RIKEN RESEARCH

SUMMER 2021

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PREYING ON PLANTS

How parasites target healthy vegetation

UPPING THE ANTI

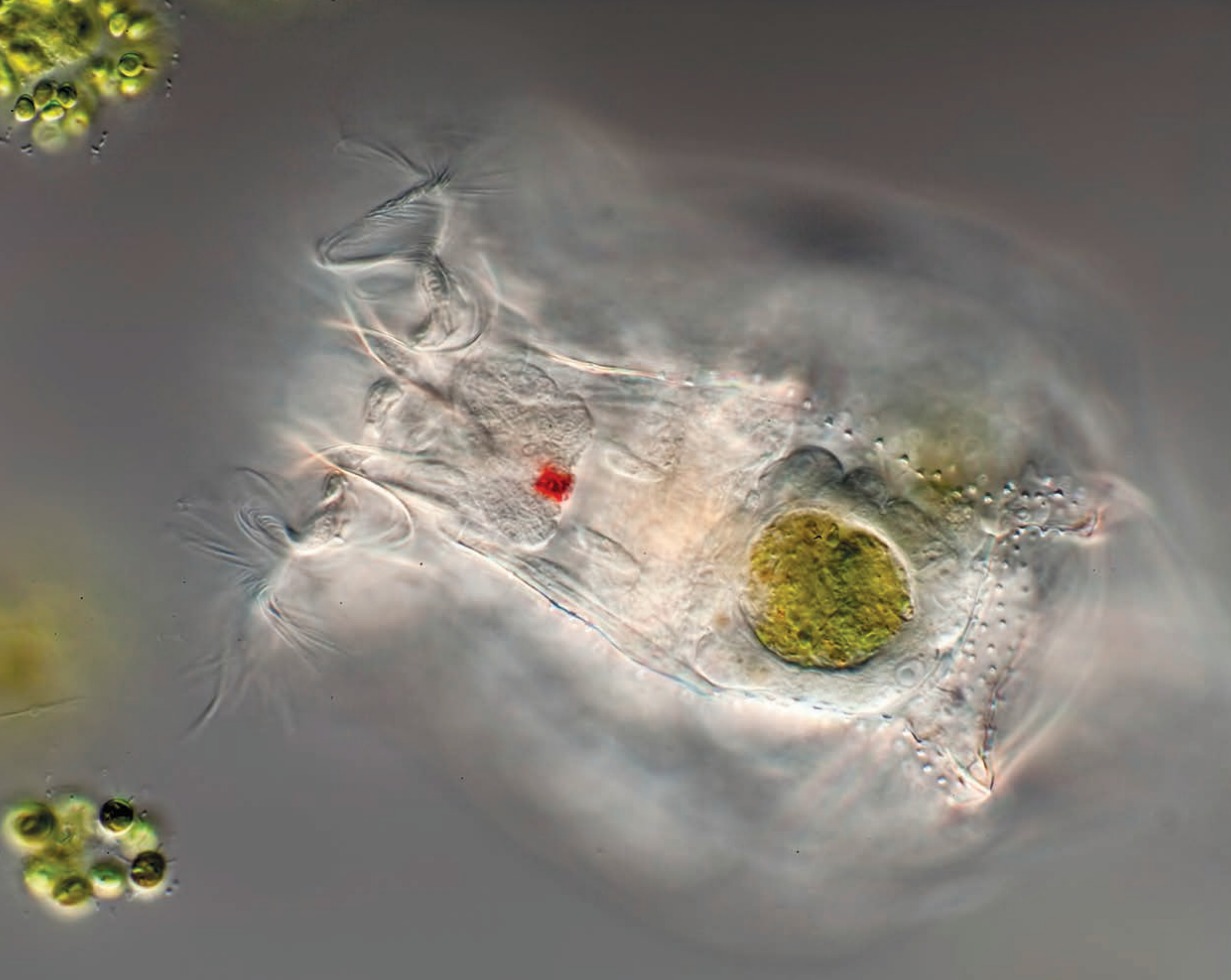
New physics possibilities from classic device

DRAWING ON DATA

AI provides answers in a crisis

HAIR TODAY, HAIR TOMORROW

Stem cells regenerate follicle growth



▲ **Bigger fish to fry**
A RIKEN-led team has developed larger strains of zooplankton by creating mutations with a heavy-ion beam. Bigger versions of this important feed stock for fish nurseries could improve fish farming efficiencies and help supply the needs of a growing global population (see page 16).

RIKEN RESEARCH

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

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

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

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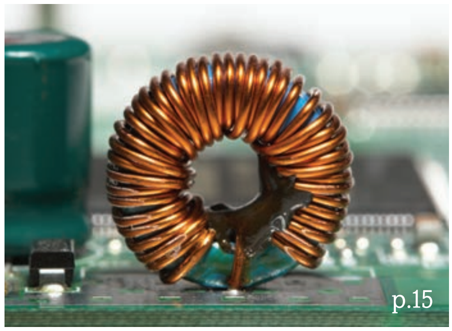

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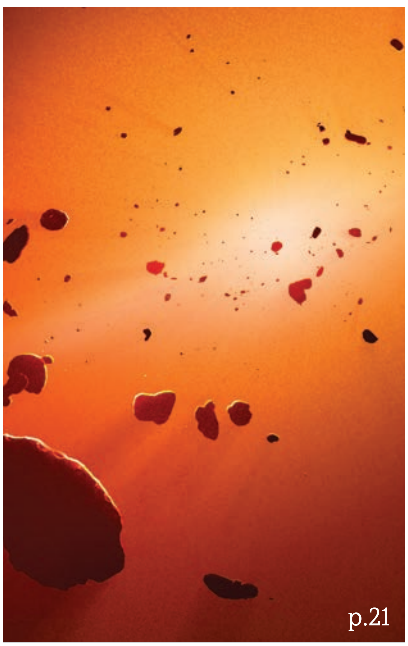
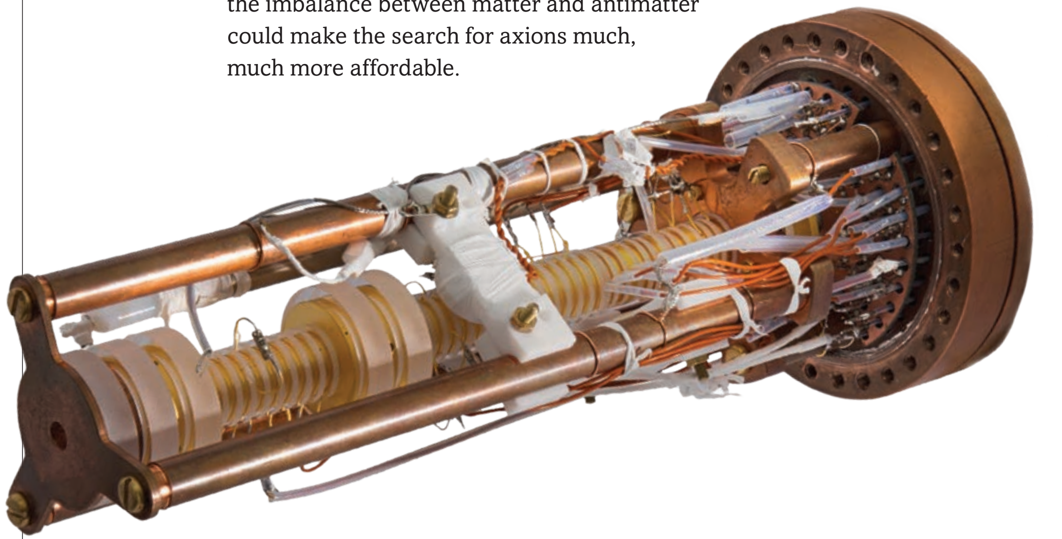
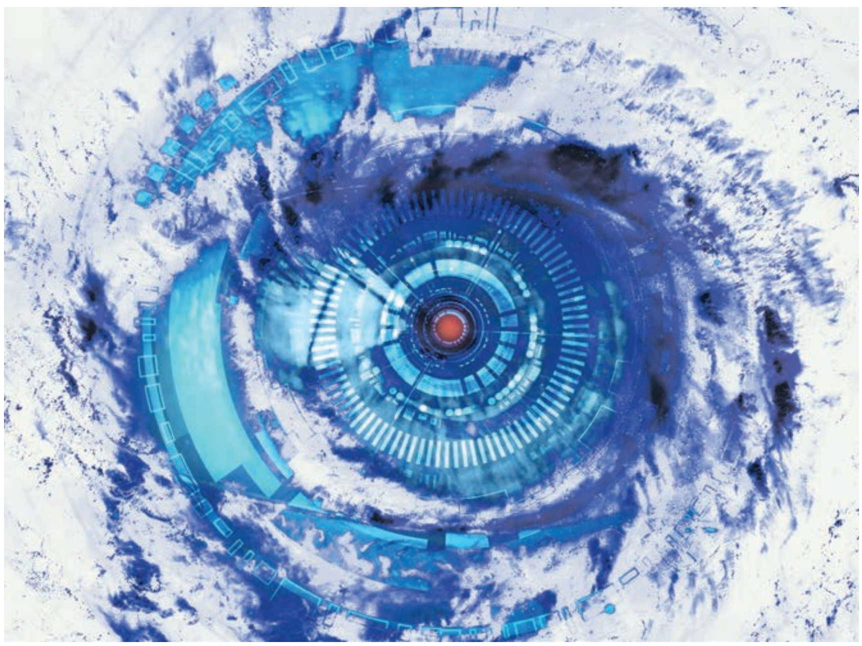
19 Research highlights



26 Feature COVER STORY



30 Perspectives COVER STORY



Calling all collaborators

Hidetoshi Kotera
Executive Director, RIKEN

One of our goals in publishing and distributing this magazine is to provide information with the potential to stimulate new collaborations between RIKEN and partners around the world. Today, I would like to update our readers on some exciting developments regarding our collaborations.

At RIKEN, our collaborations are now managed by a new organization called the Science, Technology, and Innovation Hub. As the name implies, it is meant to act as a hub for collaborations. One of its functions is to promote collaboration inside RIKEN, through initiatives such as our Engineering Network, which brings together people working on joint research projects beyond each discipline. Another important function is to promote projects between RIKEN researchers and other institutes and universities.

The basic method we use to find collaborators is to analyze the fields where we have strengths, and then identify partners that we can work with to enable us to pioneer new research fields, nurture young scientists, and ultimately return the results of our research to society in the form of innovation. For this, we work with universities and research institutes, as well as with a number of companies in the private sector.

We have seen many positive results from such collaborations, including the establishment of a new research organization, the Interdisciplinary Theoretical and Mathematical Sciences Program, based on collaboration between RIKEN, Kyoto University, and research groups in China, India and the United States. Another collaboration with Hiroshima University has furthered cell-imaging technologies and one with Nagoya University has led to the development of a new rice strain that is currently being evaluated in Kenya. We are looking to expand these networks to many more universities and companies outside of Japan.

We hope that you will find examples of research in this issue of *RIKEN Research* that will lead to future collaborations.

小寺秀俊

COVER STORY:
The invasive organs (pictured) of parasitic plants, such as *Phtheirospermum japonicum*, respond to the plant hormone ethylene.
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Physics modeling of viral spread between cells

Catherine Beauchemin
Deputy Program Director, RIKEN Interdisciplinary Theoretical and Mathematical Sciences (iTHEMS) program

Describe your role at RIKEN

I first joined RIKEN in 2016 as a senior visiting scientist at iTHES, the predecessor of the Interdisciplinary Theoretical and Mathematical Sciences (iTHEMS) program. In 2020, I became one of four iTHEMS deputy program directors. I am in a field I call 'virophysics'; the application of physics methods to virology. Primarily, I construct computer and mathematical models to explain the experimental observations made when viruses infect cell cultures. In biology, such knowledge is usually advanced through experimental trial and error, but physics modeling can help streamline this process.

How did you become interested in your field?

As an undergraduate in computational physics, I became interested in self-organizing systems and distributed intelligence. As a graduate student, I intended to work on social insect behavior, but my doctoral advisor wanted me to work with him on cancer. He gave me a paper called *Immunology for physicists*. Reading it, I became fascinated by how our immune system learns about new pathogens and retains that memory over a long time. Coincidentally, this happened around 2003, when the original SARS virus (SARS-CoV-1) hit China, Canada and other countries. The mathematical models in the papers I was reading always assumed that a cell close to an infected cell sees the same amount of virus as one that is far away. In my first research project I constructed a simple, spatial model for the spread of a respiratory virus infection to show how local effects impact cell-to-cell virus spread, and the immune response. There was very little known about SARS-CoV-1 at that time, so I decided to construct my first model based on the influenza virus. I didn't know that influenza would become important due to the possibility of an avian influenza pandemic, which remains a threat today.

> *"I construct computer models to explain the observations made when viruses infect cell cultures.*

My research is important to society because...

Let's say we want to determine the time between giving two doses of a vaccine to confer optimal protection. In immunology or virology, this is done by testing different dosing intervals in as many people as possible, and then we can choose only from the options that were tested. Without equations, we cannot predict what happens if the interval is longer or shorter, because the system is complex and the response is nonlinear. My research is developing physics-based equations that accurately predict what happens between and beyond the scenarios tested.

How has being at RIKEN helped your research?

The iTHEMS program was designed to stimulate interdisciplinary collaborations. There are many seminars on topics ranging from physics to biology and mathematics to information theory. We have informal, iTHEMS-wide seminars and coffee meetings on many of these topics. At these meetings, new ideas and perspectives emerge, and we exchange skills and techniques across fields. ■

Managing a marmoset brain atlas

Alexander Woodward
Unit leader, Connectome Analysis Unit, RIKEN Center for Brain Science

Describe your role at RIKEN

I lead a group that is a member of Japan's Brain/MINDS project that focuses specifically on the brain of the common marmoset. My group works on neuroinformatics applied to digital brain atlases and online database development. One of our current focuses is upgrading a digital marmoset brain atlas that we previously developed for Brain/MINDS.

Digital atlases are important to large-scale brain-mapping projects because you need a common digital space for integrating and organizing data from diverse experiments in 3D. Marmoset research has also become quite active in recent years, due to what it can reveal about human brain structure and function. Other activity from our group includes the work of Rui Gong, who has worked on how to improve atlas construction using artificial intelligence, and Takuto Okuno, who has developed a new method for causal analysis of functional brain networks where different regions are defined by a brain atlas.

How did you become interested in your current research?

I studied computer vision at the University of Auckland, New Zealand. A big focus was on how to get in-depth information from images by using a computer. I now apply these techniques to neuroimaging data.

How and when did you join RIKEN?

I joined RIKEN about six years ago as a member of Yoko Yamaguchi's Neuroinformatics Unit. Before that I completed a post-doc at the University of Tokyo with Takashi Ikegami. The lab there focused on complex systems and artificial life.

How has being at RIKEN helped your research?

Being able to interact with RIKEN's world-class researchers in neuroscience has definitely helped further my understanding of the brain. Additionally, working at RIKEN has meant we have always been able to get the computer equipment we need. Being a core part of Japan's Brain/MINDS project has also expanded my network within the neuroscience community.

What are some technologies you use?

We are always processing and mapping datasets on to one another or on to brain atlases. To do this we rely on image registration (mapping) algorithms. One of the key pieces of software we use to do this is called ANTs (Advanced Normalization Tools). We also use popular deep-learning libraries such as TensorFlow and PyTorch, and have recently been looking at how to use artificial intelligence running through web browsers. We have also been leveraging a high-performance computing cluster to batch process thousands of brain images.

What has been your most memorable experience at RIKEN?

I have fond memories of traveling, which has often been linked to the International Neuroinformatics Coordinating Facility (INCF). ■

Careers at RIKEN
For further information, visit our Careers page:
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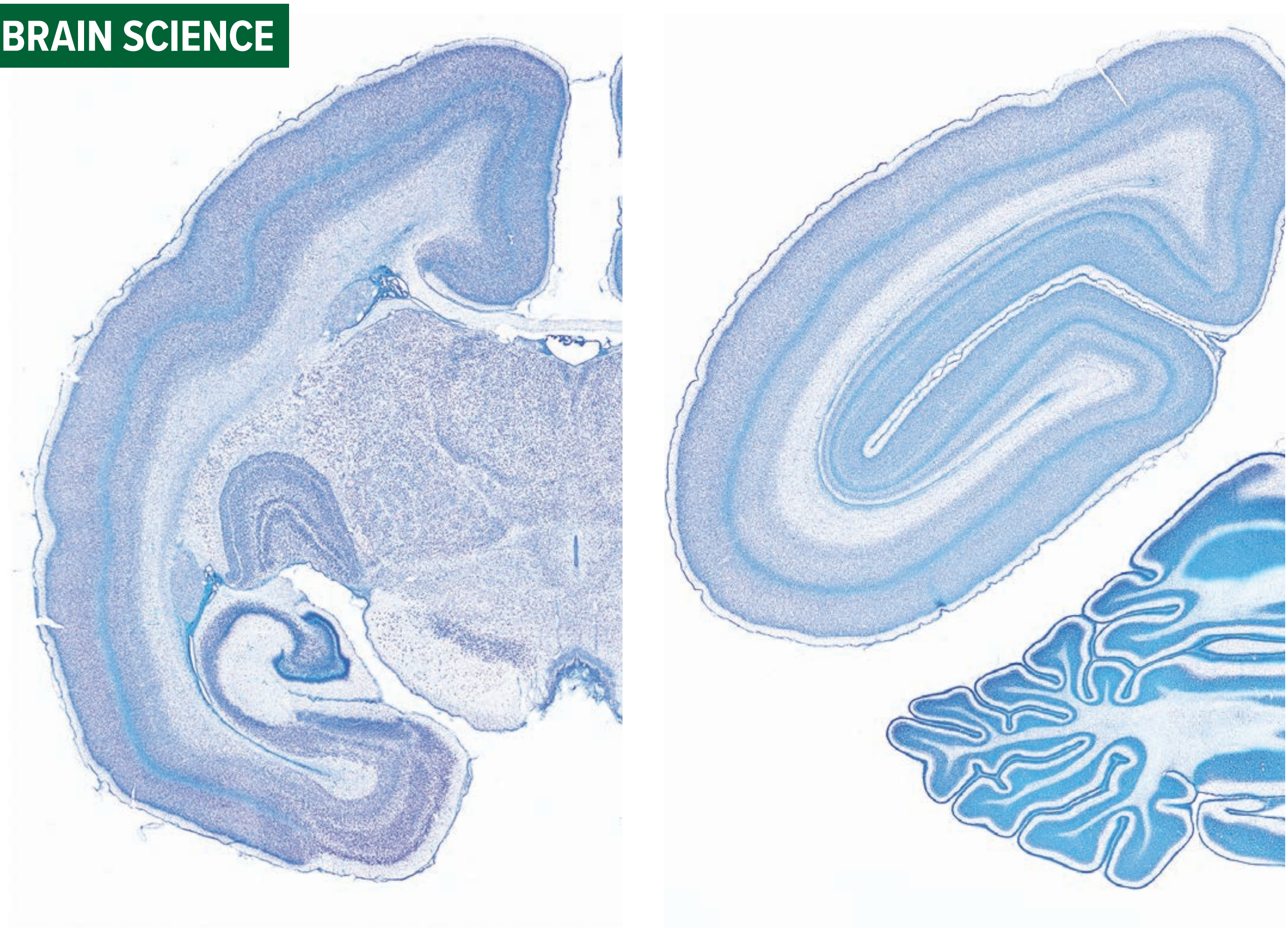
BRAIN SCIENCE



One of the aims of a new database of marmoset genes linked to developmental and psychiatric disorders is to identify the key brain regions involved.

