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RESEARCH
SPRING 2019
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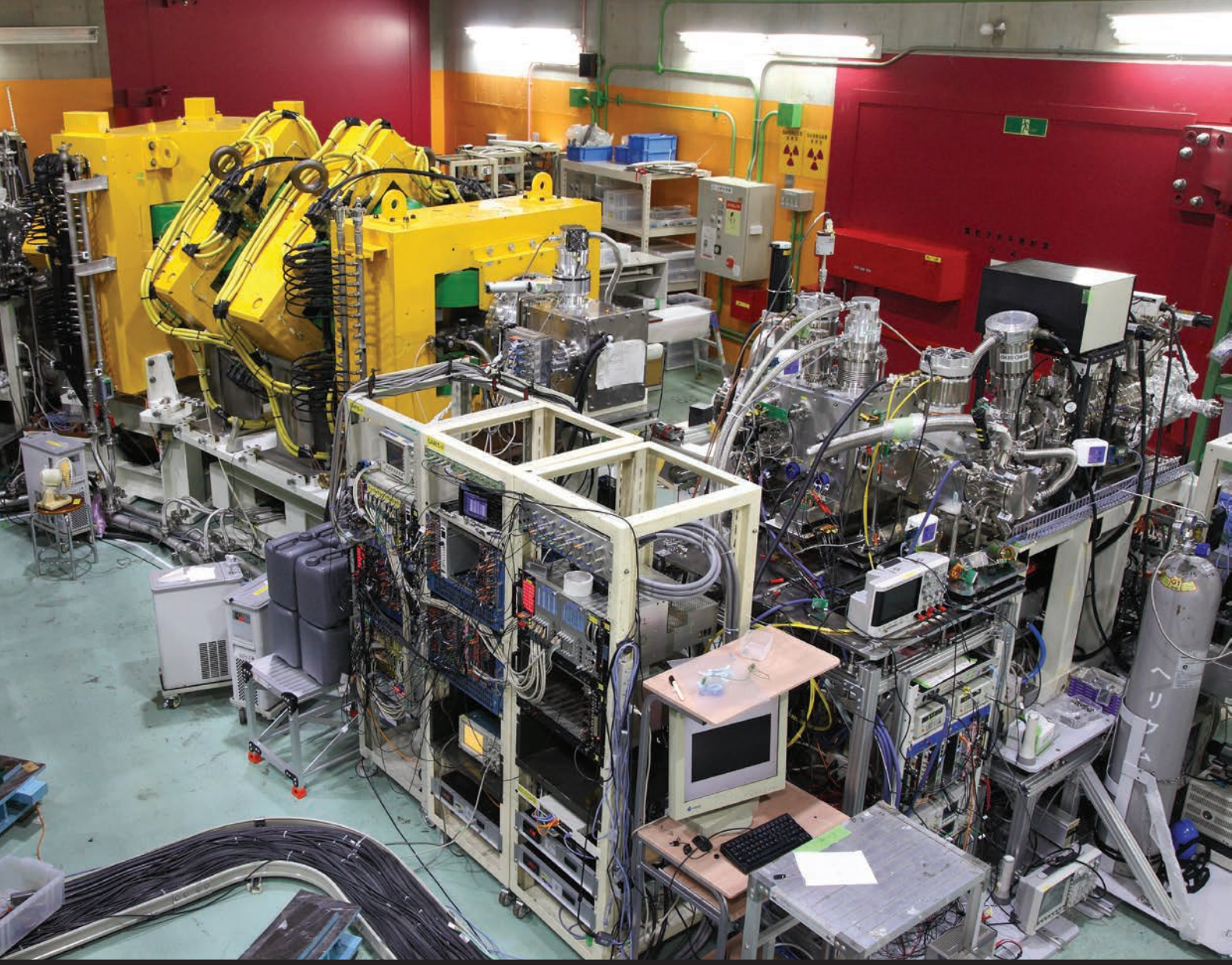
IN HOT PURSUIT

