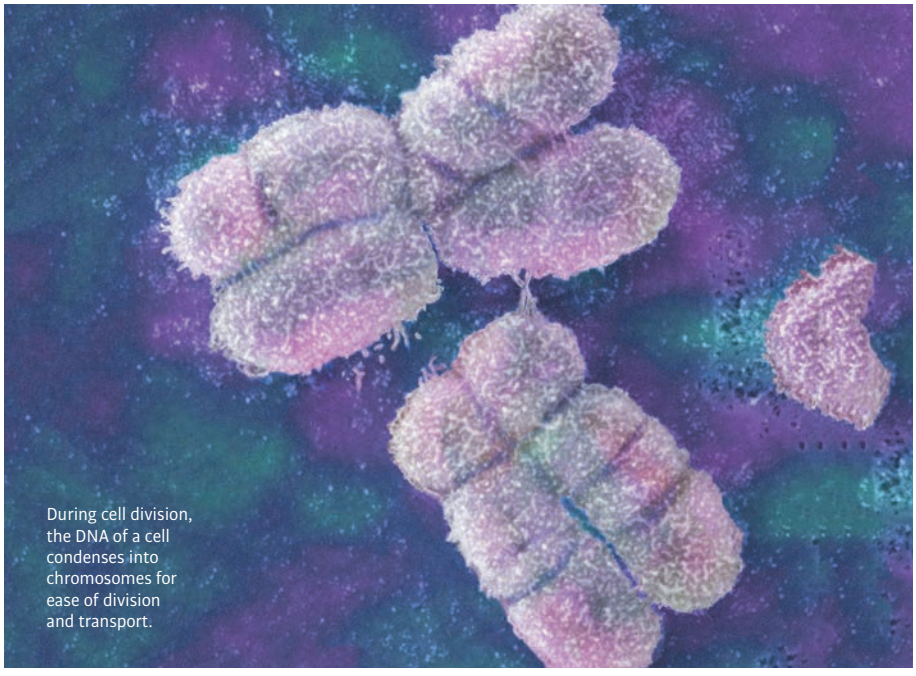
BIOLOGY

Making do with less

Fewer components are needed for chromosome assembly during cell division than previously supposed



During cell division, the DNA of a cell condenses into chromosomes for ease of division and transport.

In a discovery that could lead to the rewriting of biology textbooks, RIKEN researchers have found that tightly wound strands of DNA, known as chromosomes, can form even in the near absence of substructures that were thought to be essential for their production[1].

Before a cell divides to form two daughter cells, its DNA is packed into chromosomes (pictured above). But the exact mechanism for this process is still unknown. "It's one of the oldest and most fundamental problems in cell biology," says Tatsuya Hirano, who heads the Chromosome Dynamics Laboratory at RIKEN.

Textbooks on cell biology present a model in which chromosomes assemble in a hierarchy that starts from the assembly of 'beads-on-a-string' structures on DNA, known as nucleosomes. Two decades ago, Hirano discovered condensins—large protein complexes responsible for the higher-order folding of nucleosome fibers. It was thus thought that nucleosome assembly underlies higher-order chromosome assembly mediated by condensins.

To test this supposition, Hirano's team used a 'cell-free' experimental system in which chromosomes can be assembled by mixing sperm DNA with an extract prepared from frog eggs that contains all the ingredients to build chromosomes. "We simply mimicked fertilization in a test tube," says Hirano. In the current study, the team mixed mouse sperm DNA that lacks nucleosomes with an extract depleted of a protein needed for nucleosome assembly (called Asf1). In this way, just the nucleosome assembly step could be blocked, leaving the other steps intact, including those mediated by condensins.

> **"We were all very excited by that. It may require revising the standard textbook view."**

"We thought that we wouldn't see anything because many people, including us, believed that nucleosome assembly was a prerequisite for the large-scale organization of mitotic chromosomes," recalls Hirano.

To the team's great surprise, the experiment produced chromosomes, although they were somewhat diffuse and fragile. "We were all very excited by that. It may require revising the standard textbook view."

The team then tested the effect of depleting condensins while interfering with nucleosome

assembly. Simultaneous depletion of Asf1 and condensin I had no big effect, whereas depletion of Asf1 and condensin II together led to severe defects in the chromosomes' architecture. The condensin complexes are already known to act on DNA independently of the nucleosome, at least partially; the new findings hint at complex functional crosstalk between the different components involved in chromosome assembly.

Hirano hopes his lab will eventually unravel the biochemical and biophysical mechanisms of these interactions and how they drive chromosome assembly. "Because I was one of the discoverers of these protein complexes, I feel responsible for fully describing their activity or function," he comments. ●

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CHEMISTRY

Lasers pick up good vibrations

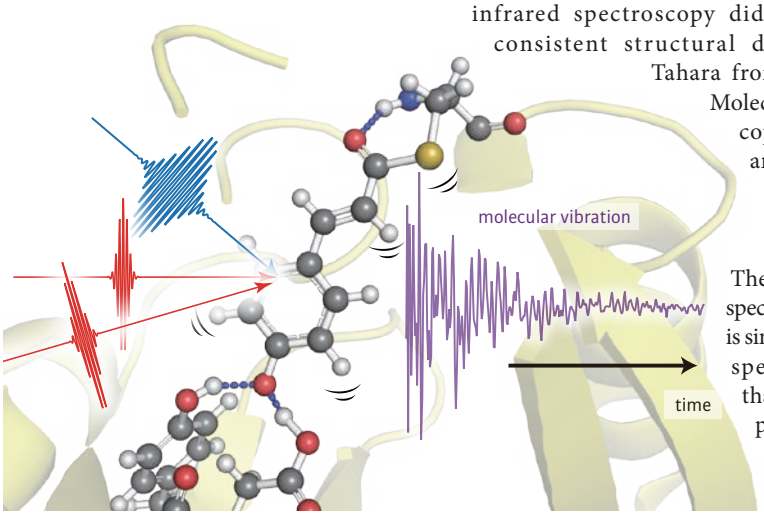
The changes to the structure of a light-sensing protein have been tracked over incredibly short time scales

Captured just a few quadrillionths of a second after it absorbed a photon, a light-absorbing protein has been observed for the first time using a newly developed ultrafast technique. This information will provide scientists with valuable clues about why some proteins are so sensitive to light.

Light-sensitive proteins form a key part of the sensory systems by which organisms detect light around them. For example, the aquatic light-harvesting bacterium *Halorhodospira halophila* detects blue light using the photoactive yellow protein (PYP). The organism swims away from blue wavelengths—a response thought to avoid exposure to harmful blue light.

Previous studies had shown that blue light triggers a structural twist known as *trans*-to-*cis* isomerization at the light-capturing heart of PYP. But this photon-triggered rearrangement of the protein occurs so rapidly that it has proved difficult to observe, generating contradictory results.

Since previous studies using x-rays and infrared spectroscopy did not provide consistent structural details, Tahei Tahara from the RIKEN Molecular Spectroscopy Laboratory and co-workers adopted a different approach. They used Raman spectroscopy, which is similar to infrared spectroscopy in that it uses laser pulses to probe the molecular vibrations of compounds, but employs visible light rather than longer wavelength infrared radiation.



Three light pulses were used to excite vibrations in photoactive yellow protein molecules.

The team used a Raman technique that they had developed called time-resolved impulsive stimulated Raman spectroscopy (TR-ISRS). "I believe TR-ISRS is one of the ultimate forms of Raman spectroscopy," Tahara says.

Using three precisely timed light pulses, the team could trigger photon uptake in the PYP molecules in a sample, synchronize their motion, and then monitor any changes in the protein's structure over the next few hundreds of femtoseconds (see image; one femtosecond is 10^{-15} second).

Most of PYP's vibrational signals remained steady over this time frame, showing that the protein does not flip from the *trans* to the *cis* conformational state until later in the process. But one vibrational signal dropped rapidly in intensity following photon absorption. The team showed this change relates to the rapid weakening of a hydrogen bond that normally anchors the protein's light-capturing portion, allowing PYP to flex during the subsequent isomerization.