Gene database

A team led by Tomomi Shimogori and Henrik Skibbe of the RIKEN Center for Brain Science has created a database containing 2,000 marmoset genes linked to expression patterns in developmental and psychiatric disorders and has identified risk genes for the disorders. Comprehensive analysis revealed that genes involved in psychiatric and neurological disorders are expressed in specific brain regions and neuron clusters. Analysis of expression patterns in marmoset, mouse and human brains showed many common patterns between marmosets and humans. The database will identify brain regions at the root of psychiatric disorders and the causes of genetic neural circuit dysfunction.

https://doi.org/10.1073/pnas.2020125118

RIKEN protects cherry blossoms

Climate change may be why the cherry trees in Kyoto reached full bloom on March 26 in 2021—the earliest date in 1,200 years of records. The reason: the common Somei Yoshino breed requires a protracted cold spell before spring to flower profusely, a pattern that is becoming less common in southern Japan. In 2010, RIKEN's Abe Tomoko and her colleagues scrambled cherry-cutting DNA via irradiation using a particle accelerator. The result was the Nishina Otome variety, which still flowers after a mild winter. Registrations have also recently been granted for two new varieties, Shinriko and Shinseiko, which bloom without low temperatures, and are being sold from this year on.

BDR Symposium

The virtual RIKEN BDR Symposium 2021 was held between March 1 and 3. The theme was Structuring Biosystems: Functions Emerging from Molecules. Twenty-five leading scientists talked about biomolecules that sustain essential cellular functions to 345 registrants from 22 different countries. Eisuke Nishida, BDR Center Director, noted that, while the cancellation of last year's symposium due to the pandemic was regrettable, the new online format has allowed many who may not have been able to join to participate. Next year's symposium, themed Emergence in Biological Systems: Challenges to Bridging Hierarchies, will be held online in March 2022.

https://www2.bdr.riken.jp/sympo/2021/

RNA diagnostic test for COVID-19 faster than current PCR detection

Scientists from the RIKEN Cluster for Pioneering Research have developed a new technology that can diagnose COVID-19 in minutes, by detecting single molecules of the SARS-CoV-2 virus' RNA. Unlike when testing using PCR, the most common method, RIKEN's method cuts out the time required for amplification of the RNA. The breakthrough, led by chief scientist Rikiya Watanabe and published in *Communications Biology*, was developed using a method called SATORI, which is a combination of leading-edge microchip technology and CRISPR-Cas13, which is used to detect nucleic acids. What is more, the cost per test is relatively close to that of the PCR test. In addition to detecting COVID-19, it is hoped SATORI technology could also be used to detect biomarkers of other diseases, including cancers.

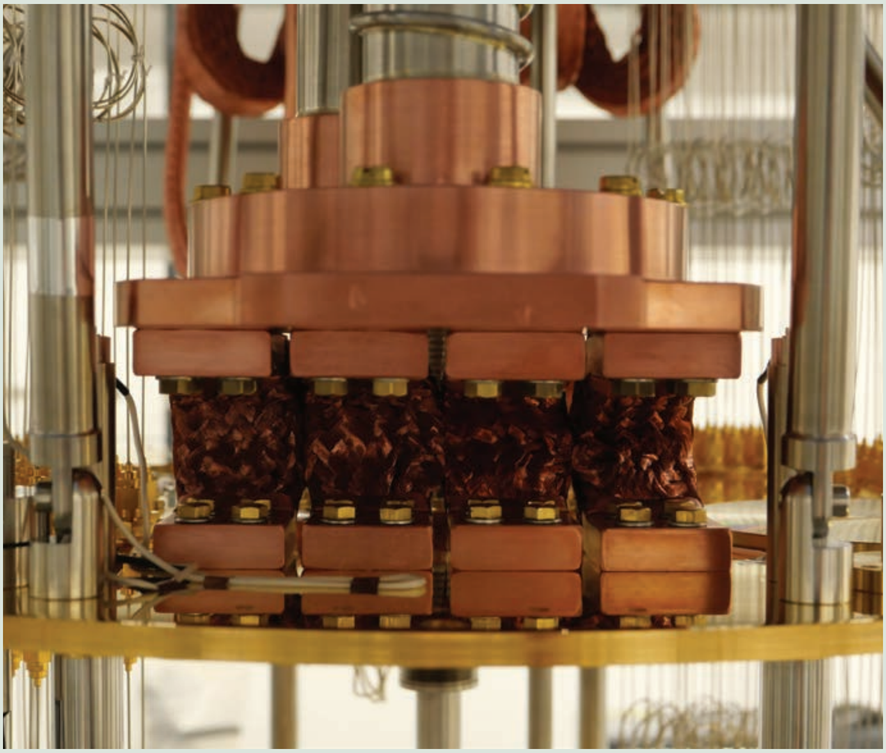
Read the paper: 10.1038/s42003-021-02001-8

More: www.riken.jp/en/news_pubs/news/2020/20210419_2/index.html

Virtual open day

On April 17, a virtual Open Day was held for three RIKEN campuses in Wako, Tsukuba and Sendai. During the online event, Shun-ichi Amari, from the RIKEN Center for Brain Science, discussed the brain and artificial intelligence, Atsushi Yoshiki of the RIKEN BioResource Research Center lectured on mouse models, and Tomoko Abe from the RIKEN Nishina Center for Accelerator-Based Science talked about creating novel plants using heavy-ion beams.

The Sendai campus offered a virtual lab tour and multimedia information on terahertz-wave research. The International Affairs Division also organized an informal virtual talk by Junichi Aikawa from the RIKEN Innovation project. Aikawa studies protein in termites. Another speaker at this virtual 'science cafe', Alia Oktiavani, from the RIKEN Center for Sustainable Resource Science, gave a talk titled 'Unraveling how spiders spin their silk'.



At the new RIKEN Center for Quantum Computing, researchers are already creating the complex architecture required of superconducting qubit computer processing.

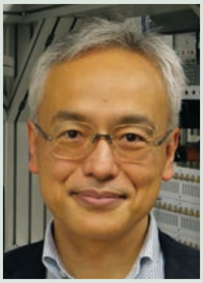
Japan's new quantum center

The new RIKEN Center of Quantum Computing (RQC) was established on April 1, 2021.

It forms a focal point for a national strategy aimed at innovation in quantum information technology. The center will focus on the basics of quantum information, as well as creating quantum computing systems and different types of qubits (see page 8).

The new center will focus on superconducting qubits, based on the work of director Yasunobu Nakamura and team leader Jaw-Shen Tsai, as well as optical quantum computers led by Deputy Director Akira Furusawa, and hardware relating to the use of various types of physical systems including electron spins in semiconductors and atoms in vacuum. Software will also be explored with regards to quantum computing theory, quantum algorithms and quantum architecture.

Partners outside RIKEN include Fujitsu Limited, with which a joint research center was recently established.



Yasunobu Nakamura.

RIKEN also serves as the headquarters of the Quantum Technology Innovation Hubs (QIH), which are also linked to the government plan and have been set up elsewhere, including at the Tokyo Institute of Technology, the National Institute for Materials Science, the National Institutes for Quantum and Radiological Science and Technology, the National Institute of Information and Communications Technology, Osaka University, the National Institute of Advanced Industrial Science and Technology, and the University of Tokyo.

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

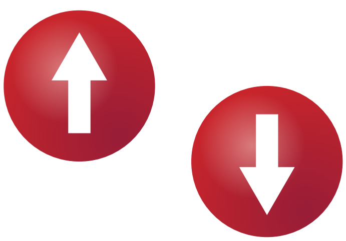
QUANTUM QUESTIONS

The new RIKEN Center for Quantum Computing (RQC) is co-ordinating the Japanese-government's quantum agenda, and exploring a number of important approaches for qubits, quantum circuits and quantum architecture.

QUANTUM COMPUTING AND QUBIT 101

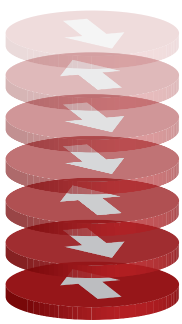
Researchers have long predicted that harnessing the complex quantum-mechanical properties of atoms and subatomic particles for computer processing could help tackle certain types of problems—especially those involving a daunting number of variables and potential outcomes, like simulations or optimization questions—faster than any classical computer.

Quantum computers can process information using 'qubits', which act in much the same way as classic binary bits. But while a bit represents either of two distinct states (0 or 1), the unique properties of a qubit means it can be in more than two states (see right).



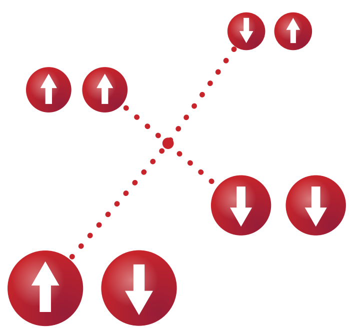
BITS (0 OR 1)

A qubit is unique in that it can be in two states simultaneously. For example, it can be placed into superpositions, in which one state is imposed over another, as if the qubit then exists in both states at once.



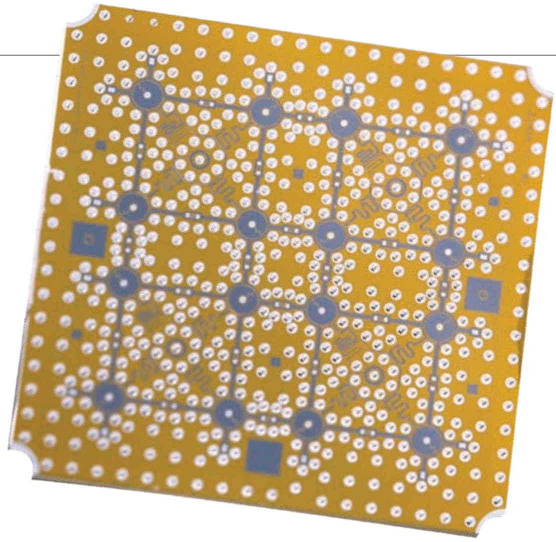
QUBITS (SUPERPOSITION)

Qubits can also be subject to entanglement, in which the state of one qubit is correlated to the state of one or more others, even if they are separated by space.



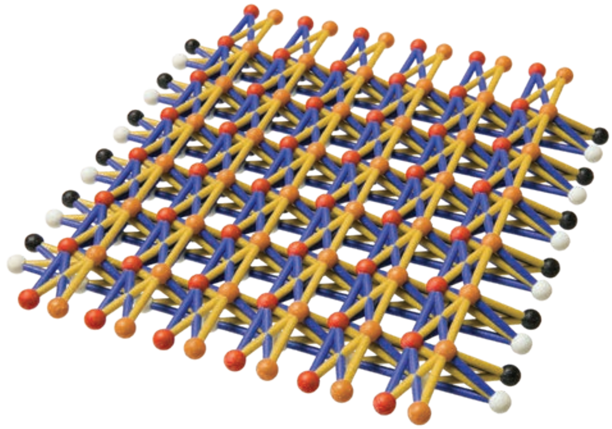
QUBITS (ENTANGLEMENT)

The newly established RIKEN Center for Quantum Computing is exploring quantum frontiers. Four examples of their approaches are shown to the right.



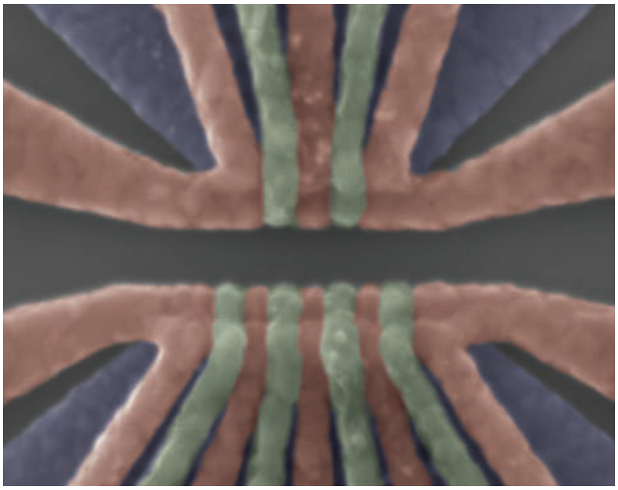
1 SUPERCONDUCTING QUANTUM BIT

Superconducting circuits are macroscopic in size, but feature quantum properties such as quantized energy levels, superposition states and entanglement. Their qubits are manipulated by using electromagnetic pulses that control the magnetic flux, the electric charge or the phase difference across a Josephson Junction (a device with nonlinear inductance and no energy dissipation). On this RIKEN designed 16-qubit superconducting circuit on a 1 cm^2 silicon chip, the qubits are placed at the gray dots with rings. A number of holes in the chip electrically connect the top and bottom surfaces. Coaxial wires for microwave signals are attached to the backside of the chip to help with control and to read the states of the qubits.



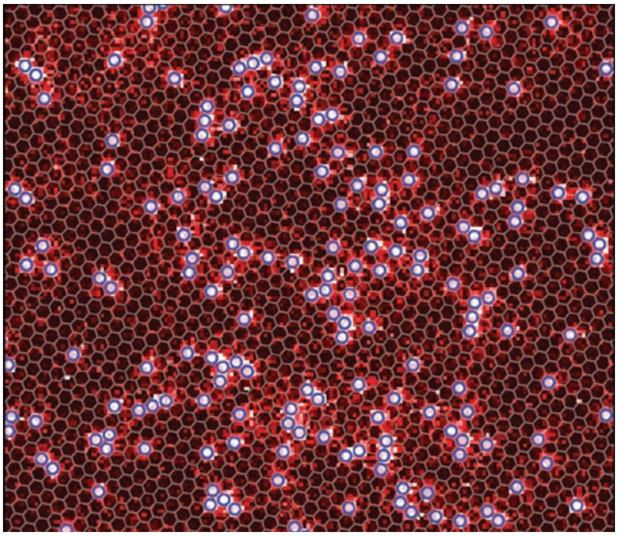
2 OPTICAL QUANTUM COMPUTING CLUSTERS

Developing useful qubit cluster states is key to scaling up quantum computers, as they will help facilitate complex control over many qubits. These clusters can be formed by entangled qubits—in which the state of each qubit is correlated to the state of one or more other qubits. Cluster states that use optical modes and multipartite entangled states could act as a sort of index for quantum information. The RQC wants to use the uncertainty associated with the amplitude and phase of the state of light. If this quantum uncertainty is unequally distributed, the state is said to be squeezed; and the more the state is squeezed, the more photons are correlated. Processing information via multi-photon squeezed light could be a basis for optical quantum computing in cluster states.



3 SEMICONDUCTOR ELECTRON SPIN

Spin is an intrinsic property of electrons, which can be thought of as rotating around an axis in either a clockwise or anticlockwise manner. Based on their spins, electrons react to magnetic fields in different ways, for example, by aligning themselves with other electrons in a specific pattern. In 2020, RIKEN researchers created a useful qubit system by controlling the synchronization of electron spins of natural silicon quantum dots (found at the end of the red and gray lines, above) using microwave drive. The group showed that a resonant drive controlled the electron spins of two silicon quantum dots that aligned with an accuracy of 99.6%, the highest reported for two-spin synchronization.



4 ULTRACOLD ATOMS/ FLOATING ELECTRONS

Patterns of ultracold atoms or 2D formations created by electrons and using electrostatic charge to make them hover above liquid helium could provide the basis for new qubit systems. In 2020, RIKEN researchers demonstrated single-atom resolved imaging of ultracold rubidium (^{87}Rb) atoms in a triangular optical lattice. They managed a detection fidelity of 96.3% during imaging through machine-learning-based automatic optimization of the Raman sideband experimental parameters for fluorescence imaging.

SKYRMIONS

Revealing the origins of skyrmion lattices

Interactions between electrons help to organize magnetic whirlpool structures into a repeating grid

RIKEN physicists have discovered how interactions between electrons can stabilize a repeating arrangement of swirling magnetic patterns known as skyrmions, which could help to further exploit these structures[1].

The spin of an electron causes it to behave like a miniature magnet. In a skyrmion, many of these spins are arranged in a swirling pattern that resembles a tiny tornado. Skyrmions are highly promising as a means of carrying information in a new generation of high-density, low-energy data-storage devices.

Skyrmions behave as if they are distinct particles, and multiple skyrmions can arrange themselves into a regular grid within certain types of material. But researchers are still debating how these stable skyrmion lattices form.