The search for answers to a supermassive mystery

GUIDING LIGHT
Tissue probe speeds up breast-conserving surgery

LUCKY 113
Celebrating nihonium and 150 years of the periodic table

2020 VISION
Post K-computer will run laps around its predecessor



▲ **GARIS-II at the RIKEN heavy-ion linear accelerator (RILAC) facility**
A new gas-filled recoil ion separator, GARIS-II, will be used to detect the creation of atoms of element 119 from vanadium and curium. The researchers will use hot fusion, which can accommodate larger mass differences between the elements being fused. Cold fusion, which was used to create nihonium (see page 32), could take centuries to produce the desired element.

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: www.riken.jp/en/research/rikenresearch Please visit the website for recent updates and related articles. Articles showcase RIKEN's groundbreaking results and are written for a non-specialist audience.

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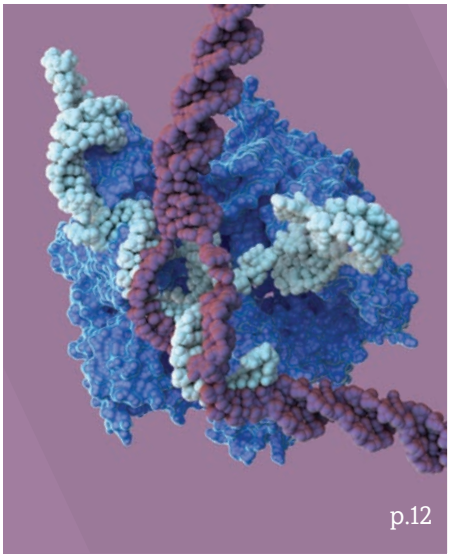

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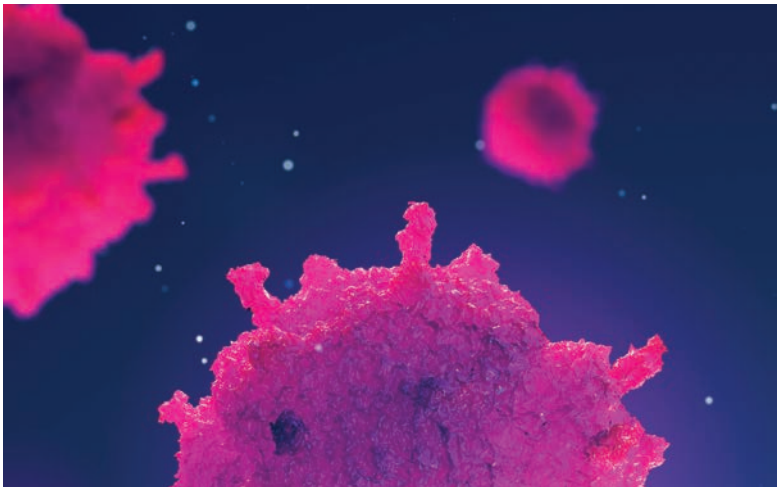

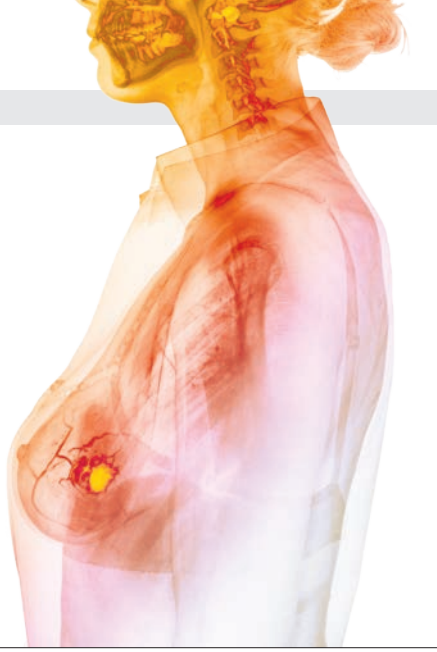

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Expanding our global network—Singapore, Beijing, and now Brussels

Motoko Kotani
Executive Director, RIKEN

I am happy to announce a very significant milestone in RIKEN's strategy for international collaboration. On 29 November 2018, we held a ceremony to celebrate the opening of our new Europe office, which is located in central Brussels, Belgium, just a short stroll from the headquarters of the European Parliament. This is our third overseas office, joining our Singapore office (established in 2006) and our Beijing office (established in 2010).