"TR-ISRS is a very versatile vibrational spectroscopic method, having extremely high time resolution and sensitivity," Tahara says. "We would like to apply it to a wide range of problems, from studying fundamental molecules to understanding the mechanism of newly found photoresponsive proteins, as well as new materials. We have already started research in this direction," he adds. ●

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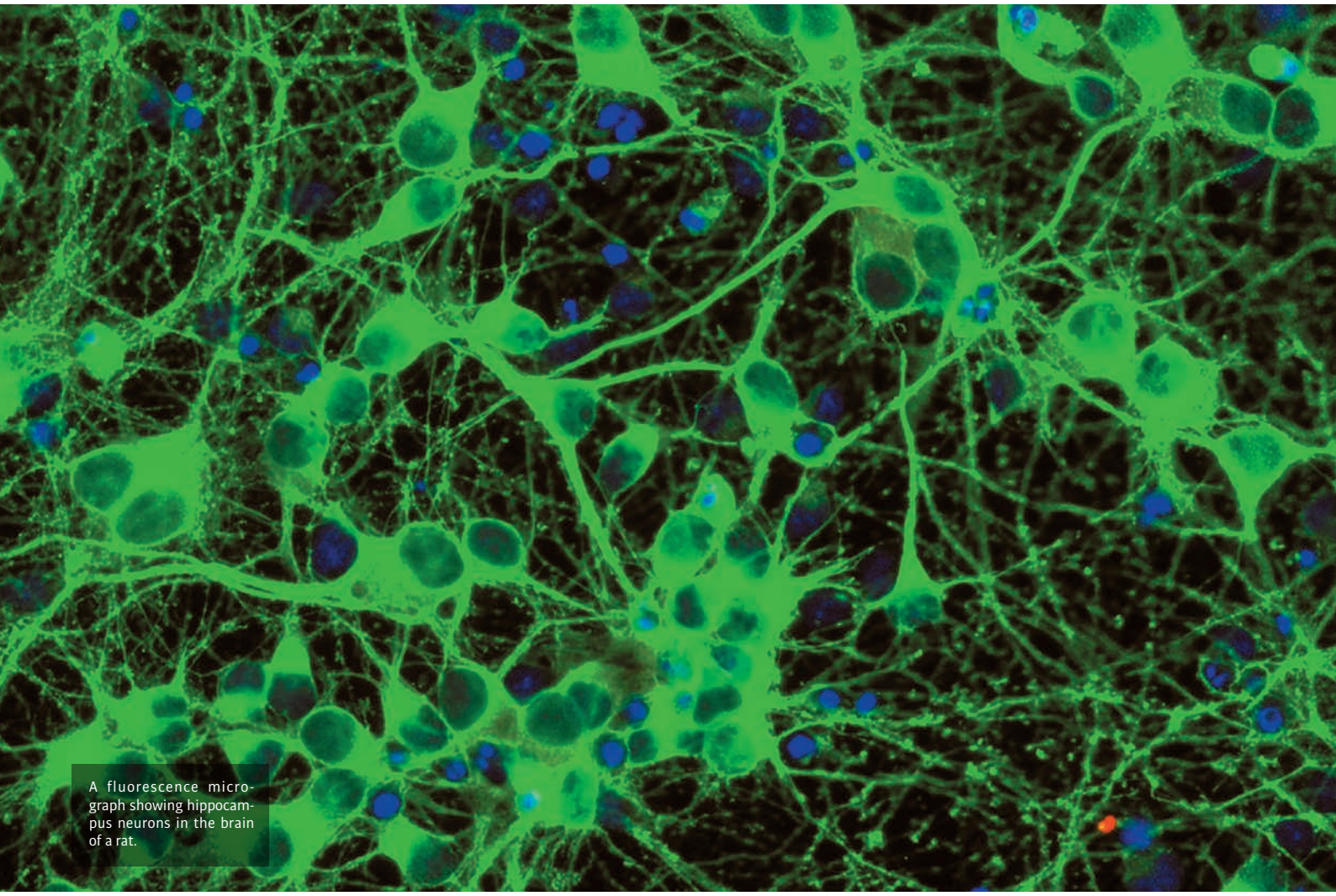

A fluorescence micrograph showing hippocampus neurons in the brain of a rat.

BIOLOGY

How are memories of events stored?

The brain's hippocampus can organize memories of events as well as places

A rat's hippocampus stores memories of events in sequence by varying neural codes in the brain, find RIKEN researchers[1]. These 'event cells' may aid decision-making later.

Neurons mainly signal to each other by changing the timing or frequency of their firing. Shigeyoshi Fujisawa at the RIKEN Brain Science Institute and colleagues examined how these two parameters changed in the central hippocampal area CA1 when rats chose different sound–odor combinations to obtain a water reward. Many cells displayed elevated activity in response to one or both stimuli. Furthermore, they retained this activation through the decision phase, indicating that the inputs were being integrated by the brain and retained in a specific order to facilitate a subsequent choice.

The hippocampus has a refresh rate of around 8 hertz—the theta cycle—which guides how often neurons update their activity, a phenomenon called the theta phase precession. The researchers were interested in how this cyclic organization of information is modified by inputs, like a smell event, followed by a sound event, followed by a decision. Among the neurons responsive to smells, the theta phase precession occurred only for preferred odors, and their activity was subsequently locked to the theta cycle. This occurred for

about 90 per cent of smell-sensitive cells and for a similarly high proportion of choice-sensitive cells.

On a more global scale, assemblies of hippocampal neurons can also form theta sequences—coordinated sequential activation patterns representing past, present and future locations during animal navigation. The researchers discovered that theta sequences were formed by this cue-combination task.

The team could decode whether neural spikes at different phases of the theta cycle represented real-time inputs—the moment when the smell or sound event happened—

> **"Spikes that were locked to different phases of the cycle could even tell us if the rat had made a correct, rewarded choice or chosen the wrong cue combination."**

or future periods—the decision-making moment. "Spikes that were locked to different phases of the cycle could even tell us if the rat had made a correct, rewarded choice or chosen the wrong cue combination," says Fujisawa.

Finally, the team reversed the experimental conditions: the previously rewarding sound–odor combination became incorrect, and vice versa. Rats learned the new relationship after a few days, and their brain cell activity adapted, exhibiting the phase precession and locking that was observed before the switch.

"This neural reorganization reflects the sequence of the events and can be flexibly remapped," comments Fujisawa. "Cells that encode specific cues, combinations or choices can collectively represent an entire sequence of events when they become temporally organized with the hippocampal theta phase."

The researchers surmise that the hippocampus organizes networks of relational elements, whether these are locations or events, as a fundamental process of episodic and spatial memory.

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PHYSICS

Heavy krypton shifts shape

A first look at extra-heavy isotopes of krypton has provided new insights into the forces affecting atomic nuclei

Extra-heavy isotopes of the element krypton have been studied for the first time at RIKEN's Nishina Center for Accelerator-Based Science, with scientists intrigued by the new atomic nuclear shapes this experiment has revealed[1].

Krypton, a noble gas, usually exists as the isotope ^{84}Kr, which has 36 protons and 48 neutrons. But an international team has used spectroscopy to explore extremely neutron-rich isotopes ^{98}Kr (62 neutrons) and ^{100}Kr (64 neutrons).

The arrangement of protons and neutrons in a nucleus depends on the strong nuclear force that binds them together. This force, still poorly understood, gives rise to sometimes sudden and surprising quantum phenomena such as the complete spatial rearrangement of nuclear particles when the number of neutrons increases from 59 to 60 in zirconium (40 protons) and strontium (38 protons) isotopes.

Until now, krypton isotopes had been studied up to ^{96}Kr, which has 60 neutrons and was known to be the stopping point for the shape transition. The experiment conducted at RIKEN enabled scientists to determine the energies of the first excited states in ^{98}Kr and ^{100}Kr. They discovered that, in contrast to neighboring isotopes of rubidium, strontium and zirconium, which change shape suddenly at neutron number 60, these isotopes experience a gentle onset of deformation with the addition of neutrons.

These changes in shape illustrate the complex interplay between the collective properties of nuclear systems, like shapes, and their intrinsic degrees of freedom, such as neutron and proton numbers. Understanding this interplay is essential for constraining nuclear models, and this study marks a decisive step toward understanding the limits of this quantum phase transition region.

Furthermore, an excited state measured at low energy hints at the presence of another competing configuration. Theoretical models link the presence of these low-lying states to the coexistence of two ellipsoidal shapes at low energy: a football and a discus.

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Two extra-heavy isotopes of krypton produced at the Radioactive Isotope Beam Factory at RIKEN provided vital information about the forces inside atomic nuclei.

The results were made possible by the production of very neutron-rich nuclei at the Radioactive Isotope Beam Factory at RIKEN (see image). About 150 billion uranium 238 nuclei per second were accelerated to 70 per cent the speed of light and collided with a beryllium target. The fission products created by this collision were sorted in-flight by a magnetic spectrometer and sent to a cryogenic liquid-hydrogen target to synthesize nuclei of interest via proton knockout. These knockout reactions were identified by a time projection chamber around the target. Finally, the electromagnetic de-excitation of the nuclei was detected using a gamma-ray detector. The combination of these instruments and technologies was essential for studying these previously inaccessible nuclei.

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BIOLOGY

Untangling depression in Huntington's disease

New research implicates clumps of insoluble, misfolded proteins in the development of mental illness

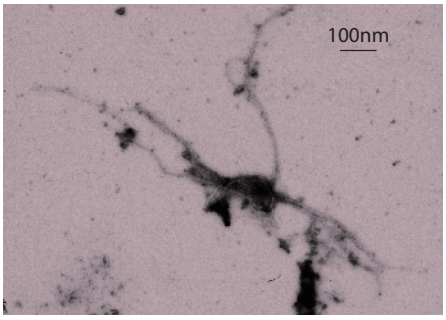
A new discovery by RIKEN researchers could offer fresh insights into not just depression related to Huntington's disease, but also mental illness more generally. The scientists have identified a molecular signaling pathway linked to psychiatric symptoms in Huntington's disease[1].