This could provide researchers with a useful tool to study skyrmion lattices in other materials

To discover more about skyrmion lattices, Yuuki Yasui at the RIKEN Center for Emergent Matter Science and colleagues studied a metallic material called gadolinium ruthenium silicide ($GdRu_2Si_2$; see image). Electrons in the material's gadolinium atoms are largely responsible for its magnetic properties, while the ruthenium atoms contribute 'itinerant' electrons that are more mobile.

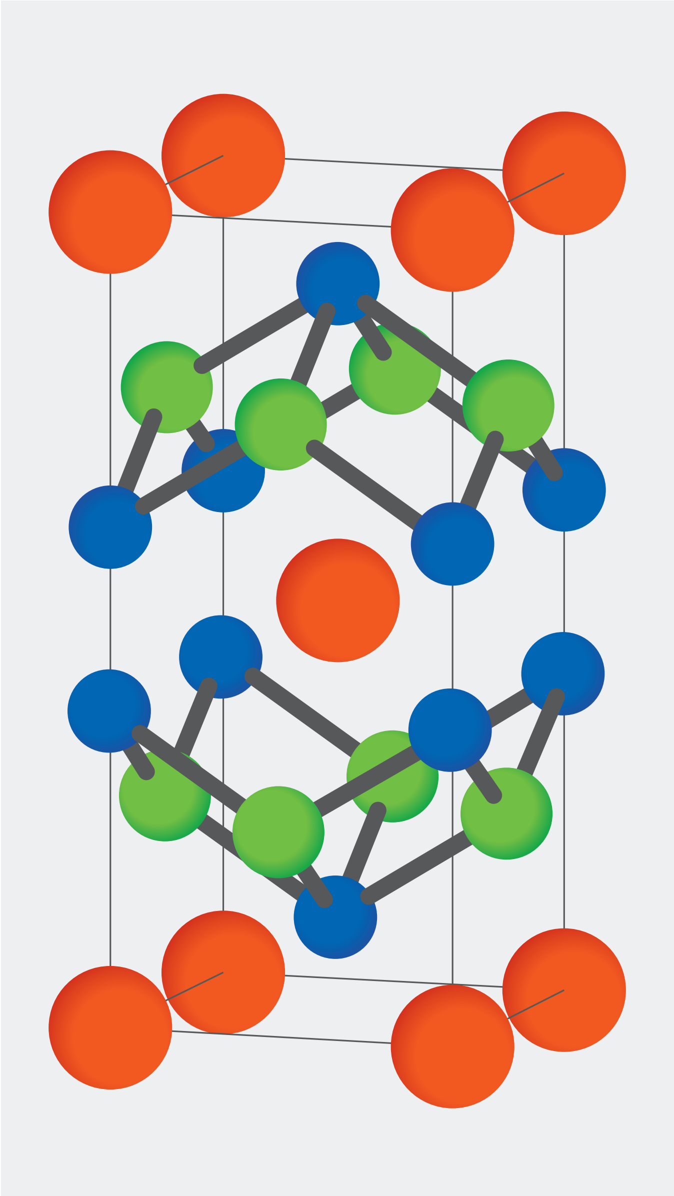
The team had previously found that by applying a magnetic field to the material, they could create a square lattice of skyrmions arranged in a grid pattern at intervals of about 2 nanometers. In the new study, they used a technique called spectroscopic-imaging scanning tunneling microscopy (SI-STM) to study the itinerant electrons in $GdRu_2Si_2$.

The researchers cooled the material to –271 degrees Celsius and applied a range of magnetic fields to generate different magnetic patterns. SI-STM measurements showed that changes in the material's magnetic patterns were reflected in the distribution of itinerant electrons. Crucially, the team also saw that the skyrmion lattice pattern is imprinted on the material's itinerant electrons, due to interactions between the spins of localized and itinerant electrons.

The researchers suggest that these interactions could play an important role in the formation of the square skyrmion lattice. "The proposed mechanism stabilizes skyrmion lattices," says Yasui.

The team also performed theoretical calculations, based on the interactions between localized and itinerant electrons, to predict the distribution of itinerant electrons in the material under different magnetic fields. These distributions were very similar to the patterns observed by SI-STM, lending support to the mechanism proposed by the researchers.

In addition to providing clues about how skyrmion lattices are stabilized, the research shows that SI-STM can be used to indirectly monitor the behavior of skyrmions. "This could provide researchers with a useful tool to study skyrmion lattices in other materials," says Yasui. ●



The crystal structure of gadolinium ruthenium silicide, which can host a square lattice of swirling magnetic skyrmions (orange = gadolinium; green = ruthenium; blue = silicon).

Reference

1. Yasui, Y., Butler, C. J., Khanh, N. D., Hayami, S., Nomoto, T., Hanaguri, T., Motome, Y., Arita, R., Arima, T., Tokura, Y. & Seki, S. Imaging the coupling between itinerant electrons and localised moments in the centrosymmetric skyrmion magnet $GdRu_2Si_2$. *Nature Communications* **11,** 5925 (2020).

COVID-19

Glycans play crucial role in COVID-19 infection

Simulations by a pair of supercomputers reveal how glycans help SARS-CoV-2 to invade cells

Efforts to design drugs for preventing and treating COVID-19 stand to benefit from the discovery by RIKEN scientists that sugar molecules called glycans play an important role in the structural changes that occur when SARS-CoV-2, the virus that causes the disease, invades a human cell[1].

When invasion occurs, a spike protein on the virus' surface binds to an enzyme called ACE2 on the surface of the cell. The spike protein consists of three polypeptide chains, and it has glycans attached to its surface. These glycans are thought to help viruses to evade attack by antibodies produced by the body's immune system.

Structural analyses have shown that the spike proteins of SARS-CoV-2 have up- and down-form structures. While these analyses have advanced our understanding of the three-dimensional structure of the spike proteins, the detailed molecular structure of the highly fluctuating glycans is still not understood and the role glycans play in the process of cell invasion remains unclear.

"We need to develop better preventative and therapeutic measures to bring the pandemic to an end"

Now, a team led by Yuji Sugita of the RIKEN Center for Computational Science (R-CCS) has conducted molecular dynamics simulations for the up- and down-form structures of the proteins, using two supercomputers—Fugaku at the R-CCS and Oakforest-PACS at the University of Tokyo. Using these powerful machines, they performed molecular dynamics simulations of the spike proteins at a time scale of 1 microsecond.

"Research projects like this show us how the new generation of powerful supercomputers will allow us to gain new insights into many phenomena by performing simulations at a level of detail that would have been impossible previously," says Sugita.

The study provided new insights into how glycans help to stabilize the dynamic structure of the proteins. From the calculations, the team was able to identify specific glycan-attached amino acids in the spike protein that play an important role in stabilizing the structure of the receptor-binding domain. Their results suggest that electrostatic repulsion between the domains drives the conformational change to the up-form structure. They also indicate that glycans that stabilize the down-form structure are dislodged and replaced by other glycans after the domains are displaced.

Information like this is valuable for combating the pandemic. "We need to develop better preventative and therapeutic measures to bring the pandemic to an end," says Sugita. "It would be very useful to be able to design drugs taking the structural changes of spike proteins into account, by stabilizing the down-form or inhibiting the change to the up-form, for example." ●

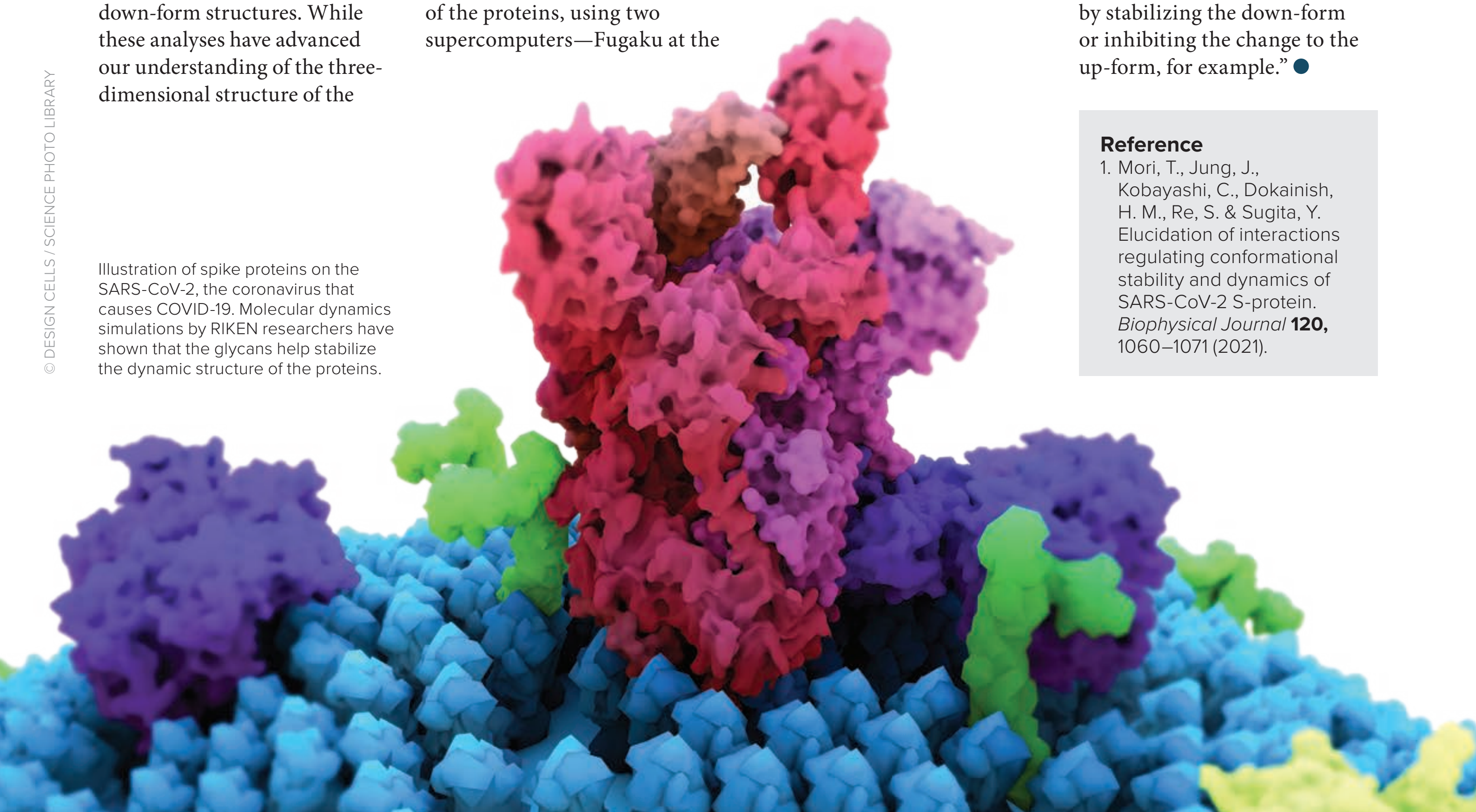


Illustration of spike proteins on the SARS-CoV-2, the coronavirus that causes COVID-19. Molecular dynamics simulations by RIKEN researchers have shown that the glycans help stabilize the dynamic structure of the proteins.

Reference

1. Mori, T., Jung, J., Kobayashi, C., Dokainish, H. M., Re, S. & Sugita, Y. Elucidation of interactions regulating conformational stability and dynamics of SARS-CoV-2 S-protein. *Biophysical Journal* **120,** 1060–1071 (2021).

ROOT GRAVITROPISM

Choreographing the downward dance of plant roots

The identification of a transporter protein involved in root gravitropism should benefit agriculture

In a finding that could be used to improve the nutrient uptake of crops, a RIKEN-led team has identified a transporter protein that is involved in the tendency of plant roots to grow downwards in response to gravity, a phenomenon known as root gravitropism[1].

Charles Darwin was among the first scientists to investigate root gravitropism in plants. Through simple but elegant experiments, Darwin showed that plant root tips sense gravity and that they transmit the signal to neighboring tissues so that roots bend toward gravity. We now know that the plant hormone auxin plays a key role in this gravitropic response.

This should improve the uptake of water and nutrients by roots

Plant hormones serve many physiological functions and help plants withstand fluctuations in their environment. To function properly, their distribution and activity in cells and tissues must be precisely choreographed. This often involves transporter proteins that mediate the uptake or export of hormones or their precursors by cells.

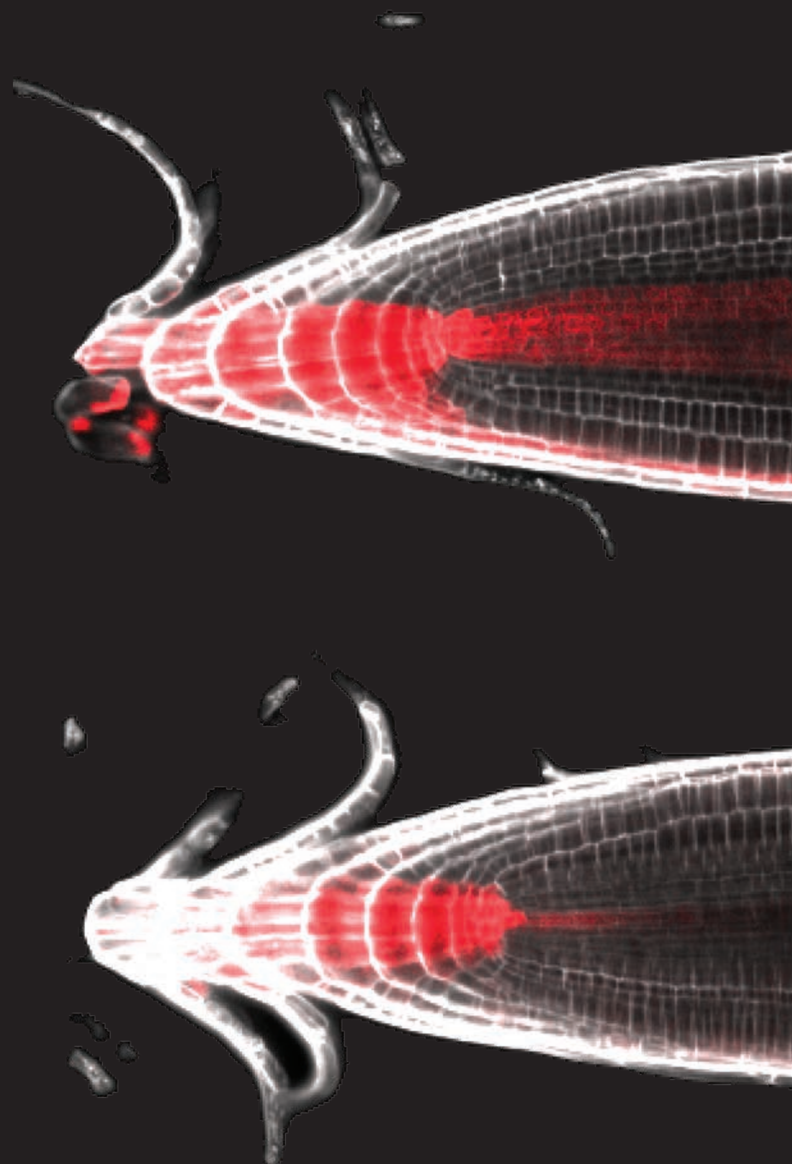
RIKEN biologists have now shown that a previously described transporter protein, NPF7.3, regulates auxin responses and root gravitropism in the model plant *Arabidopsis*.

"We noticed that seedlings in which the gene encoding NPF7.3 was mutated displayed abnormal root growth," says Mitsunori Seo of the RIKEN Center for Sustainable Resource Science. "Closer inspection revealed specific defects in gravitropic responses, which were not explained by previously reported functions of NPF7.3 as a nitrate and potassium transporter. This made us suspect that this protein might have additional, previously uncharacterized functions."

Subsequent experiments demonstrated that NPF7.3 functions as a transporter of indole-3-butyric acid (IBA), and that IBA taken up by specific root cells via NPF7.3 is converted into indole-3-acetic acid (IAA), which is the major naturally occurring plant auxin. This helps establish auxin gradients in root tissues, which in turn direct the gravitropic response.

IBA is a minor precursor of IAA, and the involvement of IBA-derived IAA in gravitropism was previously unknown. However, it seems likely that other plants, including crop species, share similar regulatory mechanisms, which could lead to agricultural and horticultural applications.

"We will be able to modify root architecture by regulating IBA transport," says Seo. "This should improve the uptake of water and nutrients by roots, and hence promote crop production."



Asymmetric distribution of auxin activities (shown in red), which is required for proper gravitropic responses, is observed in wild type (top), but not in roots in which the gene encoding NPF7.3 is mutated (bottom).

NPF proteins were originally identified as nitrate or peptide transporters, but it is becoming clear that they are more adaptable than previously thought. "Recent studies, including this one, indicate that this transporter family conveys various compounds including plant hormones and secondary metabolites," says Seo. "As a next big question, we want to know how NPF proteins recognize such a variety of substrates."

Reference

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THE CRAB PULSAR

Giant pulses have gigantic levels of energy

After decades of observations, astronomers have finally found clear evidence of an increase in x-ray emission associated with giant pulses previously observed in the radio band

The giant pulses emanating from the Crab pulsar may be hundreds of times more energetic than previously believed, observations by RIKEN astronomers suggest[1]. They found an increase in x-ray emission associated with the giant radio pulses.

A dozen pulsars in our Galaxy emit extremely short (microsecond duration) pulses of radio waves known as giant radio pulses. Little is known about the mechanism that causes them. They may be the origin of the mysterious phenomenon known as fast radio bursts—rapid bursts of radio waves that are believed to originate from energetic events in the extragalactic universe.

To gain insights into these phenomena, the RIKEN-led group made coordinated observations of the Crab pulsar—one of the most famous and well-observed pulsars. Chinese and Japanese observers witnessed the explosion of this star in a supernova explosion in 1054, and it led to the formation of the beautiful Crab Nebula that can still be seen today.