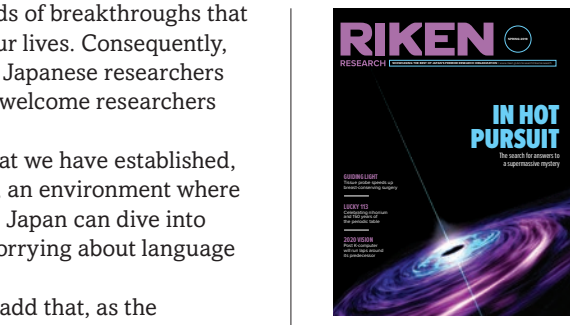
The newest office is part of our ongoing efforts to strengthen collaborations with partners around the world. We believe that now, more than ever, it is critical for researchers around the world, in both the private and academic sectors, to collaborate to solve many pressing problems, some of which threaten the continued existence of our civilization.

We also believe it is crucial for scientists to acquire a broad and international perspective if they are to make the kinds of breakthroughs that will truly revolutionize our lives. Consequently, at RIKEN, we encourage Japanese researchers to go abroad and also to welcome researchers from overseas.

I should emphasize that we have established, and continue to improve, an environment where researchers from outside Japan can dive into their research without worrying about language or cultural barriers.

Lastly, I would like to add that, as the establishment of our new office demonstrates, we are always looking for new collaborations with overseas partners. We hope these will help address the great challenges we face globally, both scientific and social. I encourage you to browse through the research achievements highlighted in this and other issues of *RIKEN Research*, and to consider whether your own institution has any potential collaborators.

We look forward to collaborating with you.



COVER STORY:
The magnetic field hypothesized to heat supermassive black hole coronae to more than a billion degrees turned out to be no stronger than a fridge magnet.
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Is there a bit of virus in our genome?

Nicholas F. Parrish
Hakubi Team Leader
Genome Immunobiology RIKEN Hakubi Research Team
RIKEN Center for Integrative Medical Sciences (IMS)

Please describe your current research. Why is it important?
I'm the team leader of the Genome Immunobiology RIKEN Hakubi Research Team. With mentorship from Haruhiko Koseki and Piero Carninci, who are global leaders in epigenetics and genomics, I'm studying parts of the genome that are derived from viruses other than retroviruses. These kinds of sequences were first reported by my mentor at Kyoto University, Keizo Tomonaga.

Until recently, nobody thought to look for these types of sequences in our genomes, because there is no reason that they should be there. My project is testing whether they could be contributing to making us immune to the viruses from which they're derived. We will use genome engineering to test this. If our hypothesis is confirmed, it would reveal another type of mammalian immune system. This could have the potential to generate trans-generational immune memory, similar to the CRISPR–Cas immune system in bacteria.

What excites you about your current research?
The possibility that viral sequences might be captured by the host and stored as a form of memory for immune purposes is quite new and interesting.

How did you become interested in your current field of research?
As an undergraduate, I was bothered to learn that only about two percent of our genome codes for proteins—this is the part of the genome that we understand best. During my PhD, I studied retroviruses, which cause diseases such as AIDS. Pieces of ancient retroviruses (called endogenous retroviruses) actually make up almost 10 percent of our genome. When I heard about sequences in our genome derived from viruses that are not retroviruses and thus "have no business being there," I thought that they might reveal something cool.