A hereditary neurological condition that gets progressively worse, Huntington's disease is mainly characterized by involuntary, dance-like movements. It is caused by mutations in the Huntingtin (HTT) gene, which result in the production of misfolded Huntingtin protein molecules. These molecules aggregate to form insoluble clumps, leading to nerve cell death in the striatum—a region of the brain involved in voluntary movements.

Huntington's disease has traditionally been considered a movement disorder, but its classic symptoms are now known to be accompanied by psychiatric ones, particularly depression. Very little is known about the underlying molecular mechanisms for these symptoms, however.

Motomasa Tanaka at RIKEN Brain Science Institute and his colleagues examined genetically engineered mice carrying a mutated human HTT gene. These mice exhibited the pathological hallmarks of Huntington's disease, including HTT aggregation.

The researchers performed a series of biochemical assays and found that misfolded



A transmission electron microscopy image of an aggregate of cellular protein DISC1.

HTT protein binds to another cellular protein called DISC1, causing them to aggregate (pictured). This boosts the activity of PDE4—an enzyme that breaks down a small signaling molecule called cAMP. DISC1 normally binds to PDE4 to restrict its activity, but in Huntington's disease it binds to HTT instead. Consequently, PDE4 becomes overactive, leading to reduced cAMP levels.

The team then examined brain tissue samples obtained from Huntington's disease patients after death and found that they too contained insoluble clumps made of mutant HTT protein bound to DISC1. In contrast, tissue samples from three individuals who died of other causes did not contain these aggregates.

Behavioral testing further revealed that the mutant mice showed no preference for a sugar solution over water, indicating that they have anhedonia, or an inability to experience pleasure and reward, one symptom of depression. However, their preference for the sweet drink could be restored by injecting them with a shortened form of DISC1 that does not bind to mutant HTT. This suggests that the alterations in this signaling pathway are associated with anhedonia.

"Reduced levels of soluble, functional DISC1 due to co-aggregation with HHT is responsible for anhedonia in Huntington's disease," says Tanaka, "so DISC1 supplements could reduce this symptom."

"This study leaves a critical question unanswered," he adds. "Can our co-aggregation hypothesis explain diverse psychiatric symptoms, including social deficits, in other neurodegenerative diseases? We are keen to investigate this."

Reference

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CHEMISTRY

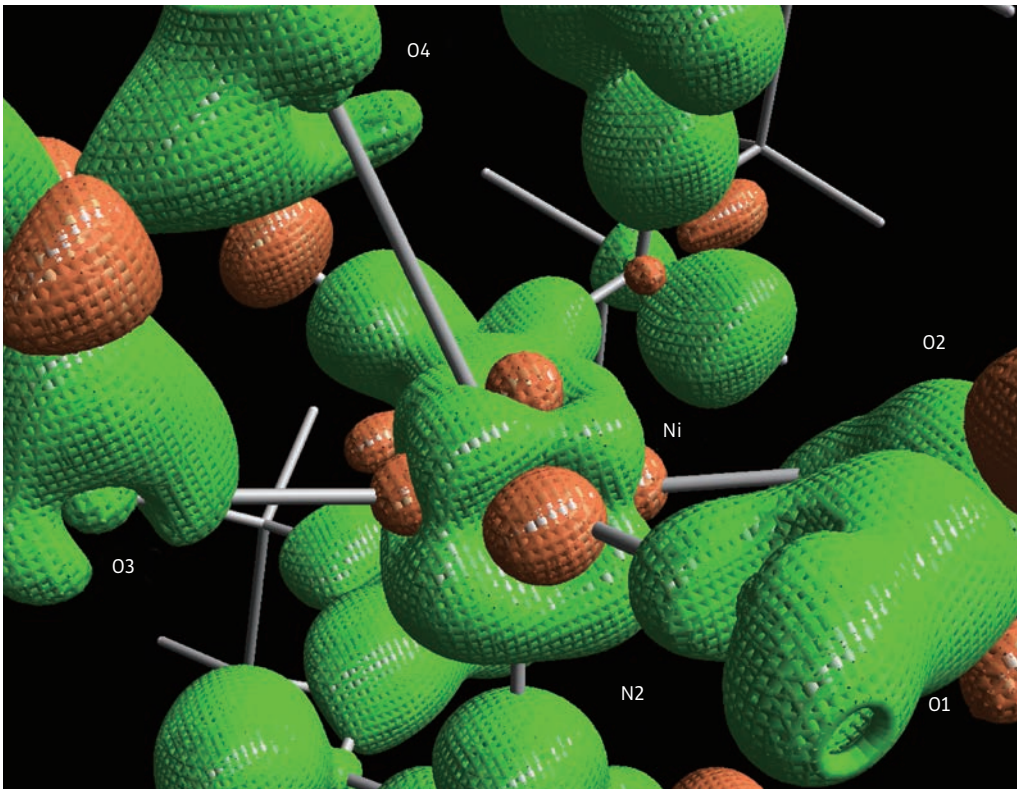
Electron analysis reveals catalyst is both acid and base

Crystallographers and synthetic chemists show how a common nickel catalyst acts to assemble molecules

Assembling the components of new drugs could be a lot easier thanks to RIKEN researchers' work mapping the distribution of electrons in a catalyst.

Nickel-based catalysts are powerful agents for assembling complex organic molecules such as drugs, but they tend to be developed by trial and error. A cross-disciplinary team of RIKEN researchers has studied a nickel catalyst in more detail, developing a deep understanding of its electronic structure and resulting chemical activity[1]. The research paves the way for wider use of this catalyst and provides a pathway by which all catalysts could be improved.

Catalysts typically act as chemical matchmakers, bringing together two molecules and facilitating the exchange of electrons that bond them together. To make molecules such as drugs, there is an added complication. In nature, most organic molecules are chiral: like your left and right hands, they exist in mirror-image forms known as enantiomers. Catalysts can help guide the reactants together so that only the desired enantiomer of a drug is formed. To do this, chemists usually test a range of catalyst structures and pick the one that works best.



X-ray diffraction data reveals the electronic structure at the heart of a nickel catalyst.

> **"A nickel complex has two 'hands', one acid and one base."**

To develop a new nickel catalyst to selectively pair two chiral molecules in a transformation known as a [3+2] cycloaddition, Mikiko Sodeoka, Yoshihiro Sohtome and their colleagues at the RIKEN Synthetic Organic Chemistry Laboratory and the RIKEN Center for Sustainable Resource Science took a different approach. By teaming up with crystallographer Daisuke Hashizume at the RIKEN Center for Emergent Matter Science, they probed the catalyst with x-rays to understand its activity by first understanding its electronic structure.

"X-ray diffraction data contains information on all electron densities in the crystal," says Hashizume. Using this data, the team mapped the electrons spread across the complex, a process they called electron density distribution (EDD) analysis. The analysis revealed a partially naked, electron-deficient *d* electron orbital, a feature that gives the catalyst acidic properties. They also found that one of the catalyst's ligand arms is weakly bound and so can act as a base.

"We experimentally showed that a nickel complex has two 'hands', one acid and one base," says Sohtome. The two hands work cooperatively to catalyse the cycloaddition.

"Our collaboration demonstrates that EDD analysis is a useful tool to link catalyst structure and function," Sohtome says. The insight that the catalyst acts simultaneously as acid and base should inspire numerous other catalyst reactions. "We strongly believe that the catalyst design criteria of using chiral metal catalysts that merge acid and base functionalities, holds vast potential to design asymmetric catalysis," he concludes.

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Researchers have discovered a straightforward way to make a wide range of common crops more drought tolerant—just add vinegar to the soil.

BIOLOGY

Vinegar survivors

Adding vinegar to the soil of common crops is a simple way to boost drought tolerance

Adding vinegar to the soil increases the drought tolerance of a wide range of common crops such as maize, rice and wheat, RIKEN researchers have shown[1]. This curious finding is the result of a newly identified biological pathway, activated by acetate, one of the components of vinegar.

Researchers Jong-Myong Kim and Motoaki Seki at the RIKEN Center for Sustainable Resource Science say their work could have global significance. "Although transgenic technologies can be used to create plants that are more tolerant to drought, we must also develop simple and less expensive technologies because genetically modified plants are not available in all countries," says Kim. "We expect that external application of acetate to plants will be a useful, simple, and less expensive way to enhance drought tolerance in a variety of plants."

The discovery began with the identification of unique drought-tolerant *Arabidopsis* mutants. The plants were found to have a mutation for an enzyme called HDA6 (histone deacetylase 6), and the initial goal of the study was to determine exactly how this mutation allows the plants to grow in severe and extended conditions without water.

Initial testing of non-mutant *Arabidopsis* in drought conditions showed that

genomic-wide expression of HDA6 was linked to activation of the biological pathway that produces acetate, the main component of vinegar.