The group began looking to see if there was an increase in x-ray emissions associated with giant radio pulses. Despite many observations over several decades, researchers had been unable to make any unambiguous detections in x-rays. The observations were based on a coordinated international campaign of simultaneous space-based x-ray and ground-based radio observations. The space-based observations were done with NICER, a new instrument aboard the International Space Station, while the radio observations were made by two observatories in Japan. After continuing the campaign for three years, the team eventually found a clear signal indicating an enhancement of x-ray emissions associated with an increase at the radio wavelength.

The enhanced emission detected in the x-ray band was similar to that previously reported in the visible band, but nothing similar has ever been observed from any of the other 2,800 known pulsars. "Our measurements imply that these giant pulses are hundreds of times more energetic than previously thought," says Teruaki Enoto, the leader of the Extreme Natural Phenomena RIKEN Hakubi Research Team.

These observations also impose important constraints on models of fast radio bursts, which are thought to be associated with pulsars and possibly young ones like the Crab pulsar. "However, the relationship between the two is still controversial," says Enoto. "These findings, along with upcoming discoveries regarding fast radio bursts, will help us to understand the relationship between these phenomena."

"Our result not only has a broad impact on pulsar and fast radio burst science but also represents a fitting legacy for the Kashima 34-meter telescope, which was a valuable instrument for the radio-astronomy community but was irreparably damaged by a typhoon in 2019," adds Enoto.

Giant pulses from the Crab pulsar in the Crab Nebula (shown) may be hundreds of times more energetic than previously thought.

Reference

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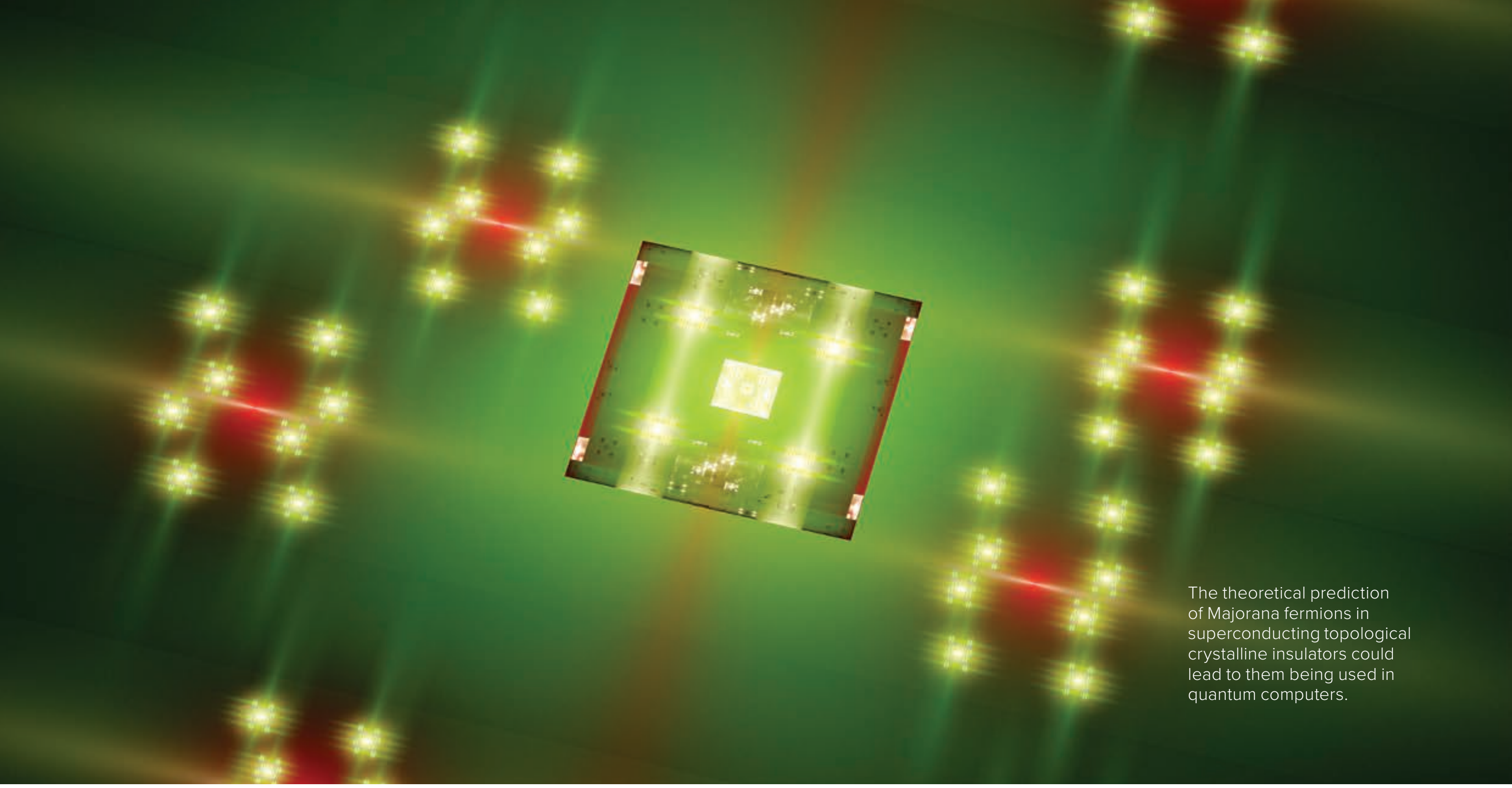

The theoretical prediction of Majorana fermions in superconducting topological crystalline insulators could lead to them being used in quantum computers.

TOPOLOGICAL SUPERCONDUCTORS

New way to create particles for quantum computers predicted

A large class of quantum materials could host hypothetical particles useful for quantum computers

A broad class of quantum materials could be used to create particles for use in quantum computers, calculations by two RIKEN theoretical physicists have predicted[1].

Every fundamental particle has an antiparticle counterpart with the same mass but the opposite electric and magnetic characteristics. For example, the antiparticle of the negatively charged electron is the positively charged positron.

A special class of particles that are their own antiparticles has been theoretically predicated. These so-called Majorana fermions have not yet been identified in experiments that probe the physics of elementary particles. However, composite particles or quasiparticles that mimic the same properties have been created in exotic materials.

Quasiparticle Majorana fermions have been observed at the interface between superconductors and topological insulators—materials that are electrically insulating on the inside but conduct a current on their surfaces. Majorana fermions observed in this two-component system maintain their state even in the presence of defects and disturbances. This robustness makes them promising as a platform for quantum computation.

"Recent experiments have found evidence for a Majorana fermion at vortices in hybrid systems of topological insulators and superconductors," explains Shingo Kobayashi from the RIKEN Center for Emergent Matter Science (CEMS). "But it is still highly challenging to create Majorana fermions."

Kobayashi and his CEMS colleague Akira Furusaki are hoping to make it easier to form Majorana fermions through identifying a broader range of materials that can support them. So they theoretically investigated a type of topological insulator known as a topological crystalline insulator, in which the surface is conducting due to the symmetry of the material's atomic structure.

"Recent work that combined calculations and material databases has theoretically uncovered several thousand topological materials with topological phases enabled by crystalline symmetry," notes Kobayashi.

The calculations performed by Kobayashi and Furusaki showed that the crystalline symmetry that creates the surface states in a topological crystalline insulator also plays an important role in protecting Majorana fermions.

Furthermore, the pair discovered that these systems can support states with multiple Majorana fermions. Unlike a single Majorana fermion, these multiple Majorana fermions can react to external perturbations such as magnetic fields or physical strain. This finding offers ways to manipulate the fermions, which is vital if they are to be implemented in a topological quantum computer.

"The next step will be to apply our generalized mechanism to material databases and predict materials that are suitable for achieving these Majorana fermions," says Kobayashi. ●

Reference

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INDUCTORS

Bringing inductors down to size

Inductors are set to join other electronic components in being miniaturized thanks to a quantum effect

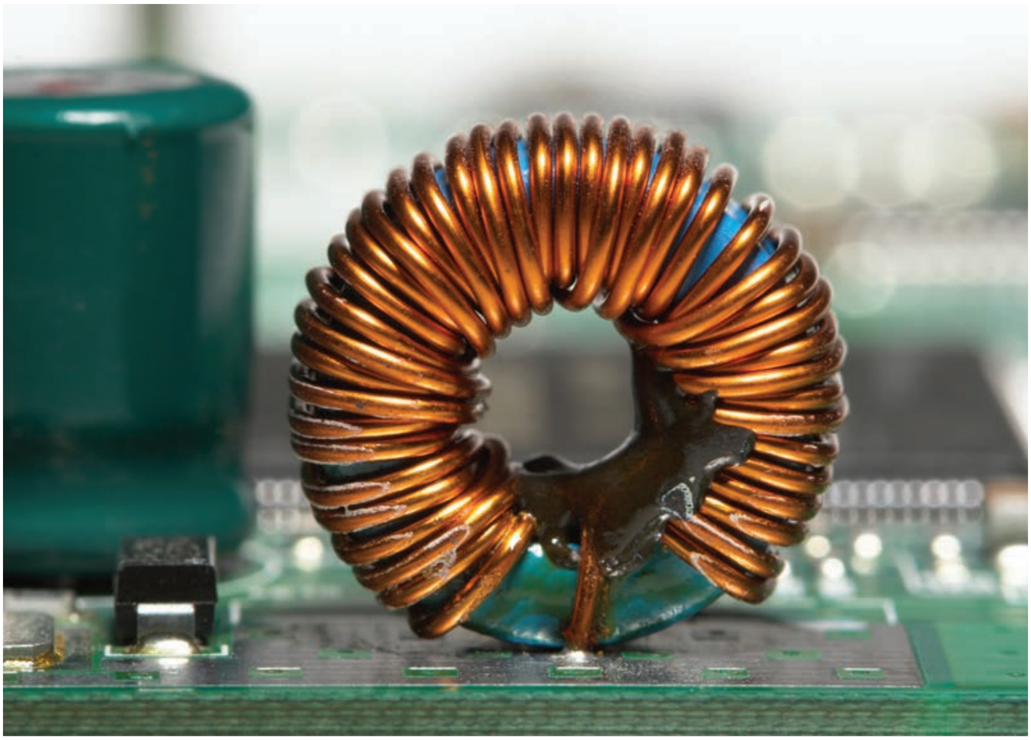
Mobile-phone chargers and other devices could become much smaller after an all-RIKEN team of physicists successfully shrunk an electrical component known as an inductor to microscale dimensions using a quantum effect[1].

Inductors are a basic component of modern electrical circuits, and they are used in a wide range of applications including information processing, wireless circuits and chargers for mobile devices. They are based on the law of induction that English physicist Michael Faraday discovered in 1831. But while physics has made great leaps since then, the fundamental principles of inductors remain essentially the same—they are basically coils of wire.

Unlike other electrical circuit components, inductors have been difficult to miniaturize because the size of their inductance diminishes with their volume, such that if you halve their volume, the inductance drops by half too.

Now, Yoshinori Tokura, Tomoyuki Yokouchi and their co-workers, all at the RIKEN Center for Emergent Matter Science, have generated an inductance equivalent to that of commercial inductors but in a component whose volume is about a million times smaller.

They achieved this by using a new mechanism for generating inductance that depends on quantum effects. Inductors based on this mechanism will be easy to shrink since their inductance actually increases with decreasing cross-sectional area.



A conventional inductor mounted on a printed circuit board. Inductors have resisted miniaturization until now, but the demonstration of a quantum source of inductance by RIKEN researchers promises to result in much smaller inductors.

"We discovered an electromagnetic inductance of quantum-mechanical origin," says Yokouchi. "This has big potential for the miniaturization of inductors, one of the most fundamental parts of contemporary electric circuits."

One of the authors, Naoto Nagaosa, had previously theoretically proposed a totally new mechanism for electromagnetic induction based on emergent electromagnetism, a new form of electromagnetism that arises from the quantum-mechanical properties of conduction electrons in specially engineered systems. In the present study, the team realized this effect by using a micrometer-scale magnet. The electron spins that give rise to the magnetism are arranged in a spiral-like arrangement, mimicking the coils of a conventional inductor.

Yokouchi notes that the success of the study hinged on the collaborative environment at RIKEN. "Strong collaboration between theorists and experimentalists was essential for this project," he says. In particular, the experimentalists have tremendous expertise in fabricating advanced quantum materials.

The team's nanoscale inductor operates only at very low temperatures, so they are now looking for materials that behave similarly at high temperatures. "For applications, we have to find a material that generates emergent inductance at and above room temperature," says Yokouchi. "We've already started searching for prospective materials." ●

Reference

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MUTATION BREEDING

Supersized snacks for growing fish

Larger strains of zooplankton could improve survival rates in fish farms

A RIKEN-led team has developed larger strains of zooplankton, which are an important feed stock in fish nurseries, by creating mutations with a heavy-ion beam[1]. These new strains could improve the survival rate and optimize the growth of juvenile fish in farms.

Food shortages due to population growth and increased consumption are a major global concern, and countries around the world are seeking ways to increase food production. Resources from the oceans, which cover 70% of the Earth's surface, are one promising solution to this challenge.

The bred rotifers were approximately 1.2 times larger than other strains

Economically important fish species, such as bluefin tuna, yellowtail and flatfish, are fed live bait until they are sufficiently large to be fed with artificial foods. Rotifers (see image) are a type of animal plankton, and they are commonly used as the initial live food. Fish need progressively larger bait as they grow, but rotifers are often too small to satisfy the growing fish, leading to cannibalism or growth abnormalities that curb the survival rate.

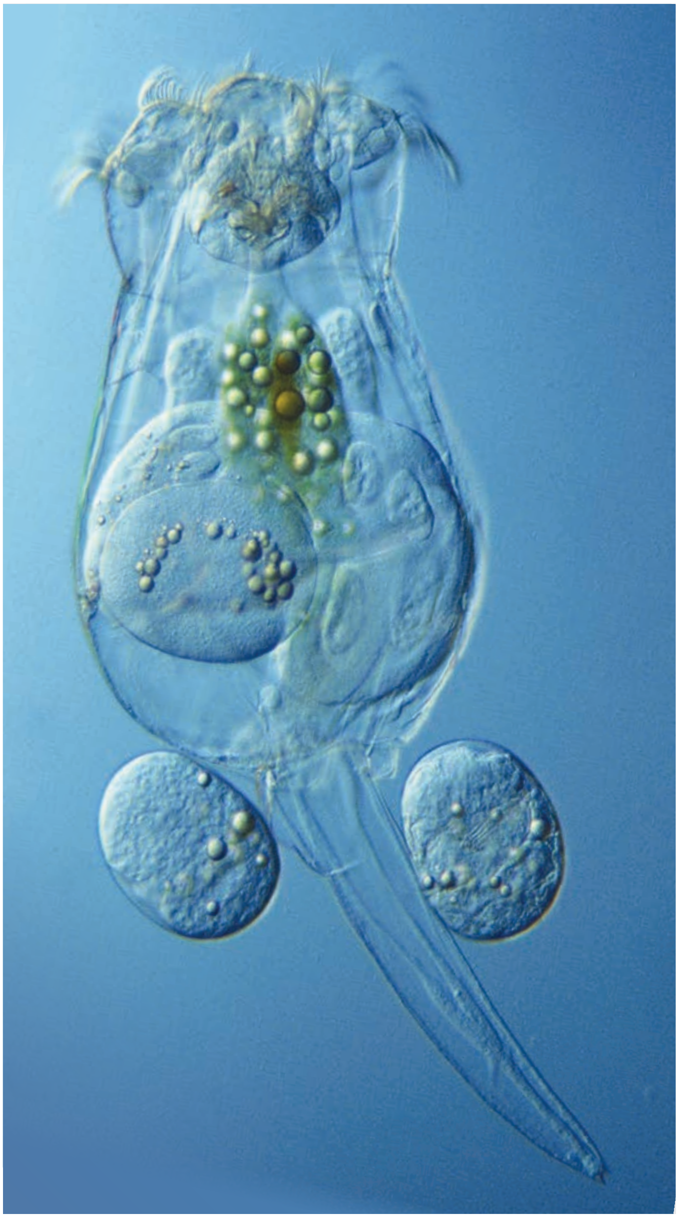
"We decided to try to do something to improve the survival rate of fish larvae, as this would help to increase aquaculture productivity," says Tomoko Abe of the RIKEN Nishina Center for Accelerator-Based Science. "We thought that if we could create a large rotifer strain using our expertise, it would contribute to stabilizing the income for aquafarmers."

The team used a technique known as heavy-ion-beam irradiation to create larger rotifers. It involves exposing cells to a beam of heavy atomic nuclei. By adjusting the type of ion and dose, the beam can induce random mutations in the genome, and strains with desirable phenotypes can be selected.

Using the RIKEN RI Beam Factory, the team irradiated proliferating rotifers with beams of argon and carbon ions. They then selected larger individuals and cultured the plankton for several generations to create a large mutant line. The bred rotifers were approximately 1.2 times larger than other strains, which the team judged would be an ideal size for growing juvenile fish.

Some of the strains were not only larger, but also grew faster than the parent strains. "In general, larger mutants grow more slowly than normal rotifers, but we were lucky to discover a line that grows not only larger but faster as well," says Abe. "However, picking a large mutant among live rotifers that are moving quickly around under a microscope was far more difficult than we had anticipated and actually was the hardest part of this study."

The enlarged rotifers could provide a stable supply of larger rotifers at low cost, enhancing aquaculture. The team now plans to see if the larger rotifers survive longer in field tests. ●



A differential interference contrast light micrograph of a rotifer. RIKEN researchers have created larger strains of the zooplankton, which is used for feeding fish in fish farms.

Reference

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Chemists at RIKEN have found that the photoionization of phenol occurs 10,000 times faster at the interface between water and air than entirely within water.

INTERFACE CHEMISTRY

Chemical reaction zips along at water surface

A light-induced reaction proceeds much faster at the surface of water

A chemical reaction powered by light occurs about 10,000 times faster at the interface between air and water than within water, three RIKEN chemists have demonstrated[1]. This finding could improve our understanding of the many important chemical and biological processes that occur at the water surface.