In the mutated plants, they found a greater activation of this pathway under the same conditions and noted the plants produced larger amounts of acetate. Analysis found the HDA6 enzyme acts as a switch, controlling which type of metabolic pathway is active. Normally, plants break down sugar for energy, but in times of drought, they switch to the acetate-producing pathway.

> **“More than 70 per cent of the plants treated with acetic acid survived, whereas virtually all the other plants died”**

The team next measured acetate levels in normal plants and found that the amount of acetate produced by plants during drought directly correlated with how well they performed. To confirm this, they tested plants with mutations in two of the genes found in the acetate synthesis pathway. Results showed that these plants produced less acetate and were more sensitive to drought than normal plants.

To definitively confirm that the amount of acetate in plants helps them survive drought, the team grew normal plants either with vinegar—acetic acid—added to the soil, other organic acids, or just water. After subjecting them to drought conditions for 14 days, they found that more than 70 per cent of the plants treated with acetic acid survived, whereas virtually all the other plants died.

The scientists mapped the entire signaling pathway related to the HDA6 switch and realized that this pathway is present across many plant species.

Reference

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PHYSICS

Flaws in zinc oxide films add magnetic twist

Why does a non-magnetic material cause electrons to behave like they are interacting with a magnet?

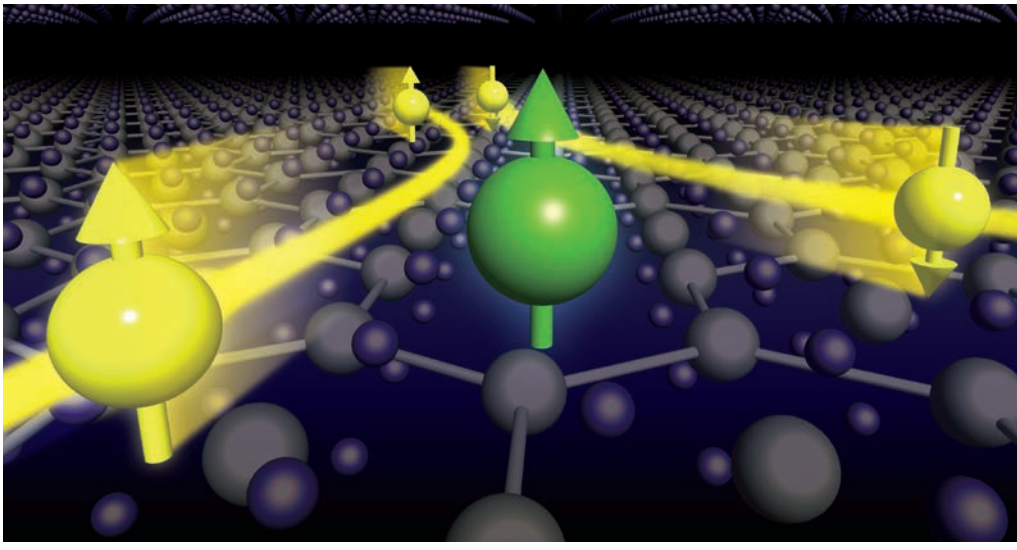
Scientists often try to eliminate flaws, or defects, from the crystal structures of electronic materials to preserve high conductivity. RIKEN researchers, however, have discovered that some crystal defects can help electrons flow rapidly and with minimal energy loss, generating a quantum state that is highly desirable in the race for low-power electronics[1].

Thin films of magnesium–zinc and pure zinc oxides (MgZnO/ZnO) have intrigued Masashi Kawasaki and colleagues from the RIKEN Center for Emergent Matter Science for over 20 years. When stacked, the faces of the two films confine electrons in a thin, nearly two-dimensional region, where they zip along with extraordinary mobility. Continuous improvements in the quality of MgZnO/ZnO crystals mean that electrons in these high-speed interfaces can now travel quite far—some micrometers—before scattering or interacting with other particles.

> **“Everyone agreed we were seeing the anomalous Hall effect, but initially no one could explain it.”**

The team investigated whether MgZnO/ZnO interfaces could act as thermoelectric materials, which generate electricity when heated. This required characterizing the response of interface to both heat and electrical stimulation. The researchers measured the interface’s power dissipation using magnetic fields to deflect electrons from their normal

CONTINUED ON PAGE 24



High-mobility electrons (yellow spheres) with different spins are scattered in different directions by a localized magnetic defect (green sphere) at the interface between the oxides MgZnO and ZnO.

flow—a phenomenon known as the Hall effect. When these experiments were performed at temperatures near absolute zero, a quantum Hall effect emerged, indicating that the system had few defects.

However, the researchers were surprised when they checked power dissipation at temperatures too high for quantum effects to occur. Instead of behaving classically, the current-generated voltages shot up far more than predicted.

"This was very unexpected," recalls Denis Maryenko. "We expected the Hall effect to show classical linear increases with applied magnetic field. But instead we saw additional, nonlinear enhancements."

"We used different samples and experimental setups, but the nonlinearity was always there," says Maryenko. "We talked to many scientists, and everyone agreed we were seeing the anomalous Hall effect, but initially no one could explain it."

Collaboration with theorists revealed one possible solution to the magnetic puzzle. If a few defects remain at the MgZnO/ZnO interface after thin-film fabrication, these would likely be filled by spin-polarized, single electrons. These defects act as effective magnetic moments that twist flowing electrons from their paths and initiate another Hall effect through a process known as skew scattering (pictured page 23).

"As a way to produce the anomalous Hall effect, one mechanism for producing skew scattering was almost completely forgotten," says Maryenko. "But if we return to low temperatures, we may see how localized magnetic moments alter the quantum Hall states with impacts for applications such as quantum computing. It proves you have to pay attention to defects—sometimes they can be very useful and bear surprises."

Reference

1. Maryenko, D., Mishchenko, A. S., Bahramy, M. S., Ernst, A., Falson, J., Kozuka, Y., Tsukazaki, A., Nagaosa, N. & Kawasaki, M. Observation of anomalous Hall effect in a non-magnetic two-dimensional electron system. *Nature Communications* **8,** 14777 (2017).

BIOLOGY

Finding real rewards in a virtual world

Mice store both virtual and real-world locations in the same regions of the brain

RIKEN researchers have demonstrated that mice use the same brain regions to remember a location in a virtual world as they do in the real world.

Mice employ the same brain regions to remember a location in a virtual world as they do in the real world, RIKEN researchers have shown[1]. This means that scientists can use virtual-reality technology to explore the brain activity of mice with the confidence that their findings will be applicable to the real world.

Monitoring the brain activity of animals performing different behaviors is a powerful way to learn about normal brain function. When animal models of neurological disorders are used, researchers can test whether different manipulations can alleviate symptoms, with the ultimate goal of helping people with similar disorders. But monitoring brain activity when animals have complete freedom of movement is challenging.

To solve this problem, scientists are using virtual-reality technology with rodents. However, the findings will be useful only if it can be confirmed that rodents use the same brain regions in the same way in a virtual setting as they do in the real world.

To test this, a team led by Masaaki Sato of the RIKEN Brain Science Institute developed a virtual-reality track for mice that requires mice to stop running and wait for a reward when they arrive at a particular location on the virtual road.

"When we first started our experiments, I was a bit skeptical because mice are not known to be visual animals," explains Sato. "So it really surprised me that they could learn the goal location."

The CA1 region of the hippocampus in the brain is necessary for learning spatial locations and remembering routes. To test whether the mice were learning locations on the virtual track in the same way they do in the real world, the researchers used a drug to reversibly inhibit the CA1 region after mice had learned to run on the virtual track and find the goal. They found that the mice did not wait at the goal and were thus less successful in getting rewarded. After the drug wore

off, the mice could find the goal just as well as before the inhibition.

The team next examined mice lacking a protein called Shank2, which is normally found in hippocampal output neurons. The *SHANK2* gene is associated with autism spectrum disorders, and the model mice are known to have difficulty learning the locations of platforms in water mazes. These mice did not learn as well when tested on the virtual track.

"By using a mouse model of autism, we demonstrated that our virtual-reality system and behavioral paradigm are useful for studying brain disorders," says Sato.

Reference

1. Sato, M., Kawano, M., Mizuta, K., Islam, T., Lee, M. G. & Hayashi, Y. Hippocampus-dependent goal localization by head-fixed mice in virtual reality. *eNeuro* **4,** ENEURO.0369-16.2017 (2017).

BIOLOGY

The nuclear transport option

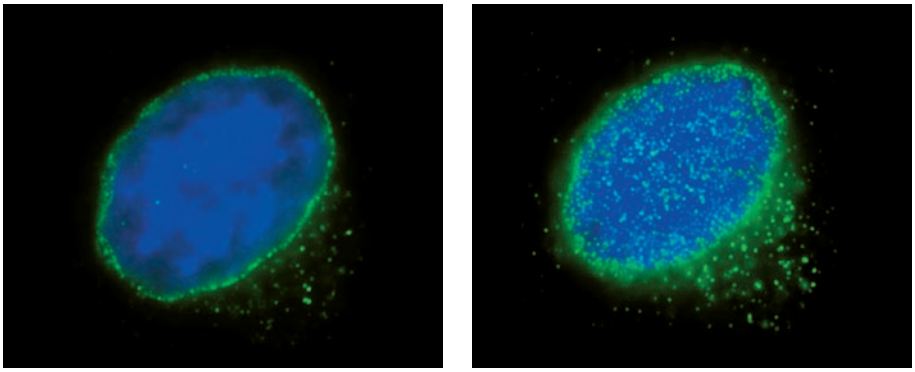
The identification of substances entering the nuclei of human cells reveals that import molecules have distinct biological roles

The molecular shuttles on which proteins hitch rides when passing in and out of the nuclei of human cells differ depending on those proteins' biological functions, RIKEN researchers have revealed[1]. This discovery could eventually help scientists to develop new ways to treat cancer and other diseases.

Vast numbers of ions and molecules are shipped into and out of the nucleus of a cell, and this transfer affects every aspect of health. Ions and small molecules can easily slip through pores in the membrane that surrounds the nucleus (see image), whereas larger cargo such as proteins can do so only after binding to receptors that pass through the pores.

In human cells, 12 such receptors, called importins, are involved in nuclear import. Mutations of specific importin genes in model organisms, including yeast and flies, have been shown to cause problems in certain biological processes. But little is known about their precise molecular functions because the cargos associated with different importins are largely unknown.

Previously, a team led by Naoko Imamoto of the RIKEN Cellular Dynamics Laboratory had developed a way to identify the cargos of nuclear import receptors. Called SILAC-Tp, this technique involves labeling cells with amino acids of different masses, extracting cell cytoplasms and nuclei, remixing these to trigger nuclear transport into the cell nuclei in a reconstituted system, and identifying cargo proteins with mass spectrometry.



Fluorescence microscopy images of nuclear pore complexes (shown in green; blue region is DNA) on nuclear surfaces. Middle section (left) and bottom surface (right) of the nucleus of a human HeLa cell.

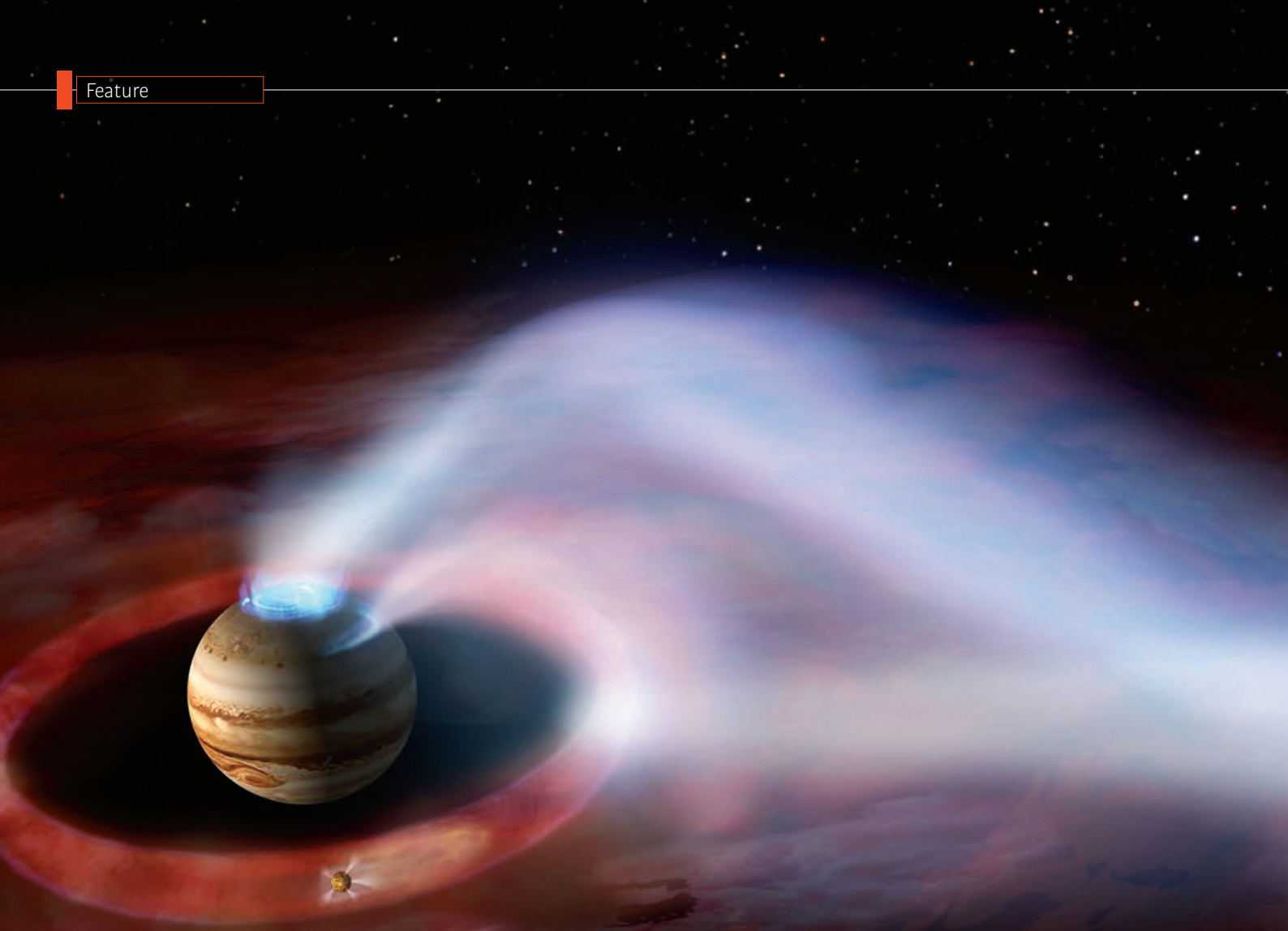
Now, by using a recent advance in mass spectrometry, Imamoto's team improved the SILAC-Tp technique to allow them to discover the nuclear cargos carried by all 12 human importins. Employing this enhanced SILAC-Tp technique, they were able to identify the specific receptors that hundreds of proteins used as shuttles into the nucleus. The researchers also found the cargos of specific importins were grouped around particular functions, such as DNA repair, cell division, programmed cell death and circadian rhythm function. All 12 importins appeared to be associated with multiple cellular functions.

While further research is needed to clarify links to physiological functions, Imamoto is confident that the present findings will advance the understanding of interactions between receptors and their cargos and that they could eventually lead to new treatments for cancer and other conditions.

"Nuclear cytoplasmic transport is a major cellular regulatory mechanism and is linked to many phenomena related to development and disease," says Imamoto. "If we can understand the physiological significance of specific importin pathways, we may be able to learn how to block those associated with disease development."

Reference

1. Kimura, M., Morinaka, Y., Imai, K., Kose, S., Horton, P. & Imamoto, N. Extensive cargo identification reveals distinct biological roles of the 12 importin pathways. *eLife* **6,** e21184 (2017).



Astronomy

Jupiter's volcano-powered auroral lights

NASA's Juno spacecraft has helped explain how volcanoes on the moon Io spew particles that are flung out by Jupiter's magnetic field, before rebounding back. A high-speed atmospheric encounter on the return leg creates the Red Giant's once mysterious transient auroras.

An international effort led by RIKEN scientist Tomoki Kimura utilized three spacecraft to finally show that Jupiter's magnetic field (red) carries charged particles (white) derived from the volcanoes on moon Io (front) in a system-wide journey to create transient auroras.

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Io is a violent moon. Trapped in an incessant gravitational tug-of-war between the gas giant Jupiter and its other moons, Io's core is continuously kneaded by burning tidal forces. As a result, volcanoes on Io regularly throw vast quantities of molten material, dust and sulfur gas into the atmosphere.

In May 2017, an international team of researchers led by Tomoki Kimura of the Nishina Center for Accelerator-Based Science at RIKEN used data generated by NASA space probe Juno to confirm that Io's fiery volcanic activity contributes to auroral lights brightening Jupiter's upper atmosphere.

Jupiter's auroras are far more complex than Earth's. The planet's poles feature an auroral light display, which—as on Earth—is caused by solar wind, high-energy particles that escape the Sun's gravity and shoot across the Solar System. When they reach Jupiter, the planet's magnetic field guides these to the planet's poles, where they create constant auroral lights.

But Jupiter's auroras occasionally peak in brightness in events known as transient auroras—long a mystery to astronomers. It was confusing if you looked at Earth's model, says Kimura: "Sometimes aurora emission is highly correlated with the solar wind, but sometimes it's not correlated with it at all."

In 2014, the Japanese extreme-ultraviolet space telescope Hisaki observed a brightening of Jupiter's aurora that lasted 3–11 hours during a period when the solar wind was relatively quiet. Kimura was working a four-month auroral imaging campaign on interactions in the region above Jupiter's magnetic field, and, while intrigued, he needed a closer look underneath this plasma layer to unpick transient auroras.