Chemical reactions that occur at the interface between air and water abound in nature and many industrially important processes. Considerable indirect evidence indicates that chemical reactions at water interfaces differ from those in water. But reactions at liquid interfaces are difficult to study because it is so hard to isolate the molecules on the surface from those immediately below the surface.

Now, Ryoji Kusaka, Satoshi Nihonyanagi and Tahei Tahara,

> **The same reaction also occurred at an air–water interface, but roughly 10,000 times faster**

who were all at the RIKEN Molecular Spectroscopy Laboratory at the time of the study, have used an advanced spectroscopy technique to take high-speed movies of the intermediate molecules created as a chemical reaction occurred at an interface. The movie frames were obtained every 100 femtoseconds or so (1,000 femtoseconds are equivalent to one trillionth of a second).

The researchers' method used ultrashort pulses of ultraviolet light to analyze the photoionization of phenol, a reaction in which light knocks out an electron and a proton from a phenol molecule. They found that the same reaction also occurred at an air–water interface, but roughly 10,000 times faster due to the different conditions there.

"It was exciting to find that the reaction speed for phenol is so phenomenally different," says Nihonyanagi. "But in addition, our method for directly observing chemical reactions at the water surface in real time could also be applied to other reactions, and might help us get a better understanding of how reactions proceed in this special environment."

"The fact that there is a 10,000-fold difference in the reaction rate of a basic organic molecule such as phenol between the bulk water and the water surface is also very important for catalytic chemistry, the field of study that aims to promote and control chemical reactions," says Tahara, who led the trio.

The findings could have implications for environmental studies as well. "Water in nature exists as seawater, which has bubbles and aerosols, thus having a vast surface area. Our work could help us to understand how molecules are adsorbed and react on the surface of water, leading to the elucidation of chemical reactions that have an enormous impact on the global environment." ●

Reference

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RIKEN researchers have found that the gene that codes for a key regulator of the formation of synapses between neurons in the brain such as these is mutated in people with schizophrenia.

SCHIZOPHRENIA

A new drug target for schizophrenia

A protein involved in fat metabolism is also found to control synaptic growth, a process that's deficient in schizophrenia-affected brains

New therapies that improve connectivity and circuitry in the brains of people with schizophrenia could result from the discovery by a RIKEN-led team of a potential new target for drugs to treat the psychiatric disorder[1].

Treatment for schizophrenia has not changed much in 60 years. Doctors still generally prescribe medicines designed to tame psychosis by blocking neurotransmitter signaling in the brain. While the drugs ease symptoms such as delusions and hallucinations, they leave many other aspects of the illness untreated and their side effects can be off-putting to many patients. Researchers are thus keen to find new targets for drugs.

In search of new molecular targets, a team led by Takeo Yoshikawa and Motoko Maekawa from the RIKEN Center for Brain Science focused on a metabolic pathway previously implicated in the development of schizophrenia. They used targeted sequencing techniques to probe six genes, each encoding a protein from the peroxisome-proliferator-activated receptor (PPAR) family or one of its signaling partners.

By conducting a genetic analysis of 1,200 people with schizophrenia, the researchers identified several harmful mutations in the gene encoding PPARα that were absent in a large sequence database of DNA from Japanese individuals in the general population. Experiments involving cells showed that these mutations reduced the expression levels of PPARα. Additionally, mice engineered to lack PPARα displayed behavioral and molecular deficits consistent with symptoms of schizophrenia.

A gene-expression analysis of brain tissue taken from the mutant and normal mice revealed that PPARα is a key regulator of synapse formation in the brain. This adds to the protein's known metabolic role throughout the body.

To boost synaptic function—a well-documented problem in people with schizophrenia—the team gave mice a drug called fenofibrate, which activates PPARα. Fenofibrate is already taken by millions of people every day to help control cholesterol and fat levels in the blood. The researchers showed that the drug helped alleviate brain and behavioral abnormalities in various mouse models of schizophrenia.

However, because fenofibrate does not readily cross the blood–brain barrier, the scientists had to administer very high doses of the drug. That approach would be risky in people, says Maekawa, since fenofibrate can sometimes seriously damage muscle tissue. To avoid that potential side effect, drug developers may have to refine the chemistry of fenofibrate or discover new agents that activate PPARα. "To test the therapeutic strategy in people, we need more drugs that penetrate the brain for clinical trials," Maekawa says. ●

Reference

1. Wada, Y., Maekawa, M., Ohnishi, T., Balan, S., Matsuoka, S., Iwamoto, K., Iwayama, Y., Ohba, H., Watanabe, A., Hisano, Y. *et al.* Peroxisome proliferator-activated receptor α as a novel therapeutic target for schizophrenia. *EBioMedicine* **62,** 103130 (2020).

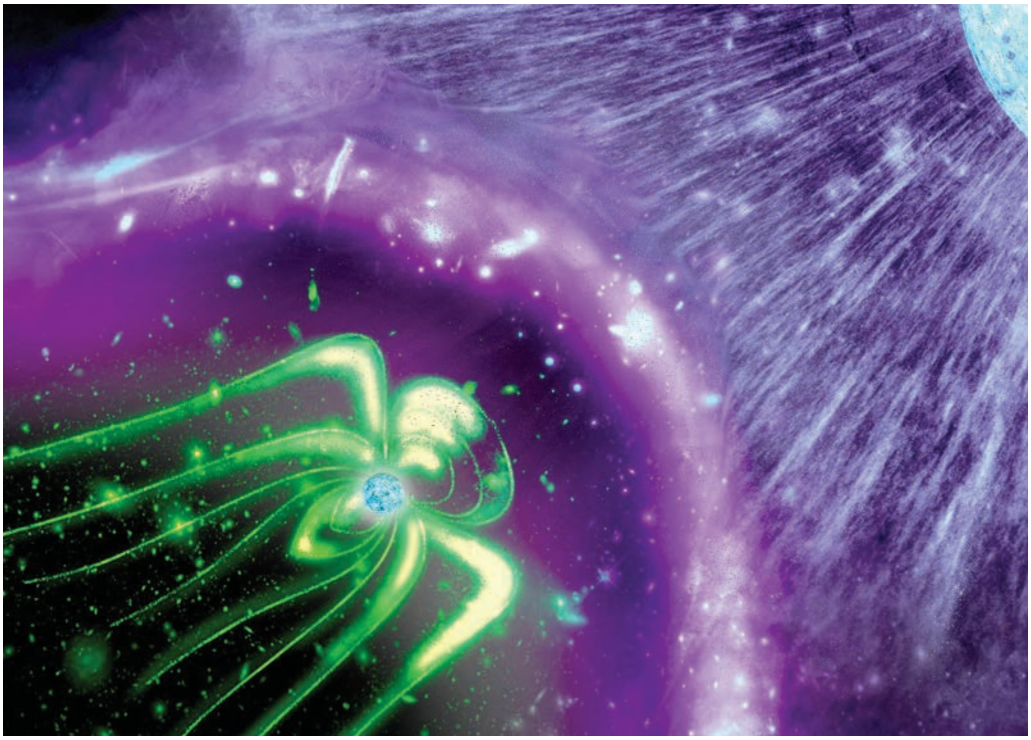
ASTROPHYSICS

Mysterious magnetar may power bright binary star

The enormous magnetic field generated by a spinning neutron star could explain the intense luminosity of a binary star system

Astrophysicists are better positioned to understand mysterious magnetars—neutron stars that boast the strongest magnetic fields in the Universe—after RIKEN researchers found evidence that the brightest gamma-ray binary star system in our Galaxy may contain a magnetar[1].

Known rather prosaically as LS 5039, the binary system consists of two stars that accelerate particles to extremely high energies, generating powerful gamma rays. One star is a hot, blue-white star about 23 times more massive than our Sun. The other was thought to be a pulsar, a spinning neutron star that emits beams of electromagnetic radiation as it rotates, rather like the beams of a lighthouse.



Observations of high-energy x-rays from the binary-star system LS 5039 suggest that it harbors a powerful magnetar (blue and white sphere on bottom left).

"Our result challenges the current most popular scenario for this binary system"

Previous observations of LS 5039 had not revealed any pulses from the pulsar, which may have been due to disruption of the telltale beams by a stellar wind—a stream of gas and particles pouring from the larger star.

Now, Hiroki Yoneda of the RIKEN Nishina Center for Accelerator-Based Science and his colleagues have studied x-rays emitted by LS 5039 that are more energetic than those investigated in previous studies and are thus less prone to this disruption.

Based on observations from two space telescopes, they found that LS 5039 emits high-energy x-ray pulses every 9 seconds. Their observations suggest that the pulsar has a mass of 1.23–2.35 times that of our Sun.

But the researchers' analysis showed that an ordinary pulsar could not supply enough energy to generate LS 5039's powerful gamma rays. Instead, they found that the star is most likely to be a rotating magnetar, with a magnetic field roughly 1,000 times stronger than typical pulsars—and about one quadrillion (10^{15}) times stronger than the Earth's magnetic field.

"We were surprised by this, because our result challenges the current most popular scenario for this binary system," says Yoneda. "So far, all magnetars have been found as isolated systems. If our findings are true, the magnetar in LS 5039 is the first one to be found in a binary system."

The researchers suggest that LS 5039 is so bright because the magnetar is immersed in its companion's stellar wind, leading to interactions that accelerate electrons in a few seconds to extreme levels (of the order of teraelectronvolts).

"The most important thing to do next is to confirm the pulsation by an additional hard x-ray observation," says Yoneda. Further observations may also pin down a more precise mass for the magnetar, which could help to reveal why they differ from normal neutron stars that have weaker magnetic fields. ●

Reference

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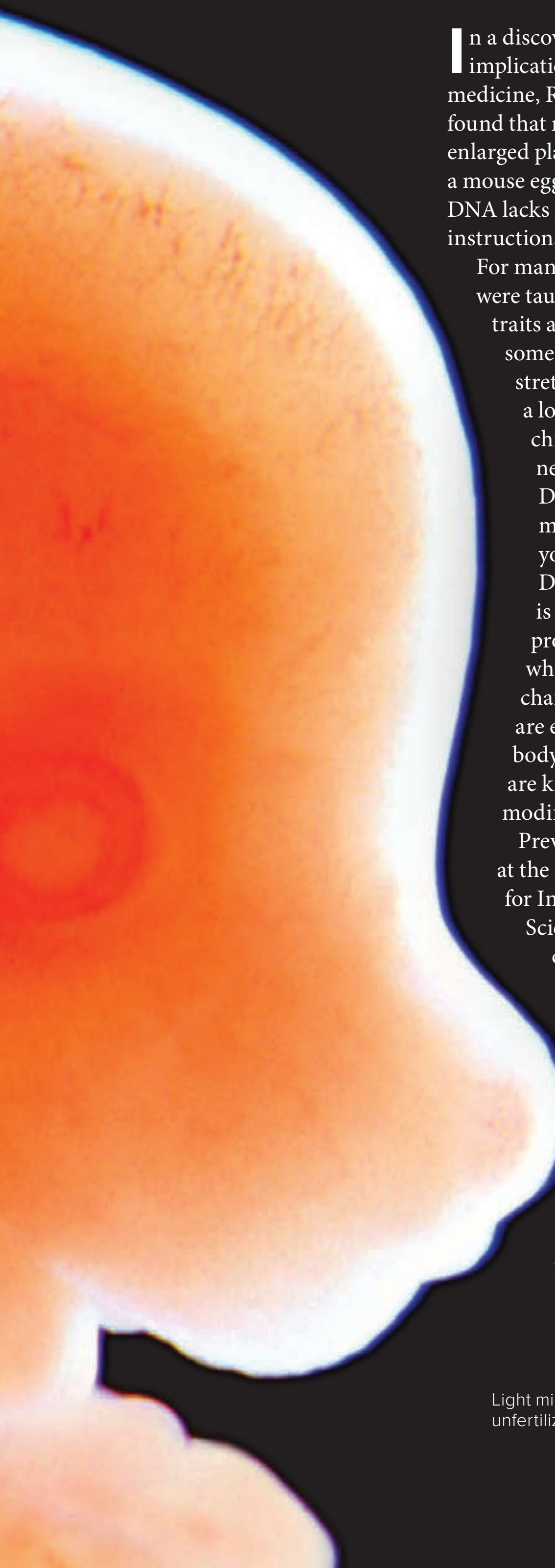
EPIGENETICS

Unfertilized egg modifications key to some traits

Two epigenetic marks in an unfertilized mouse egg cell determine inherited DNA modifications



In a discovery that has implications for reproductive medicine, RIKEN scientists have found that miscarriages and enlarged placentas can occur if a mouse egg cell with normal DNA lacks proper epigenetic instructions[1].

For many years, students were taught that acquired traits are not inherited. In some sense, this is correct; stretching your neck a lot will not result in children with longer necks. However, your DNA function can be modified throughout your life. For example, DNA in chromosomes is supported by proteins called histones, which can be modified, changing how genes are expressed in the body. These changes are known as epigenetic modifications.

Previously, Azusa Inoue at the RIKEN Center for Integrative Medical Sciences and his colleagues had found that acquired trimethylation of histone H3 at lysine 27 (H3K27me3) in mammalian egg cells can be inherited. Now, in a new study, they investigated how this happens.

The team discovered a mark left behind in unfertilized egg cells that determines which DNA modifications would be inherited if the egg is fertilized. Specifically, they found that without initial modifications to histone H2A at lysine 119 (H2AK119ub1), later inheritable modifications would not occur. One consequence of this deficit was an enlarged placenta after embryo implantation.

It was surprising to find that defects in an egg's histone modification are irreversibly inherited by embryos

The researchers first examined the timing of the two histone modifications. They found that every gene exhibiting H3K27me3 also showed H2AK119ub1 in mouse egg cells.

Suspecting its importance, the researchers knocked out two proteins that make up H2AK119ub1 in egg cells. They found that the knock-out egg cells had much less H3K27me3 than controls at a subset of genes that normally bring H3K27me3 into the next generation. Thus, H2AK119ub1 acts like a kind of marker left by a scout, identifying where subsequent H3K27me3 should follow.

"We discovered that H2AK119ub1 is necessary for maternal inheritance of H3K27me3, making the H2AK119ub1-H3K27me3 pathway a major player in transgenerational epigenetic inheritance in mammals," says Inoue.

Surprisingly, testing showed that the loss of H3K27me3 was itself inherited by fertilized embryos, and could not be reversed. Furthermore, this deficiency led to increased miscarriages and enlarged placentas. "It was surprising to find that defects in an egg's histone modification are irreversibly inherited by embryos and cause long-term consequences in development," says Inoue.

These findings have clinical implications, especially for reproductive medicine and placental defects. "The next step is to see whether any diseases or surrounding environments can affect the heritable histone modification," says Inoue. ●

Reference

1. Mei, H., Kozuka, C., Hayashi, R., Kumon, M., Koseki, H. & Inoue, A. H2AK119ub1 guides maternal inheritance and zygotic deposition of H3K27me3 in mouse embryos. *Nature Genetics* **53,** 539–550 (2021).

Light micrograph of a 13 day old mouse embryo. RIKEN researchers have found that histone modifications to an unfertilized mouse egg cell are irreversibly inherited by embryos, leading to long-term consequences in development.

Illustration of the central region of a protoplanetary disk. RIKEN astronomers have found that these infant planetary systems exhibit a surprising variation in the organic compounds they contain.

ASTROCHEMISTRY

Organic make-up of planetary systems differs from early on

Infant planetary systems show a surprising variation in the organic compounds they contain

In a finding that has implications for the origins of life on Earth, a RIKEN-led international team has discovered that 50 regions where protoplanetary disks are forming in the Perseus molecular cloud contain quite differing amounts of complex organic molecules[1]. Interestingly, the chemically rich young disks have similar compositions of organic molecules. These findings raise an important question: do solar-like systems share a common chemistry at birth?

Complex organic molecules were once thought to be rare in the Universe, and this rarity was used to explain why we have not found evidence of life outside the Earth. However, the last two decades have revealed that these molecules are actually common.

"Today, scientists have begun to systematically survey protoplanetary disks—disks where planets eventually form around a star—in the hope of determining how these molecules form, how common they are, and what impact they have on planetary systems," says Yao-Lun Yang, who was at the RIKEN Star and Planet Formation Laboratory at the time of the study.

Although astronomers have looked at individual systems, there is little comparative data to understand these young stars as a group. The RIKEN-led group decided to use observations from the ALMA observatory in Chile, whose high resolution allows scientists to study chemical compounds in protoplanetary disks.

The group surveyed the emission from organic molecules at specific frequencies in very young disks. They looked at methanol and acetonitrile, as well as two larger molecules: methyl formate and dimethyl ether. The researchers found that different regions exhibited large variations in the abundances of methanol and acetonitrile. Intriguingly, the relative abundance between the two species was remarkably similar. "This implies that there is a common production mechanism of these two molecular species, and this gives us important hints on how they form in space," says Yang.

In addition, the abundances of methyl formate and dimethyl ether tended to be higher relative to methanol in denser regions, hinting that there is something about the denser conditions that allows them to be abundant.

"This raises important questions regarding how special the chemical environment of the infant Solar System is," says Nami Sakai, leader of the RIKEN Star and Planet Formation Laboratory. "We will be able to answer this question in the future by examining the chemical evolution of the gas surrounding young protostars. We hope that such knowledge will be a base for understanding the origin of life on the Earth." ●

Reference

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NUCLEAR PHYSICS

Alpha particles lurk at the surface of neutron-rich nuclei

Measurements on neutron-rich tin nuclei uncover alpha particles in their outer layer

New insights into the structure of neutron stars and the radioactive process of alpha decay could result from a RIKEN-led study, finding evidence that alpha particles—groups of two protons and two neutrons—may lie at the surface of heavy atomic nuclei that are rich in neutrons[1].

Neutron stars are extremely dense, being composed almost entirely of neutrons. Matter exists at similar densities, albeit at a much smaller scale, in atomic nuclei.