Revelations from Juno's close-up data

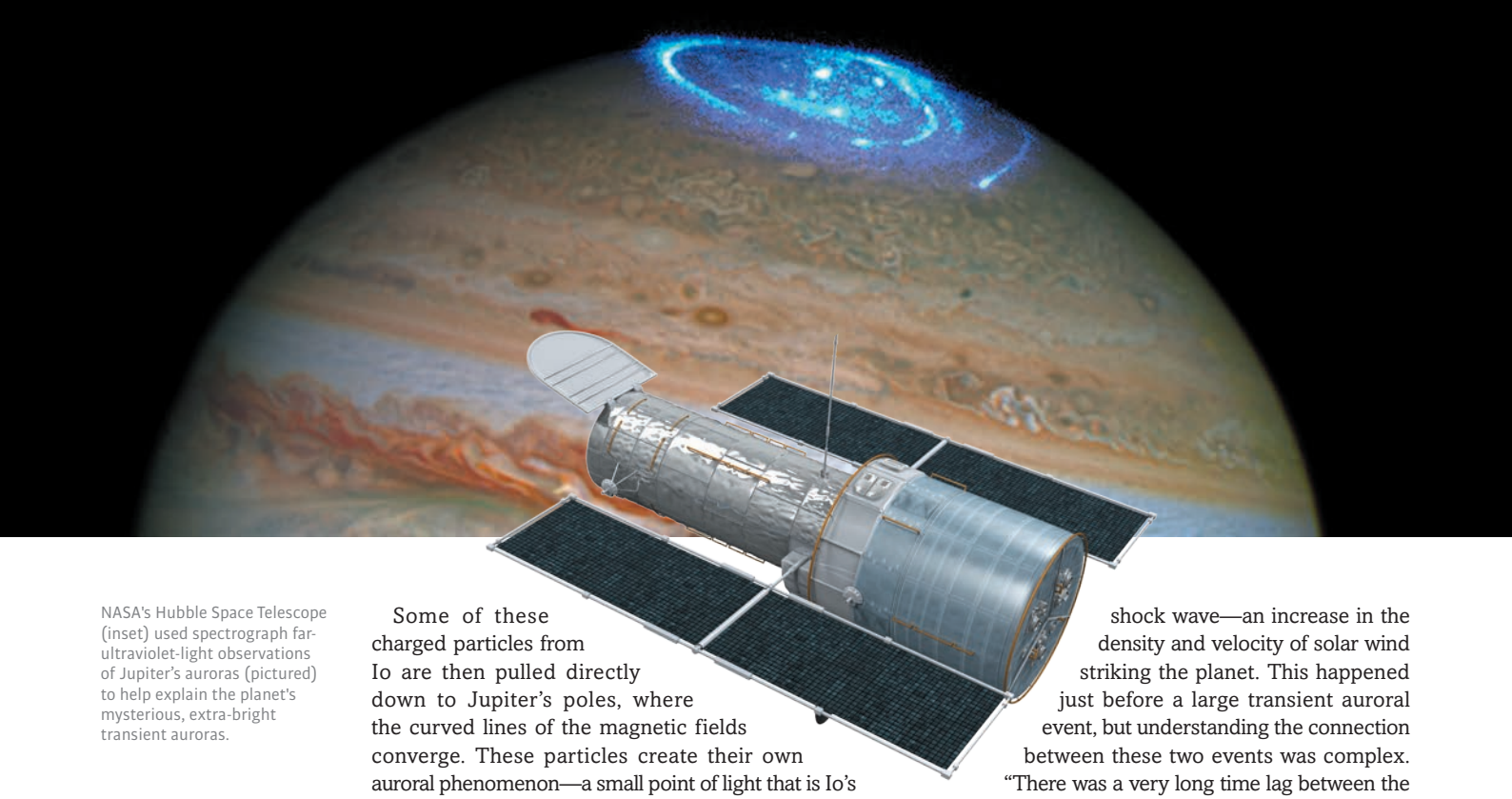
The study of Jupiter's auroras was limited to observations from Earth-orbiting satellites until the arrival of NASA space probe Juno at Jupiter in July 2016.

Finally able to look more closely into the auroras, Kimura led a team of planetary scientists from institutions all over the world, including Johns Hopkins University in the United States, Université de Liège in Belgium and the University of Leicester in the United Kingdom. The team coordinated in mid-2016 to have the Hisaki satellite and the Hubble Space Telescope both turn their electronic eyes to Jupiter and its magnetosphere—where charged particles are controlled by the planet's magnetic-field acting as a shield against solar wind. At the same time, Juno began its approach to Jupiter, travelling upstream of the solar wind, well positioned to measure the particles buffeting the gas giant.

The first thing that Hisaki's six-month monitoring revealed was that sulfur gas spewed out from Io's volcanoes is caught up in a 'tail' created by the force of the solar wind pushing Jupiter's enormous magnetic field into a windsock shape as the planet orbits. The magnetic field is strong enough to strip electrons from the sulfur molecules, making them charged.

This Feature looks at the work of Tomoki Kimura

Tomoki Kimura obtained his PhD from Tohoku University in 2010. After joining the Hisaki satellite mission and other space science programs at Japan Aerospace Exploration Agency, in 2015, he started working as a special postdoctoral research fellow at the RIKEN Tamagawa High Energy Astrophysics Laboratory. His current research interests are plasma accelerations (for example, aurora) at planetary magnetospheres and their physical and chemical impacts on icy bodies. He is also contributing to the development of the Jupiter Icy Moon Exploration (JUICE) mission led by the European Space Agency.



NASA's Hubble Space Telescope (inset) used spectrograph far-ultraviolet-light observations of Jupiter's auroras (pictured) to help explain the planet's mysterious, extra-bright transient auroras.

Some of these charged particles from Io are then pulled directly down to Jupiter's poles, where the curved lines of the magnetic fields converge. These particles create their own auroral phenomenon—a small point of light that is Io's auroral 'footprint'.

However, that is only a small part of the picture. The rest of the charged sulfur particles stripped from Io are also collected by Jupiter's magnetic field, but they take the long way around to the poles.

Jupiter's magnetosphere actually stretches roughly three million kilometers toward the Sun, and it affects the solar wind far back. It turns out that a good proportion of Io's plasma contribution actually gets flung out to the farther reaches of Jupiter's magnetosphere by the centrifugal force of the spinning gas giant, before being brought back to the planet. This process accelerates these molecules to fantastic speeds, imbuing them with enormous energy. When they do finally crash into Jupiter's atmosphere, they cause a dramatic brightening—the transient auroras.

As well as occurring outside periods of solar wind activity, transient auroras are distinguishable because they take place in a different area on Jupiter. "We found some aurora brightening that starts at the higher latitudes in the polar region and then expands into lower latitudes," Kimura says.

The speed at which these charged particles travel was also surprising. "This is very fast transport of energy, especially energetic plasma, which happens within a few hours—less than one Jupiter rotation," he says.

"This process accelerates these molecules to fantastic speeds, imbuing them with enormous energy."

Solar wind and extraterrestrial life questions

The other interesting finding was how the particles pulled from Io's surface interact with the solar wind and aurora. Previously, it was assumed that the solar wind had little to do with transient auroras. But data from Juno suggests otherwise. Just as Juno arrived upstream of Jupiter, it detected what is known as a shock wave—an increase in the density and velocity of solar wind striking the planet. This happened just before a large transient auroral event, but understanding the connection between these two events was complex. "There was a very long time lag between the shock arrival at Jupiter and the auroral brightening—an extraordinarily long time lag," Kimura says. It was roughly 10 hours. "The connection is very fast in general—a few hours, so about 10 hours is too long."

It's still something of a mystery, but Kimura suggests that a compression of the magnetosphere by the shock wave of solar wind may be somehow slowed by the heavier charged sulfur particles from Io. He hopes that looking again at the data from Hisaki and the Hubble Space Telescope will help further unravel this question.

Kimura is also intrigued by how Io's charged volcanic emissions might affect some of the other moons in the Jovian system, such as icy Europa. "There is ocean beneath the surface ice, and this is a very important environment to look for extraterrestrial life," says Kimura. He speculates that the high-energy plasma from Io, which bathes the other moons as they orbit Jupiter, might provide an energy source to fuel chemical reactions on their surfaces, which could produce organic compounds, and therefore life.

"These materials could then be transported into the subsurface ocean because of plate tectonics or some geological activity," he says. "It's just speculation, but in the future I want to explore these kinds of fascinating astrobiological questions."

Reference

Kimura, T., Nichols, J. D., Gray, R. L., Tao, C., Murakami, G., Yamazaki, A., Badman, S. V., Tsuchiya, F., Yoshioka, K., Kita, H. *et al*. Transient brightening of Jupiter's aurora observed by the Hisaki satellite and Hubble Space Telescope during approach phase of the Juno spacecraft. *Geophysical Research Letters* **44,** 4523–4531 (2017).

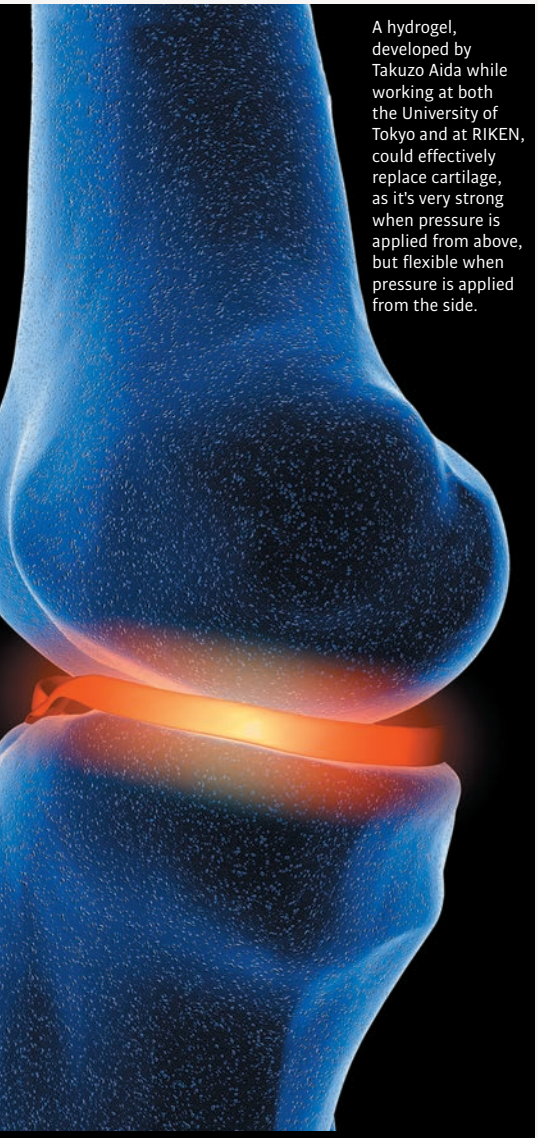
Materials science

Polymers that heal and machines with muscles

Chemists in the emerging field of functional soft matter are discovering materials that are made mostly of water, are temperature responsive, and can self-heal, opening the door to a future with less waste and more intuitive devices.

Takuzo Aida,
Group Director,
Emergent Soft Matter Function Research Group

Takuzo Aida has been group director of the Emergent Soft Matter Function Research Group since 2013. In 2010, he received a Purple Ribbon Medal of Honor from the Japanese government for work on macro- and supramolecular chemistry and for solving energy, biological resource and environmental issues. Other accolades include the Alexander von Humboldt Research Award (2011) and the Leo Esaki Prize (2015).



A hydrogel, developed by Takuzo Aida while working at both the University of Tokyo and at RIKEN, could effectively replace cartilage, as it's very strong when pressure is applied from above, but flexible when pressure is applied from the side.

Extremely fruitful partnership
The Emergent Soft Matter Function Research Group accounts for roughly one-third of RIKEN's Center for Emergent Matter Science (CEMS), a multidisciplinary center whose goal is to develop efficient technologies that will be able to generate energy in an environmentally friendly fashion in order to reduce energy use. CEMS researchers began collaborating with colleagues at the University of Tokyo in 2013, and in 2016 their partnership had become the single most productive collaborative scientific research partnership in the greater Tokyo area, according to Nature Index rankings.

In 2016, it was estimated humans generated roughly 30 trillion metric tons of waste and used about 1.6 million barrels of oil a day. To tackle this global environmental issue, chemists in the RIKEN Emergent Soft Matter Function Research Group are working toward a category of 'soft matter' materials with the potential to dramatically shrink humanity's footprint by reducing waste and fossil fuel consumption. These innovations include futuristic-seeming materials designed to have unique properties: water-based polymers that are less energy intensive to produce and easier to recycle than conventional plastics; materials that generate electricity from heat; and, more energy efficient devices that employ environmentally responsive components.

For more than a decade, researchers around the world have been exploring the new tantalizing possibilities of soft matter by tapping into fields such as chemistry, physics, engineering and environmental science to create new materials. Since the Emergent Soft Matter Function Research Group (see left) was established in 2013 within the RIKEN Center for Emergent Matter Science (CEMS), we have been leading the way. Within the last five years, our chemists have already dramatically advanced the basic science of soft matter, as well as identified some incredible properties in exotic examples, including hydrogels and liquid crystals.

Self-healing materials likely common in one to two decades

While soft matter is re-emerging as a hot topic, people have been marveling at soft-matter materials for centuries. French physicist Pierre-Gilles de Gennes, regarded as the founding father of the modern field of soft matter, noted in his 1991 Nobel Prize lecture how, more than 500 years ago, indigenous people in the Amazon basin dipped their feet in sap from the rubber tree *Hevea brasiliensis*, allowed it to dry, and *voilà*, they had rubber boots. He pointed out that this phenomenon is striking because "a very mild chemical action has induced a drastic change in mechanical properties: a typical feature of soft matter."

At around the same time as de Gennes' lecture, Jean-Marie Lehn, who won the Nobel prize in chemistry in 1987, proposed a novel way to make polymers—supramolecular polymerization. It has added several exciting properties to soft matter's arsenal, including the ability to self-heal. Traditionally, polymers—chains of smaller molecules—are made by linking the monomers with strong covalent bonds. Lehn suggested that dissolving monomers in a particular way would cause them to spontaneously link up and form a new one-dimensional structure through more dynamic non-covalent bonds. Normally, this would result in a weak structure, but Lehn discovered that under certain conditions the resulting polymer would have the same strength as an ordinary polymer. Supramolecular polymers' non-covalent bonds also reform so that broken forms fuse easily back together with the same or almost the same strength as before.

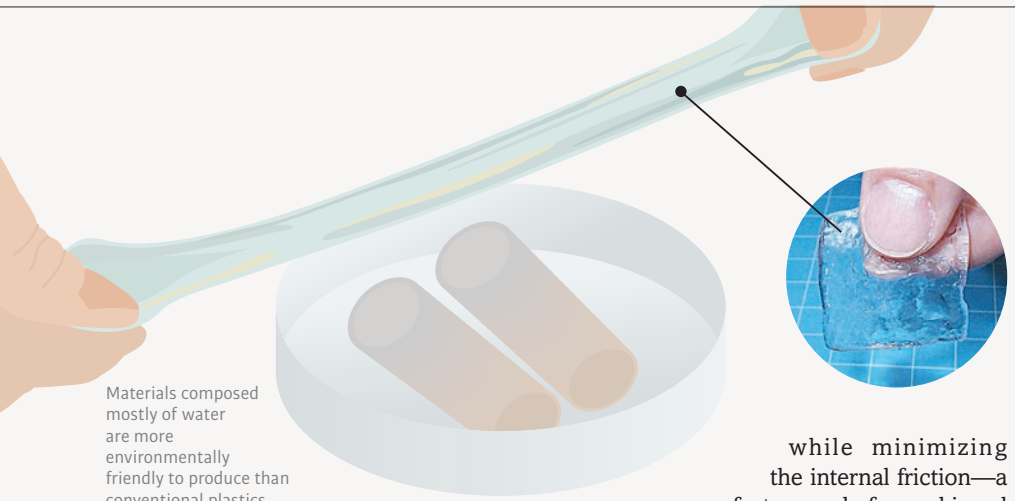
> **"The ability to self-heal will ensure that products made from these polymers will have longer lifetimes."**

Research on the topic was hampered by the fact that materials made via supramolecular polymerization were notoriously hard to control, but, in a 2015 paper published in *Science*, our soft-matter group developed the first mechanism that allowed very high precision in this area. The group's mechanism meant that the materials produced by supramolecular polymerization could be relied upon, as their chain length and molecular weight could be precisely controlled.

The ability to self-heal will ensure that products made from these polymers will have longer lifetimes. Furthermore, their weaker bonds will mean that recycling them will require less energy than conventional polymers, such as plastics made by oil-based production processes.

Water-based plastics on the horizon

'Aqua materials' are a promising basis for water-based plastics, which could replace petroleum-based plastics and also improve recyclability.



Materials composed mostly of water are more environmentally friendly to produce than conventional plastics made using petroleum, and easier to recycle.

In 2010, while at the University of Tokyo, I collaborated on the creation of a hydrogel consisting of approximately 98 per cent water, 2 per cent clay and 0.2 per cent organic components. It was the first material of its kind to be strong, self-healing and capable of maintaining biologically active proteins.