This finding has important implications for our understanding of the nuclear equation of state and neutron stars

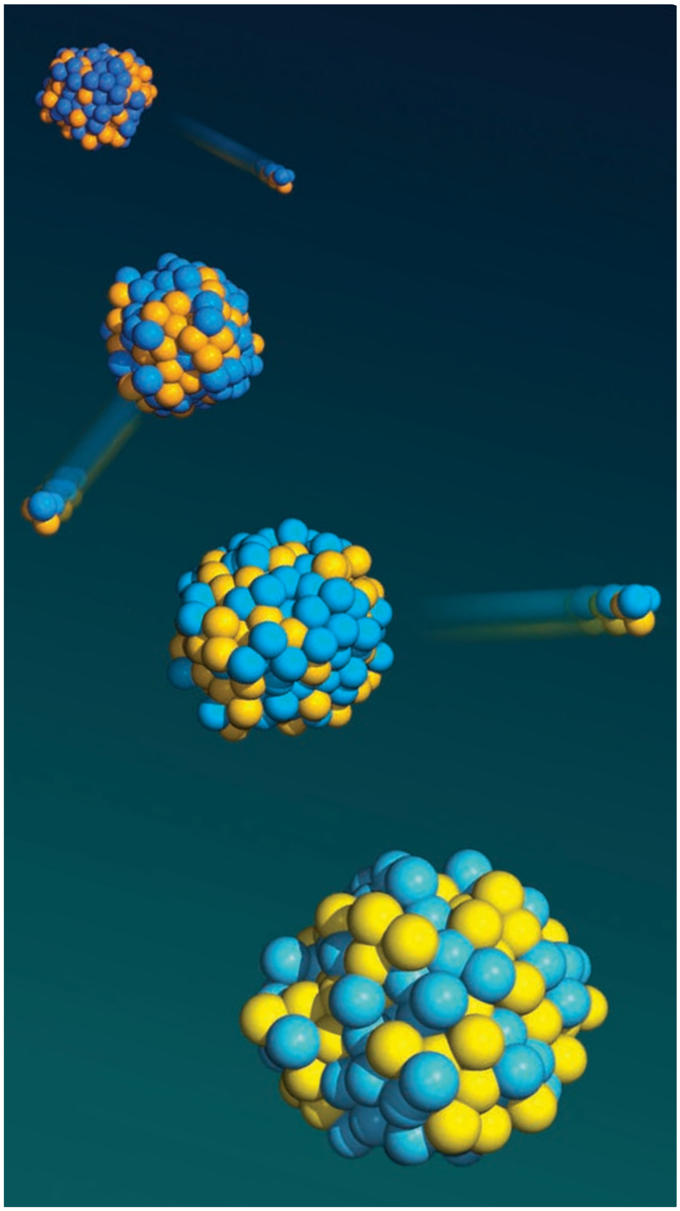
"Intriguingly, despite the vast difference in size and mass, the tiny atomic nuclei found on Earth and the enigmatic neutron star are actually governed by the same type of interactions," notes Zaihong Yang of the RIKEN Nishina Center for Accelerator-Based Science. This connection is expressed by the nuclear equation of state, which relates the pressure and the density of nuclear matter.

The researchers investigated a series of neutron-rich isotopes of tin ranging from tin-112, which has only 62 neutrons, to tin-124, which has 74 neutrons and hence a much thicker neutron skin. They knocked out alpha particles from the nuclei by bombarding them with protons and then examined how frequently they were able to observe alpha particles in progressively heavier isotopes.

The team identified alpha clusters in the very surface region of neutron-rich tin atomic nuclei, implying that the so-called neutron skin does not consist only of neutrons, but also contains alpha clusters. Importantly, they discovered that the probability of finding alpha clusters in nuclei decreased gradually with the number of neutrons. The researchers attributed this decrease to the interplay between alpha-cluster formation and the thickness of the neutron skin that surrounds the nucleus.

This finding has important implications for our understanding of the nuclear equation of state and neutron stars. In the near future, electromagnetic and gravitational-wave observations will provide more-accurate data on the properties of neutron stars.

The study is also a key step toward a full understanding of alpha decay—radioactive decay in which an atomic nucleus spontaneously emits an alpha particle. About 90 years ago, physicist George Gamow proposed that alpha decay occurs due to quantum tunneling of preformed alpha particles or clusters. However, although the theory was generally accepted, it has never been conclusively shown that such clusters exist in heavy atoms. Hence, the finding that alpha clusters exist at the surface of heavy nuclei could shed light on the origin of alpha particles in alpha decay. ●



Nuclear physicists at RIKEN have discovered that the neutron skin at the surface of neutron-rich tin nuclei contain alpha particles.

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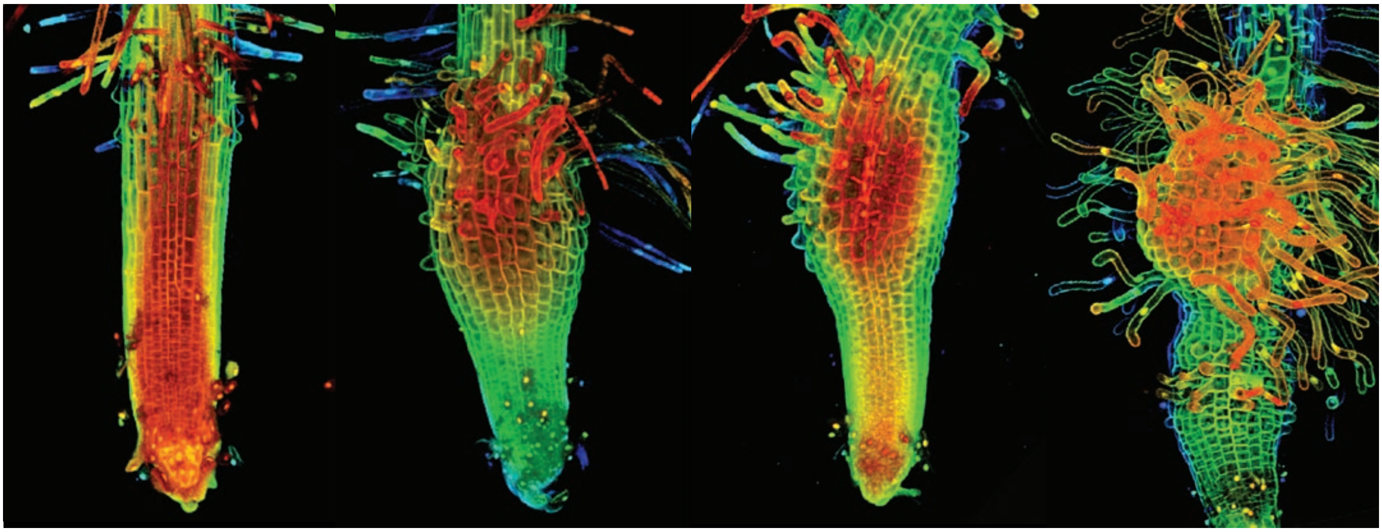

The formation of haustoria in *Phtheirospermum japonicum* seedlings grown on agar under different conditions.

PLANT DEVELOPMENT

Parasitic plants make their point with ethylene

The hormone ethylene plays a critical role in the infectious activity of parasitic plants

The invasive organs of parasitic plants such as witchweeds and broomrapes respond to the hormone ethylene when invading the roots of their hosts, RIKEN researchers have found[1]. This finding could provide researchers with new avenues for controlling these destructive plants.

Striga is a devastating parasitic weed that is particularly problematic in sub-Saharan Africa, Europe and parts of Asia. It is estimated to cause global agricultural losses that exceed US$1 billion.

Striga and other broomrapes invade plant roots using an infectious organ known as a haustorium (see image). To investigate haustorium development, a team led by researchers at the RIKEN Center for Sustainable Resource Science produced various mutants of the model broomrape *Phtheirospermum japonicum* and looked for plants that developed abnormal haustoria. They found two mutants in which the haustoria grew longer than usual and also began to produce transport tissues even in the absence of a host root.

The team then used whole-genome sequencing to identify the mutations. Surprisingly, both mutants had defects in genes in the same pathway—the signaling pathway of the hormone ethylene. “I couldn’t believe we were that lucky,” says lead author Songkui Cui, who has since moved to the Nara Institute of Science and Technology.

When the researchers treated *P. japonicum* plants with ethylene, they found that even a very small amount was enough to reduce the number of haustoria in normal plants, but this effect was absent in the ethylene-signaling mutants. Haustorium formation thus seems to be very sensitive to ethylene signaling, but since the mutations did not affect the number of haustoria, ethylene signaling is not needed early in haustorium development.

Turning to the later stages of haustorium growth, the team found that cell proliferation continued for longer in the apex of mutant haustoria, and this was accompanied by continued activity of another plant hormone, auxin. The mutant haustoria also proved less effective at invading roots, sometimes failing to form invasive cells and instead continuing to elongate around the host root.

Finally, the researchers tested whether haustorium development responds to ethylene from the host. Host plants with defects in ethylene biosynthesis were infected 35% less than wild-type plants, suggesting that host-derived ethylene is perceived by the parasite.

Taken together, these findings indicate that ethylene signaling guides the various stages of haustorium development. Cui believes that uncovering the basic biology of the parasite will lead to strategic ways to tackle it. “I’m continuing this work to understand the molecular mechanisms of this interaction in more detail, because many basic questions remain,” says Cui. “There may be more specific processes we can eventually target.” ●

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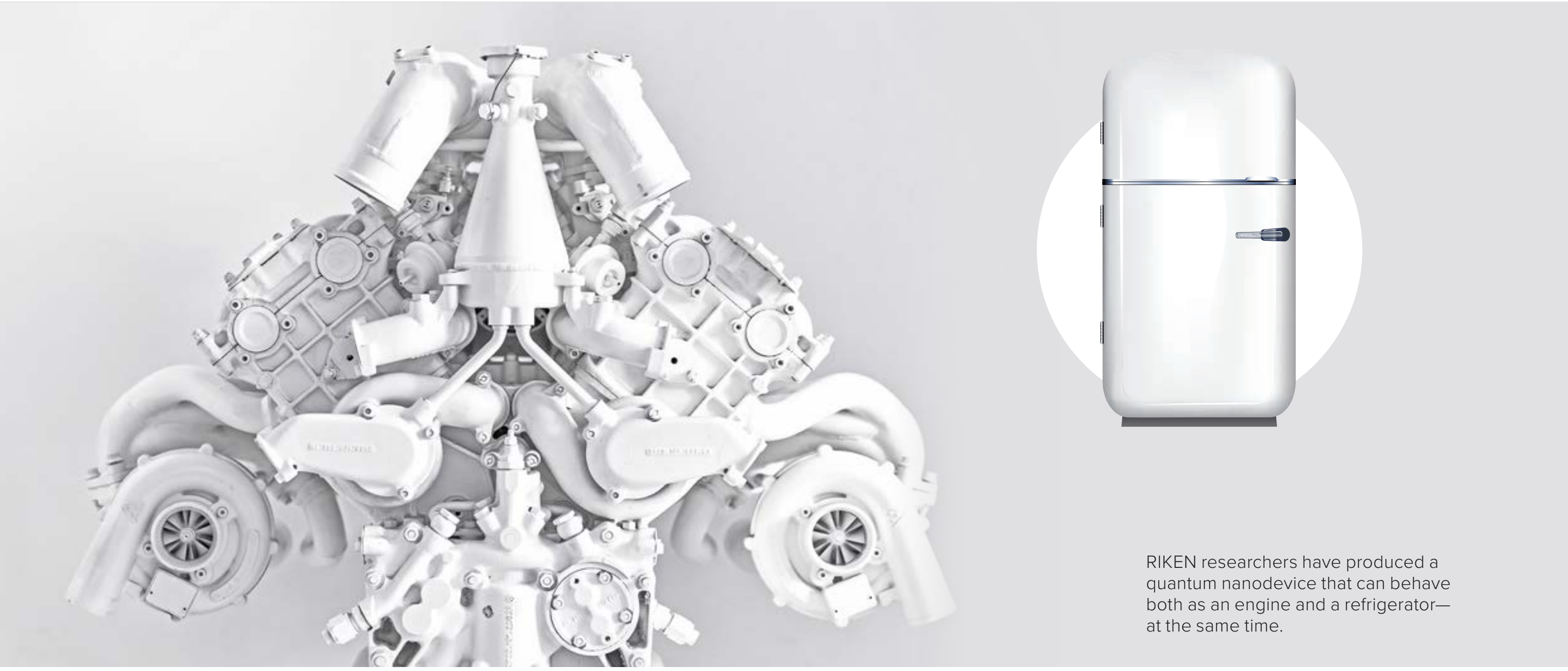

RIKEN researchers have produced a quantum nanodevice that can behave both as an engine and a refrigerator—at the same time.

QUANTUM THERMODYNAMICS

Quantum nanodevice can simultaneously do work and cool

A quantum nanodevice can simultaneously act as a heat engine and a refrigerator

A multitasking nanomachine that can act as a heat engine and a refrigerator at the same time has been created by RIKEN engineers[1]. The device is one of the first to test how quantum effects, which govern the behavior of particles on the smallest scale, might one day be exploited to enhance the performance of nanotechnologies.

Conventional heat engines and refrigerators work by connecting two pools of fluid. Compressing one pool causes its fluid to heat up, while rapidly expanding the other pool cools its fluid. If these operations are done in a periodic cycle, the pools will exchange energy and the system can be used as either a heat engine or a fridge.

It would be impossible to set up a macroscale machine that does both tasks simultaneously—nor would engineers want to, says Keiji Ono of the RIKEN Advanced Device Laboratory. “Combining a traditional heat engine with a refrigerator would make it a completely useless machine,” he says. “It wouldn’t know what to do.”

But things are different when you shrink things down. Physicists have been developing ever smaller devices, sometimes based on single atoms. At these tiny scales, they have to account for quantum theory—the strange set of laws that says, for instance, an electron can exist in two places at the same time or have two different energies. Physicists are developing new theoretical frameworks and experiments to try to work out how such systems will behave.

The quantum version of the heat engine uses an electron in a transistor. The electron has two possible energy states. The team could increase or decrease the gap between these energy states by applying an electric field and microwaves. “This can be analogous to the periodic expanding–compressing operation of a fluid in a chamber,” says Ono, who led the experiment. The device also emitted microwaves when the electron went from the high-energy level to the lower one.

By monitoring whether the upper energy level was occupied, the team first demonstrated that the nanodevice could act as either a heat engine or as a refrigerator. But then they showed something far stranger—the nanomachine could act as both at the same time, which is a purely quantum effect. The researchers confirmed this by looking at the occupancy of the upper energy level, which combined to create a characteristic interference pattern. “There was an almost perfect match between the experimental interference pattern and that predicted by theory,” says Ono.

“This may allow rapid switching between the two modes of operation,” Ono explains. “This ability could help create novel applications with such systems in the future.”

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REGENERATIVE THERAPY

Regenerating hair in the lab

By nourishing stem cells with just the right combination of nutrients, scientists have succeeded in growing hair that cyclically grows and falls out

New clinical therapies for hair regeneration could come from a recipe discovered by RIKEN researchers for realizing continuous cyclical regeneration of mouse hair follicles cultured from stem cells[1].

Regenerative medicine, which exploits the ability of special cells known as stem cells to differentiate into a wide variety of specialized cells, is an exciting emerging field in modern medicine. A team led by Takashi Tsuji of the RIKEN Center for Biosystems Dynamics Research has been working on ways to regenerate lost hair from stem cells. Now, in an important step, they have identified a recipe for realizing cyclical hair regeneration in the lab from a critical population of hair follicle stem cells harvested from the skin.

The researchers took fur and whisker cells from mice and cultured them in 220 different combinations of various biological ingredients. They achieved the highest rate of stem-cell amplification in the shortest time when they combined a type of collagen with five factors called NFFSE medium.

Our culture system establishes a method for cyclical regeneration of hair follicles from stem cells

Since hair growth in mammals is a continuous cyclical process in which hair grows, falls out, and grows again, a successful hair-regeneration treatment must replicate this cycle. To test whether stem cells cultured in the NFFSE medium produce hair that grows in cycles, the researchers placed bioengineered hair follicle stem cells in NFFSE medium or in a medium lacking one of the factors and observed the regenerated hair for several weeks. They found that 81% of hair follicles generated in NFFSE medium went through at least three hair cycles and produced normal hair. In contrast, 79% of follicles grown in the other medium produced only one hair cycle.

Knowing that stem-cell renewal can depend on what is attached to the outside of the cells, the researchers looked for markers on the surface of cells cultured in the NFFSE medium. In addition to the expected CD34 and CD49f markers, they found the best hair cycling was related to the addition of Itgβ5. “We found almost 80% of follicles reached three hair cycles when Itgβ5 was also bioengineered into the hair-follicle germ,” explains first author Makoto Takeo. “In contrast, only 13% reached three cycles when it was not present.” Analysis showed that these important cells are naturally located in the upper part of the hair follicle’s bulge region.

“Our culture system establishes a method for cyclical regeneration of hair follicles from stem cells and will help make hair follicle regeneration therapy a reality in the near future,” says Tsuji.

The team is hoping to find an outside collaborator to help them conduct clinic trials. “We are looking for a partner company to help develop clinical applications,” says Tsuji. ●

Reference

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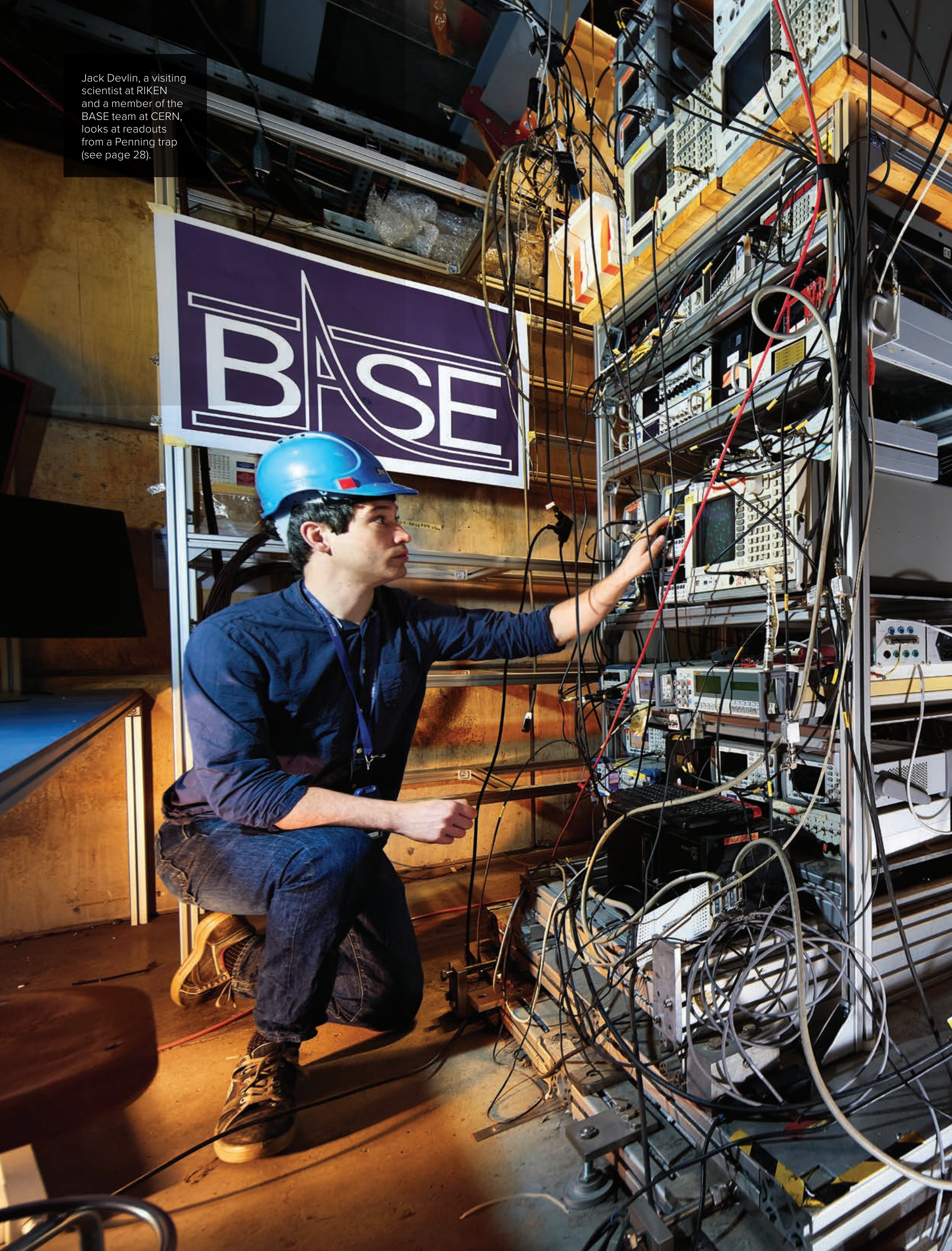
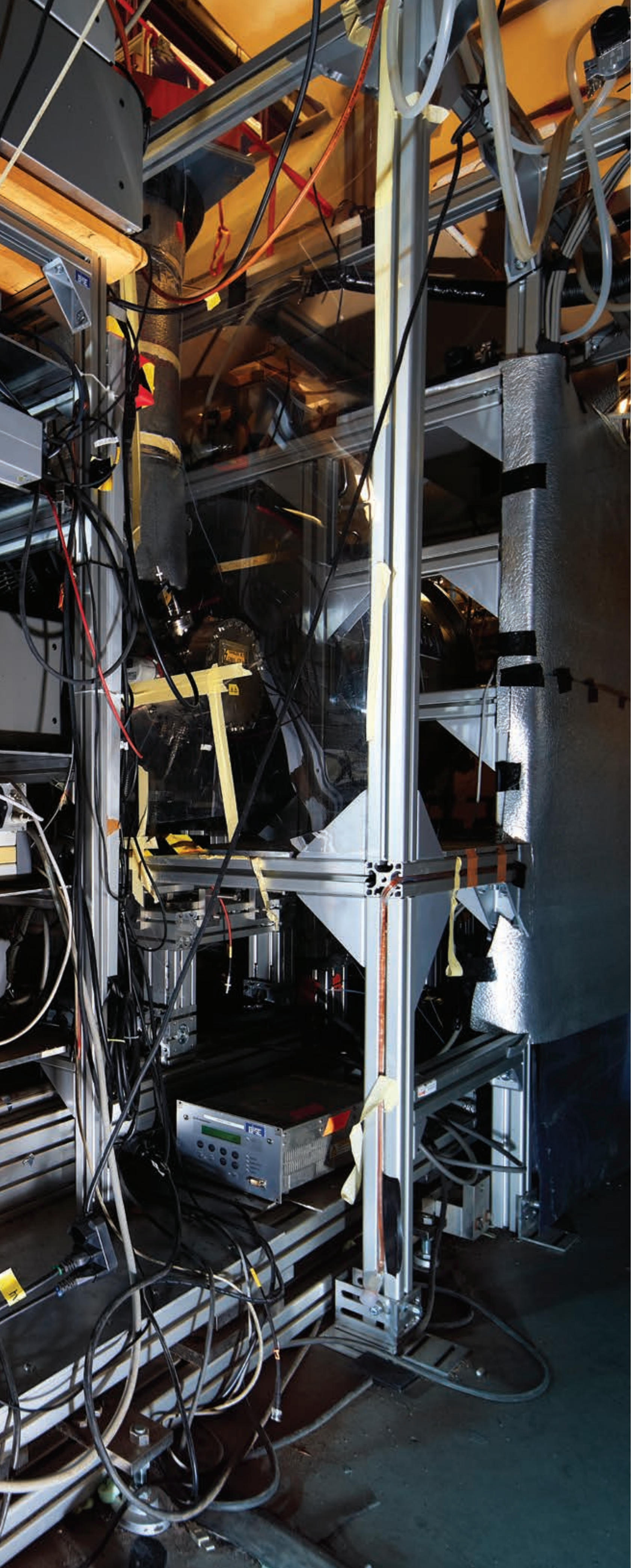
The ability to use stem cells to grow hair that regenerates itself could lead to hair follicle regeneration therapy.



Jack Devlin, a visiting scientist at RIKEN and a member of the BASE team at CERN, looks at readouts from a Penning trap (see page 28).



Hunting for big game in physics with a small trap

An instrument designed to probe the imbalance between matter and antimatter could make the search for axions much, much more affordable.

The hunt for a hypothetical particle known as an axion, which would resolve some of the biggest problems in modern physics, could be made a lot easier using the single-particle detectors in Penning traps, a team led by Stefan Ulmer of the RIKEN Ulmer Fundamental Symmetries Laboratory has demonstrated[1].

First proposed in 1977, the axion was named after a washing powder brand because, if found, it has the potential to 'clean up' a vexing quantum mechanical problem. The strong CP problem is an issue with the strong nuclear force, the strongest of four fundamental forces of nature and the one that binds protons and neutrons together in atomic nuclei. However, it doesn't play according to the expected mathematical rules.

"Many physicists are hunting for the axion at the moment," says Jack Devlin, first author of the study and a member of the Baryon Antibaryon Symmetry Experiment (BASE) team at the European Organization for Nuclear Research (CERN). "If we could convincingly detect axions, it would be huge—the biggest physics you can think of. It would answer some of the most fundamental questions."

SETTING A TRAP FOR AXIONS

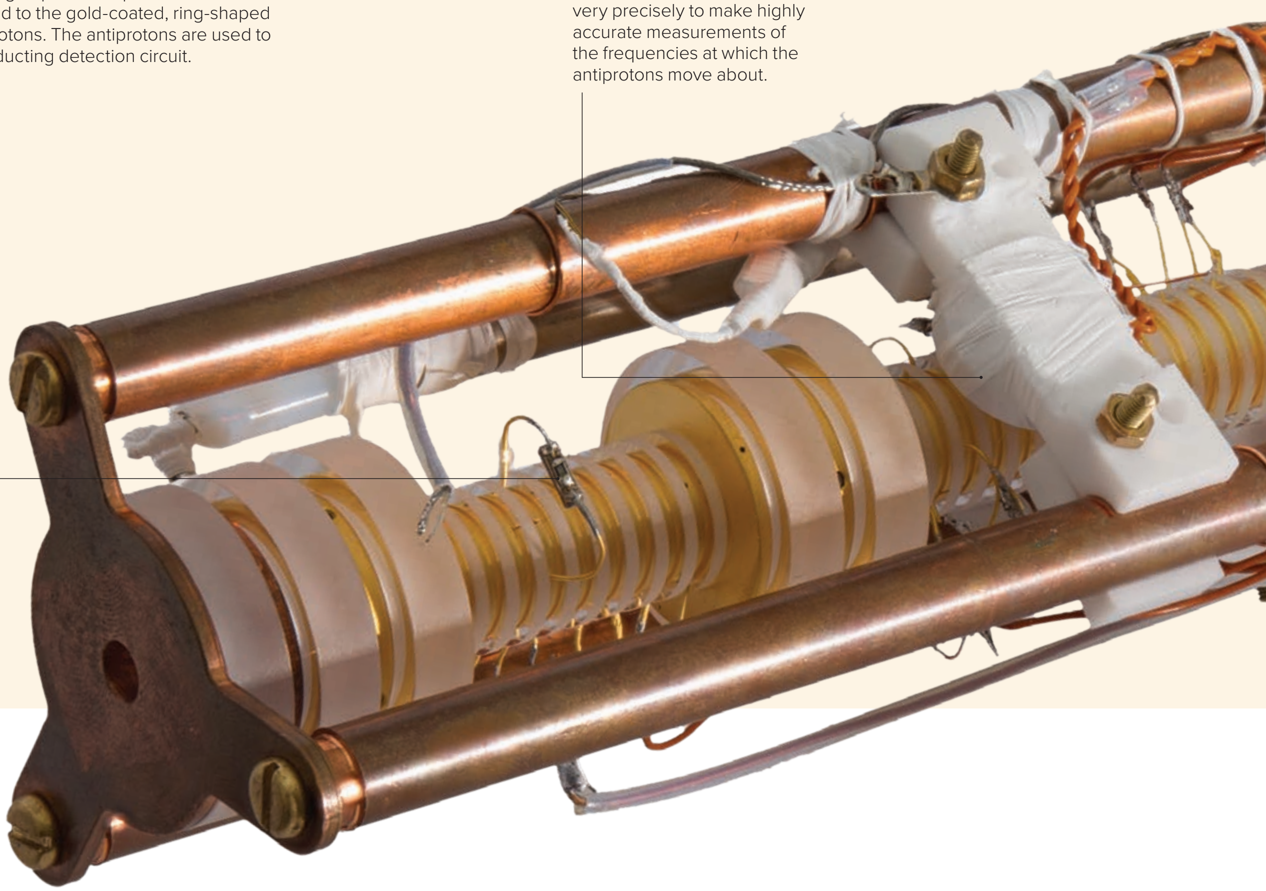
Ulmer's real passion lies in investigating another great

PENNING TRAP PRECISION

A photograph of the Penning trap used as part of the search for axions. Voltages are applied to the gold-coated, ring-shaped electrodes, trapping antiprotons. The antiprotons are used to characterize the superconducting detection circuit.

Measurement trap: A region where the magnetic and electric fields are controlled very precisely to make highly accurate measurements of the frequencies at which the antiprotons move about.

Storage trap: Stores trapped ions.



mystery in modern physics, namely why matter seems to be in much greater supply than antimatter when the present theory predicts they should be present in exactly equal amounts.

All fundamental particles have an antiparticle. For example, the electron's antiparticle is the positron, but there are far more electrons than positrons around us, and far more matter than antimatter.

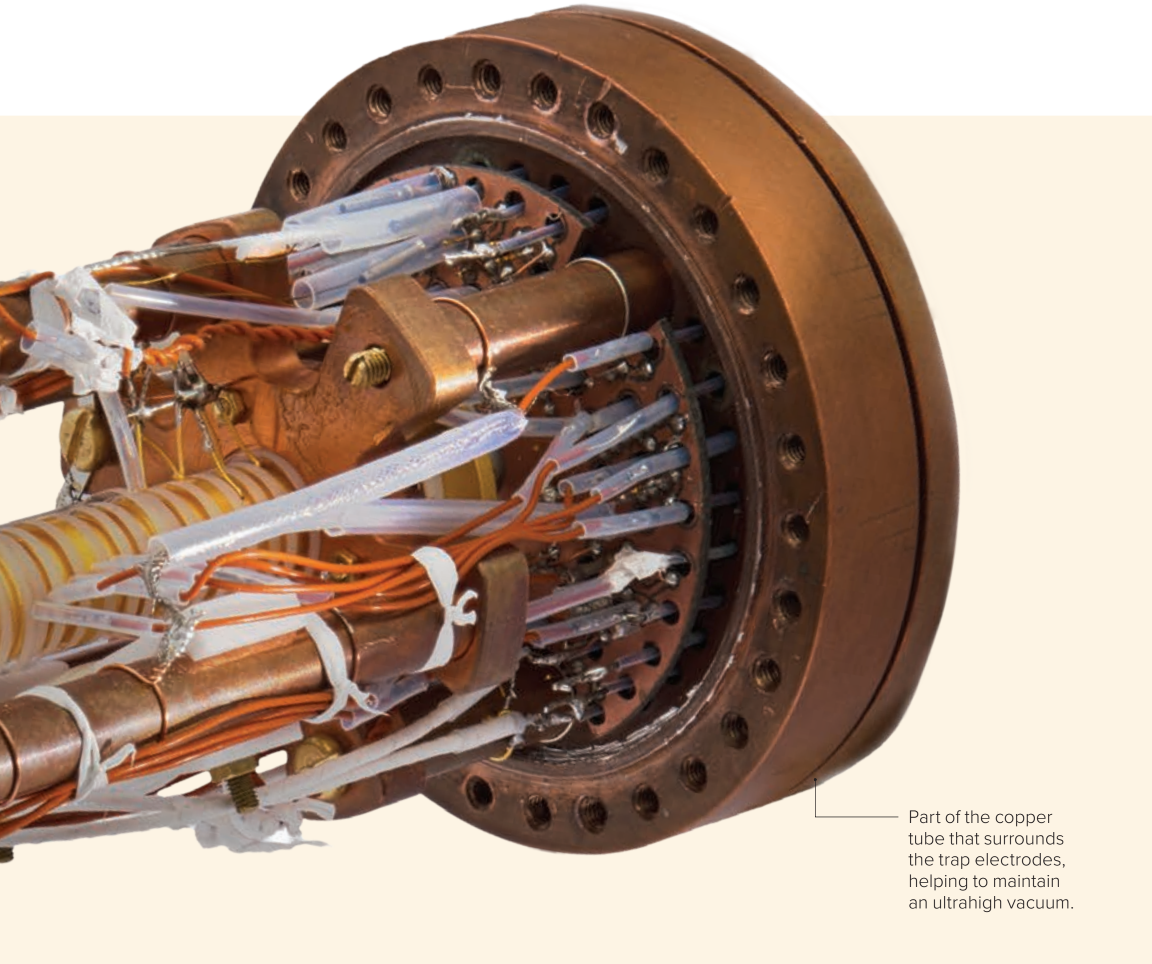
According to the most accurate experimental measurements, the binding nuclear force in atomic nuclei remains identical when you swap every particle with its antiparticle and reflect everything in a mirror. But that goes against the theory that gave birth to the standard model of particle physics, which has been such a success in every other test thrown at it.

Ulmer's team has been using the Penning trap to perform measurements on protons and antiprotons to see if they can find any subtle differences between them that might hint at the reason for the imbalance.

But it struck them that they could use the same equipment to search for the axion. While, in theory, axions are dark and don't interact with normal particles except via gravity (the weakest of the four fundamental forces), theory predicts that when placed in a strong magnetic field, an axion will decay into a photon of light once in a blue moon. This gives experimentalists an opportunity to spot telltale signs of axions in the lab.

That's where Ulmer's Penning traps, based at CERN in Switzerland, can help. Penning traps are operated in the highly uniform magnetic fields provided by superconducting coils. Using a roughly two-meter-long instrument, Ulmer's team was able to determine constraints on the rate at which axions turn into photons for a narrow range of axion masses, effectively narrowing the search.

The beauty of this demonstration is that it was at a fraction of the cost of equivalent observations by satellites or by the International Axion Observatory



Part of the copper tube that surrounds the trap electrodes, helping to maintain an ultrahigh vacuum.

(IAXO), built from an almost 10-meter-long decommissioned superconducting test magnet for the Large Hadron Collider, also based at CERN.

"And if our resonant single-particle detectors were purpose-built to search for axions, it could search a much greater area with higher sensitivity," says Ulmer.

CLEANING UP TWO PROBLEMS WITH ONE PARTICLE

The presence of the hypothetical axion, which should be at least 50,000 times lighter than the electron, would solve the strong CP problem. Some think it could also actually be the hypothetical substance known as dark matter.

The axion is also a highly attractive candidate for the enigmatic dark matter that is believed to make up 85% of the Universe's mass. Astrophysicists know that dark matter is out there because the outer regions of galaxies are spinning faster than if galaxies were just composed of normal matter. But since none of the elementary particles in the standard model of particle physics fits the properties of dark matter, physicists are searching for exotic particles such as the axion.

Compared to the highly demanding single-particle experiments that Ulmer's team normally does, the axion measurement was a doddle. "The data taking was simple—I mean, really straightforward," Ulmer says. Despite the simplicity of the measurement, the demonstration attracted a lot of interest. "I'm really surprised at the discussion this study has generated," Ulmer says. "The axion physics community is extremely interested in this project."