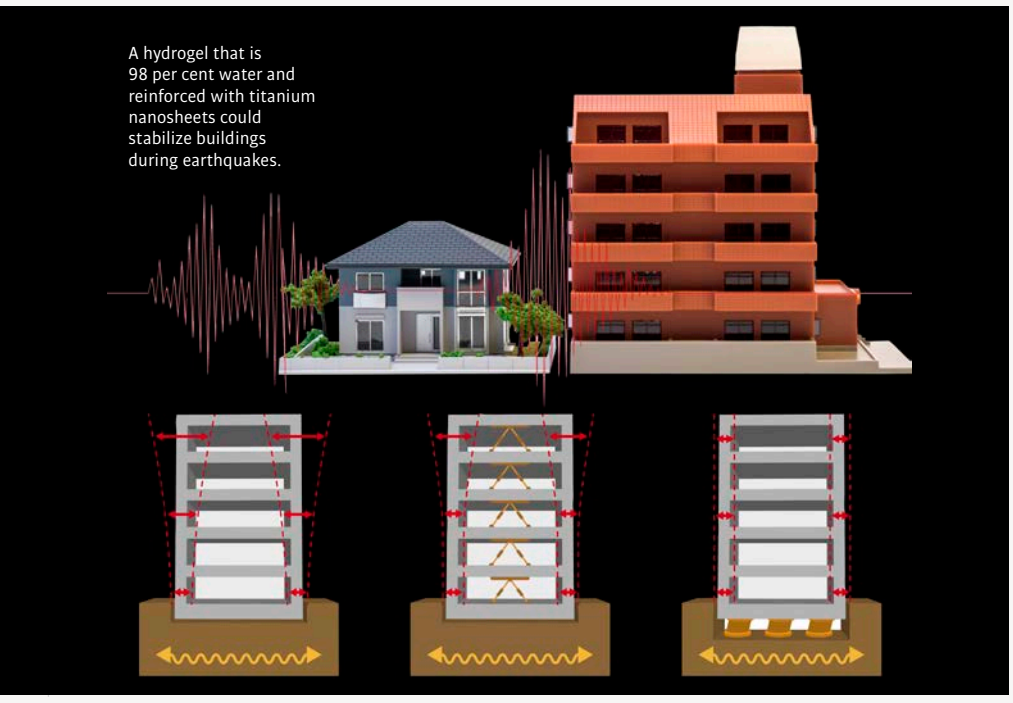
In 2015, as part of the RIKEN group, we replaced the hydrogel's clay structure with internal titanium nanosheets. The hydrogel we produced uniquely combines strength and flexibility and is promising for use as artificial cartilage and to stabilize the base of buildings by absorbing the seismic waves of earthquakes.

The orientation of these nanosheets can be controlled via a magnetic field, allowing the hydrostatic forces to be maximized while minimizing the internal friction—a feat never before achieved in two-dimensional nanosheets. This material has interesting properties. For example, it can be easily deformed when pushed from the side, but is sturdier when pushed from above or below.

Making materials that react

Soft materials could also be used as actuators to turn on or off machines when ambient temperatures change. With his colleagues, Yasuhiro Ishida, who leads one of the soft matter group's eight teams, has created just such a material using a hydrogel made with metal oxide nanosheets. The hydrogel acts like an artificial muscle, expanding in one direction and contracting in the other in response to changes in temperature—and thus could be used as a temperature-driven switch to turn machines on and off.

Another possibility is a film that could produce heat-driven mechanical energy. By heating guanidinium carbonate at high temperatures, a group led by Daigo Miyajima has produced a film composed of a carbon nitride polymer (a robust material similar to graphene). Lightweight yet strong, the film bends and straightens in response to tiny changes in surrounding humidity. It even 'walks' in a direction if one end is shielded from ambient conditions while the other is exposed. The incredible material can jump 10,000 times its own thickness and endure 10,000 bends without damage. Because it can move in response to environmental conditions such as temperature, humidity and light fluctuations, the film could be used to generate electricity from heat-driven mechanical energy. For instance, if it were embedded in window glass, it could generate electricity in response to the regular temperature changes over the day and night, and thus help meet a building's electricity needs.



A hydrogel that is 98 per cent water and reinforced with titanium nanosheets could stabilize buildings during earthquakes.

Smart skin sensors and soft robots

Soft-matter studies have the potential to revolutionize everyday objects—and to improve the efficiency of these objects from production right through to recycling. Already, a related group at CEMS has collaborated with the University of Tokyo to create inflammation-free, highly gas-permeable, ultrathin, lightweight and stretchable sensors that can be directly laminated onto human skin for long periods of time. This may soon find a use as the Internet of Things increasingly adopts soft materials and looks towards an era where—thanks to a range of collaborations—soft materials allow us to incorporate an energy source such as soft solar cells (known as photovoltaic cells) into clothing so that we can wear sensors that can continuously monitor our physiological responses including temperature or blood sugar levels. In the future, both group's researchers also hope to work on producing more human-seeming robots—in an area known as soft robotics—by using these unique materials to generate biological-appearing reactions to the external environment.

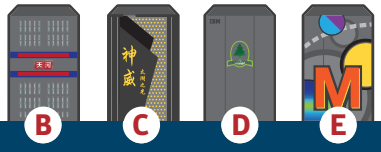
For references, visit the online version of this article at:
www.riken.jp/en/research/rikenresearch/perspectives/2017fall/

A very useful supercomputer

The K computer's no. 1 on the HPCG and Graph 500

In 1993, computer scientist Jack Dongarra built a program to measure supercomputer computation speed (floating point computing speed), creating the TOP500 list—referenced globally today by pundits who follow and compare supercomputers. But computation speed is not the only effective benchmark. In 2013, Dongarra helped create a new program, releasing the HPCG benchmark. It is intended, he and his colleagues wrote in a related paper, "to better represent how today's applications perform." While the RIKEN's K computer is currently 8th on the TOP500 list, it is number 1 in the HPCG list. Not only that, the K computer is currently number 1 in the Graph 500 list, another key benchmark in practical supercomputing. Graph 500 measures speed at the graph-type activities typically used in cybersecurity and medical informatics.

COMPARING LEADING SUPERCOMPUTERS*



How does the K computer compare to other supercomputers?

FAST DATA
The many links of 6D toruses support fast data communication between CPUs.

STORAGE
30 petabytes

NODES
82,944, each 16GB

1993
TOP500 first measures floating point computing speed

↓

2011
K computer built
Listed as no. 1 in TOP500

2013
New HPCG measures ability to solve equations relevant to industrial applications and engineering

Fall 2016–2017
K computer no. 1 in HPCG and Graph 500

↓

FUTURE
As a report on supercomputing's future released in June noted that there is an increased global emphasis on a "system's overall computer memory, interconnect, and storage infrastructure" and how these relate to executing end-to-end tasks.

increased focus on practical use

HPCG list Based on speed at tasks typically required in engineering and industrial applications

600 teraflops

- **A. K computer** — **603**, ranked **1st** on HPCG list
- **B. Tianhe-2**, China — **580, 2nd**
- **C. Sunway TaihuLight**, China — **481, 3rd**
- **D. Sequoia**, USA — **330, 7th**
- **E. Mira**, USA — **167, 11th**

Graph 500 list Based on speed at data-intensive, graph-type activities

40,000 GTEPS

- **38,621**, ranked **1st** on Graph 500 list
- **2061, 8th**
- **23,756, 2nd**
- **23,751, 3rd**
- **14,982, 4th**

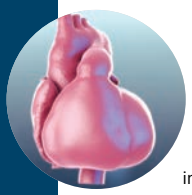
Focused on speed

TOP500 list Based on calculation speed alone

100 petaflops

- **10.51**, ranked **8th** on the TOP500 list
- **33.86, 2nd**
- **93.02, 1st**
- **17.17, 5th**
- **8.59, 9th**

WHAT CAN THE K COMPUTER DO?



170,000 TETRAHEDRA | simulate a heartbeat in **2 DAYS**

RIKEN, the University of Tokyo and Fujitsu simulated the heart's pumping mechanism by recreating the individual muscle fibers of heart tissue as 170,000 pyramid shapes. This could help predict treatment results and improve surgery success rates.

330,000 STRUCTURES | simulate an earthquake in **0.5 DAYS**

The computer modeled a shallow earthquake in 100km^2 of Tokyo, including the movements for more than 2 million people. It identified human traffic-flow bottlenecks and damage to 330,000 structures to help inform earthquake responses.

RIKEN centers and facilities
across Japan and around the world

1 Sendai
Center for Advanced Photonics

2 Tsukuba
BioResource Center

3 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 (RI Beam Factory)
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

4 Tokyo
Tokyo Liaison Office
Center for Advanced Intelligence Project

5 Yokohama
Center for Sustainable Resource Science
Center for Integrative Medical Sciences
Center for Life Science Technologies
Distinguished Senior Scientist Laboratory

6 Nagoya

7 Osaka
Quantitative Biology Center

8 Kobe
Center for Developmental Biology
Center for Life Science Technologies
Advanced Institute for Computational Science (K computer)
Quantitative Biology Center

9 Harima
SPring-8 Center
(SPring-8 Synchrotron Radiation Facility)
(SACLA X-ray Free Electron Laser Facility)

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 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.

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