When asked how he would celebrate if his team found the axion, Ulmer says that at the very least he would break open a bottle of champagne. He also notes the internal conflict when performing such measurements, "On the one hand, you measure basically expecting to find nothing because you want to avoid bias. But on the other hand, you really hope that you will find something that will revolutionize physics." ●

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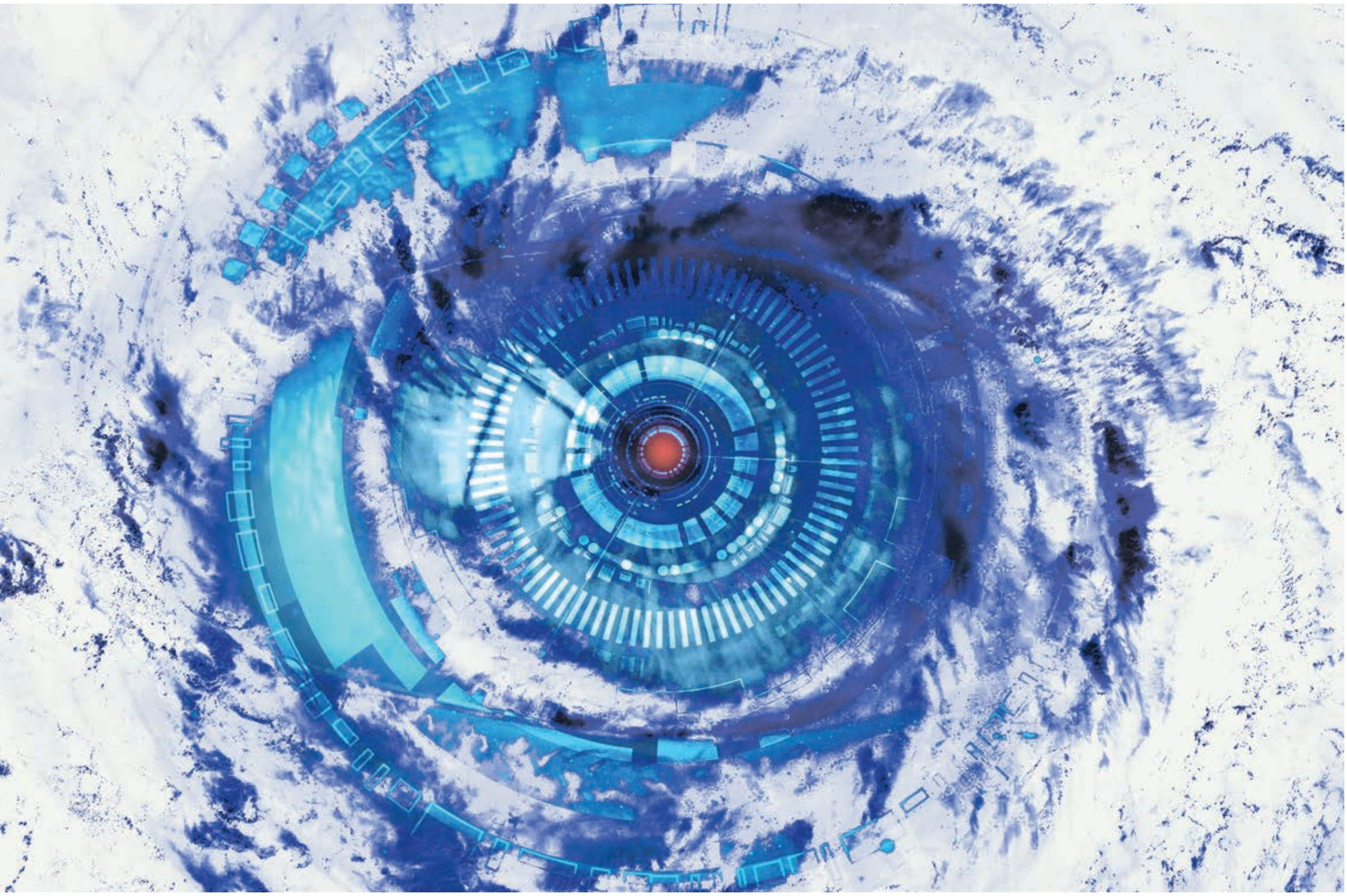
This feature looks at the work of **STEFAN ULMER**

Chief Scientist Stefan Ulmer leads the Ulmer Fundamental Symmetries Laboratory at RIKEN. He is also the founder of the BASE collaboration at the European particle-physics laboratory CERN in Switzerland. BASE performs high-precision measurements of protons and antiprotons to better understand matter and antimatter symmetry. Some of their experiments have had unprecedented sensitivity, including for magnetic moments, which allowed the first ever observation of proton and antiproton spin quantum transitions. Using their Penning traps, his group has performed several world-record measurements, including one for precision in charge–parity–time invariance in the baryon sector by comparing proton/antiproton charge-to-mass ratios. Recently, the lab has started using antiproton spins as dark-matter antennas and single-particle Penning trap detectors as antennas for axion-to-photon conversion.



AI OF THE STORM

During the pandemic, RIKEN's artificial intelligence teams have been able to advance everything from travel advice to online medicine. Has COVID-19 unlocked Japan's big data doors?

The old-fashioned sense of 'pulling together' that occurred during the SARS-CoV-2 crisis may in fact help reshape the trajectory of Japan's artificial intelligence (AI) research by opening the door to better data sharing.

For example, I believe the basis for progress toward a truly digital society in Japan will be an effective universal digital ID system. And indeed, in 2020, Japan's national digital ID system was the topic of much discussion. Twelve-digit, chipped 'My Number' cards have been available in Japan since 2016 and help manage social security, taxation and disaster-response information. However, uptake of the cards in Japan has been low and the system was plagued by problems when last year the government tried to distribute stimulus money through it to combat the effects of the pandemic.

In October 2020, Japanese Prime Minister Yoshihide Suga announced that his government would be creating a special agency devoted to digitization. Official statements followed about increasing My Number card uptake and expanding the system's uses, including to insurance, and to data on medication and medical costs via the government-run Mynaportal website.

Many AI researchers are cheering. For a number of years, it had been evident that while a focus on individual achievement has created some very successful scientific cultures, it has hindered widespread personal data sharing and the next big leaps forward in science.

AI researchers argue that big data drawn from digitized personal information—if shared in secure, ethical ways—will drive huge and important advances in everything from medical diagnostics to disaster management. That's not to say that some data privacy concerns aren't valid, but just that the advantages of a digitized, data-rich society may far outweigh the risks.

POWERING THROUGH THE PANDEMIC

Big data, high-powered computing and artificial intelligence managed largely through the RIKEN Center for Advanced Intelligence Project (AIP) and the RIKEN Center for Computational Science (R-CCS) were key to how the scientific community in Japan addressed the pandemic, for example.

A number of RIKEN teams have designed and trained AI algorithms that do everything from visualizing the risks around travel routes and virus transmission to simulating individual infections and economic activity.

Many researchers are using a secure personal-data management technology developed in Japan, called the Personal Life Repository (PLR). PLR technology encrypts personal data in such a way that only the user can manage it, and only those whom the user explicitly permits can decrypt and add to a person's PLR. Even the cloud storage service providers involved in the system cannot decrypt PLR information. This type of system could improve on standard service provider supplied records, as it makes the information easy to locate and is likely to drive electronic record system development that is more universally transferable.

PLR records could, for example, eventually add much to the work of the Business and Economic Information Fusion Analysis Team at the AIP, who have begun to try to predict COVID-19 infection severity in Japan, especially among younger people. They are currently training their algorithms on legally secured data from health insurance claims and medical check-ups using new data-fusion techniques and statistical machine learning methods.

This will complement AI modeling work through the RIKEN Medical Sciences Innovation Hub Program, which is being used to develop a personalized prediction system for COVID-19 in collaboration with the Finnish Institute for Health and Welfare (THL) and MIT spinoff, BC-Platforms. Working with deep phenotyping based on information geometry, RIKEN has already developed algorithms that can help determine who is at risk of mortality and aggravation from COVID-19. Now the group will train these algorithms further using fresh THL clinical data. The THL data comes from up to 1,000 patients with positive COVID results drawn from their COVIDprog project, a study originally aiming to identify the individual characteristics, including underlying genetics, that affect COVID-19 outcomes. This information will be processed securely through BC-Platforms technology.

RIKEN-developed machine learning is also being used to help tailor online information delivery to an individual's traits to improve reductions in high-risk public-health behaviors. This project harnesses the results of various studies in preventive medicine and behavioral economics. Abusive language and disinformation related to the COVID-19 is also being tracked at RIKEN via natural language processing technology, so that interventions can be targeted at sources or during peaks.

SOCIALLY DISTANCED SCIENCE

During the pandemic, remote medical check-ups became preferable to many. As a result, the AIP's Science, Technology and Society Team is taking a fresh look at the classifications and the ELSI (Ethics, Legal and Social Issues) of online initial medical examinations in Japan.

To remotely support older adults in cognitive decline, the Cognitive Behavioral Assistive Technology Team at the AIP has continued to develop an AI-based communication and dialogue support system for use by aged-care and healthcare providers.

This RIKEN-developed AI uses images collected during the day by older or cognitively compromised adults to help prompt group discussion, conversational participation and active recall, which helps protect against dementia and further deterioration. The idea is that the AI helps the group maintain strict rules that balance listening and speaking. More recently, as group setting have become more limited, a chat bot system called the Text-oriented Artificial Chat Operation System (TACOS) was shown to be able to provide conversational support services for up to 40 solo users in real time.

Meanwhile, the AIP's Technology and Society Team is monitoring for the potential drawbacks of remote communication, particularly at work. The project has already surveyed 300+ people to investigate the impacts of telework and identify working styles that mitigate negative outcomes, such as a lack of delineation between work and home.

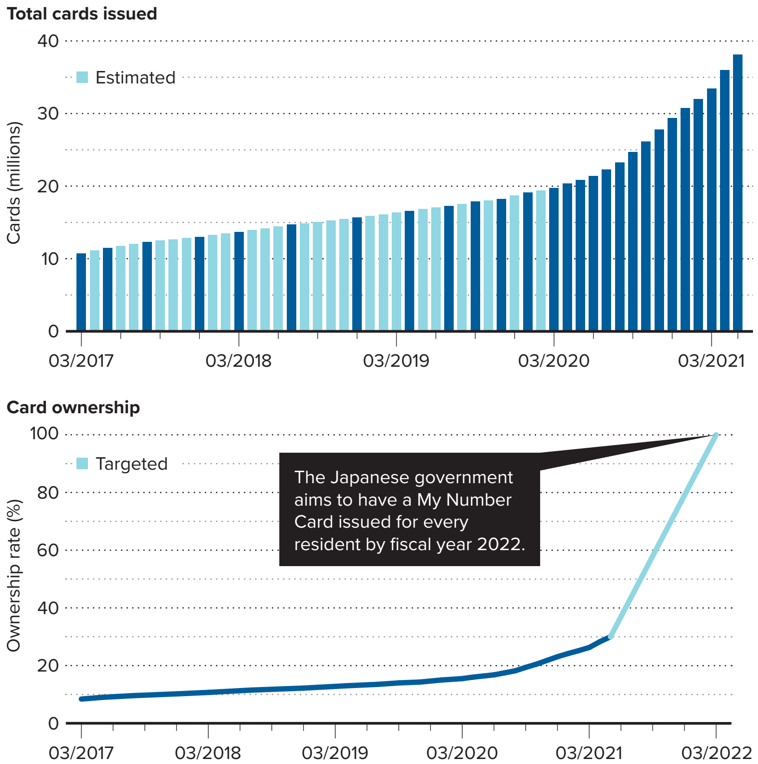
In addition, the Decentralized Big Data Team at the AIP are investigating formats and user interfaces that help people more precisely and efficiently read and

MICHIHIKO MINOH
RIKEN Executive Director, Director of RIKEN Information R&D and Strategy Headquarters

Michihiko Minoh is director of the RIKEN Information R&D and Strategy Headquarters (R-IH) and leads RIKEN's Guardian Robot Project as the part of R-IH. He became an Executive Director at RIKEN in April 2018. Previously he served as director of the Academic Center for Computing and Media Studies from 2006 to 2010 and concurrently served as vice director in the Kyoto University President's Office from 2008 to 2010. From 2010 to 2016, he was chief information officer and director-general at the Institute for Information Management and Communication at Kyoto University.

PANDEMIC PROMTS INCREASED DIGITIZATION

Government 'My Number' cards have been available since 2016 to help streamline services, including social security, taxation and disaster response. The first pandemic outbreaks in early 2020 renewed interest in these digital efficiencies. In September 2020, the Suga government issued a points reward system to promote uptake of the card. In April 2021, roughly 28% of the population had a card. The aim is full uptake by March 2022.



Source: Ministry of INternal Affairs and Communications

write in digital environments, as the pandemic is deemed to have accelerated digitization. They are also looking into AI technologies that assist composition, comprehension and other advanced uses of digital documents.

SUPPORTED BY ROBOTS

The COVID-19 outbreaks have also highlighted robotic technology's usefulness in facilitating social distancing. Robots, for example, are particularly promising prospects as carers to vulnerable populations, such as the elderly.

I lead the Guardian Robot Project, which is developing next-generation robots. The project, run through the RIKEN Information R&D and Strategy Headquarters and Innovation Hub, is developing a robot that can autonomously recognize its environment and the state of the person it is supposed to support. Five teams are using AI trained on data obtained from psychology, brain science and cognitive science to improve robotic knowledge acquisition and dialog, psychological processing, interactivity, multimodal data recognition, man–machine collaboration and behavior learning.

For example, the project will use cognitive modeling to build robotic software that helps provide adaptive and situationally responsive problem solving. It will also work to link sensors and actuators to these systems to facilitate high-level planning, prediction and reflection systems. The program is also working to develop the ability of its robots to understand natural language and to speak to their users.

JAPAN'S AI FUTURE

Overall, digitally savvy populations initially fared well during the pandemic, which will be another driver of digitization in Japan. In Taiwan, for example, Audrey Tan, the minister in charge of digital affairs, launched a successful mobile site to prevent the hoarding of masks. South Korea, which has the highest penetration of smartphones in the world, also had initial success controlling the pandemic with very precise infection tracing technology. These examples, and others, have motivated many governments to re-examine their digital infrastructure.

In addition, the AI market is also set to boast a compound annual growth rate between 2018 and 2025 of anywhere between 33% to 55%, with Asia anticipated to overtake North America's number one spot in the global market by 2025. Japan is currently number one in the world as a supplier of industrial robots and third, after China and the USA, in AI R&D. Toshiba is Japan's highest AI patent contributor, claiming the world's third spot, right after IBM and Microsoft.

On top of all of this, more than 40% of Japan will be elderly by 2030. This puts pressure on the labor force and healthcare system, but it is also an incentive to develop AI-enhanced care and industrial robots. And while the pandemic has caused a slowdown in some sectors, it has also sparked AI-driven solutions and motivated faster digitalization.

Overall, the outlook seems stronger than ever for Japanese AI researchers, although there is much work to be done. One caution I will put forth is that if a generalized negative attitude about data sharing holds us back from collecting relevant information, countries with less individually oriented cultures may overtake us in key sectors such as AI healthcare, where careful, sensitive data input is crucial. Ethical considerations and data privacy are of course important and RIKEN adopts best-practice technology, but the level of data sharing within a population may simply boil down to a feeling of safety or personal preference. Nonetheless, we are also partnering with our neighbors on many projects, and are excited about where these collaborations will go. ●

RIKEN'S CENTERS AND FACILITIES

across Japan and around the world

WAKO (RIKEN's Headquarters)

- ● Center for Emergent Matter Science (CEMS)
- ● RIKEN Center for Quantum Computing (RQC)
- ● Center for Sustainable Resource Science (CSRS)
- ● Center for Brain Science (CBS)
- ● Interdisciplinary Theoretical and Mathematical Sciences Program (iTHEMS)
- ● RIKEN Nishina Center for Accelerator-Based Science (RNC)
- ● RIKEN Center for Advanced Photonics (RAP)
- ▲ RIKEN Cluster for Science, Technology, and Innovation Hub (RCSTI)
- ▲ Cluster for Pioneering Research (CPR)
- ◆ Radio Isotope Beam Factory (RIBF)
- ▼ RIKEN Information R&D and Strategy Headquarters (R-IH)

YOKOHAMA

- ● Center for Sustainable Resource Science (CSRS)
- ● Center for Integrated Medical Sciences (IMS)
- ● Center for Biosystems Dynamics Research (BDR)
- ■ RIKEN Center for Computational Science (R-CCS)
- ▲ RIKEN Cluster for Science, Technology, and Innovation Hub (RCSTI)
- ◆ Genome Sequencing
- ◆ Nuclear Magnetic Resonance (NMR)
- ▼ RIKEN Information R&D and Strategy Headquarters (R-IH)

HARIMA

- ■ RIKEN SPring-8 Center (RSC)
- ◆ SPring-8
- ◆ SACLA

NAGOYA

LEGEND

- ● Strategic Research Center
- ■ Research Infrastructure Center
- ◆ Large Research Infrastructure
- ▲ Research Cluster
- ▼ Information Research and Infrastructure

SENDAI

- ● Center for Advanced Photonics (RAP)

TSUKUBA

- ■ BioResource Research Center (BRC)
- ◆ BioResource

TOKYO

- ● Center for Advanced Intelligence Project (AIP)
- ▼ Innovation Design Office
- ▼ RIKEN Information R&D and Strategy Headquarters (R-IH)

KEIHANNA

- ■ BioResource Research Center (BRC)
- ● Center for Advanced Intelligence Project (AIP)
- ▼ Guardian Robot Project (R-IH)

KOBE

- ● Center for Biosystems Dynamics Research (BDR)
- ■ RIKEN Center for Computational Science (R-CCS)
- ◆ Molecular Imaging

OSAKA

- ● Center for Biosystems Dynamics Research (BDR)

Since relocating its original campus from central Tokyo to Wako on the city's outskirts in 1967, RIKEN has rapidly expanded its domestic and international network.
RIKEN now supports five main research campuses in Japan and has set up a number of research facilities overseas. In addition to its facilities in the United States and the United Kingdom, RIKEN has joint research centers or laboratories in Germany, Russia, China, South Korea, India, Malaysia, Singapore and other countries. 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, Beijing and Brussels.

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