How has being at RIKEN helped your research?
The RIKEN Center for Integrative Medical Sciences is the only institute I know of with a particular expertise in functional genomics, brought to it by the Division of Genomic Medicine and the teams behind the FANTOM project, combined with long-standing thought leadership in immunology via the former RIKEN Center for Allergy and Immunology.

What are some of the techniques and technologies that you use to conduct your research?
Access to experts in CRISPR–Cas-mediated genome engineering, and next-generation and single-cell sequencing—especially those who have been using these technologies at a high level for years—is really important.

> *"If our hypothesis is confirmed, it would reveal another type of mammalian immune system*

What is the best thing about working at RIKEN?
RIKEN is an exceptionally internationally oriented institution. So many of my colleagues exemplify traits I value: diligence, truth-seeking and humility. I meet regularly with RIKEN's president and other Hakubi members to promote collaboration and cross-disciplinary thinking. RIKEN's leaders are invested in making sure their young scientists develop into global leaders. I was recruited through the Hakubi program, a new junior principal investigator program that launched in 2018. The kind of blue-sky research that the first batch of us want to try is risky and difficult, but President Matsumoto has put "his money where his mouth is"—to use an American phrase—in terms of his funding commitment. ■

Making the most of zeros

Ade Irma Suriajaya
Special Postdoctoral Researcher
Interdisciplinary Theoretical and Mathematical Sciences (iTHEMS)

How and when did you join RIKEN?
As I was finalizing my PhD thesis in 2016, I saw an ad saying that RIKEN wanted to hire pure mathematicians to become part of its interdisciplinary group.

Please describe your role at RIKEN
I'm a postdoctoral researcher in mathematics, specializing in analytic number theory. I'm able to contribute to a number of projects as part of the Interdisciplinary Theoretical and Mathematical Sciences (iTHEMS) team.

Please briefly describe your current research?
I look at how to apply the analytic properties of zeta functions and L-functions, especially the distribution of zeros, across many scientific disciplines. For example, it has been known for quite some time that zeta functions of various kinds often appear in quantum physics. They are also used as a means to regularize divergent sums, which sometimes appear in physics. I hope to be able to help these fields make even better and more complex use of zeta functions.

"My research is important to society because…."
...without the nontrivial zeros of the Riemann zeta function, nobody could trust online platforms to keep their personal information safe, for example. Classical cryptography relies on the zeros of the Riemann zeta function and Dirichlet L-functions, the simplest form of zeta function and L-functions, and these allow people to lock their electronic devices and make online payments safely!

Without the nontrivial zeros of the Riemann zeta function, nobody could trust online platforms to keep their personal information safe

How did you become interested in your current field of research?
I originally started an undergraduate course in Aeronautical Engineering, but I fell so hard for calculus that within two or three years I was sure that pure mathematics was what I wanted to work on for the rest of my life. I am so thankful. I know I can never be any happier than I am now, and I'm sure I will feel the same way for the rest of my life. Integrals here and there are the best things to find!

What excites you the most about your current research?
When I encounter new things in scientific talks. I always (unintentionally) want to see if they can be linked to zeta functions. I just love zeta functions, even the ones that do not look like classical zeta functions and don't have interesting zeros. I still want to try to understand how people might make use of them.

Please tell us about your personal goals.
I'm also pretty obsessed with languages. I'm fluent in six and I'm currently working on another.

How has being at RIKEN helped your research?
RIKEN provides access to mathematical papers and technology. For example, we work with Wolfram Mathematica, a computing system that deals with technical computing—including neural networks, machine learning, image processing, geometry, data science, visualizations, and more. Furthermore, I get to travel a lot internationally to learn techniques and methods from prominent figures in analytic number theory and zeta function theory.

What is the best thing about working at RIKEN?
I appreciate the encouragement I get to try new things, not only financially, but also in terms of enthusiasm. For example, I've been allowed to organize seminars on cutting-edge mathematics as well as a conference, which will be held in March 2019. ■

Careers at RIKEN
For further information, visit our Careers page:
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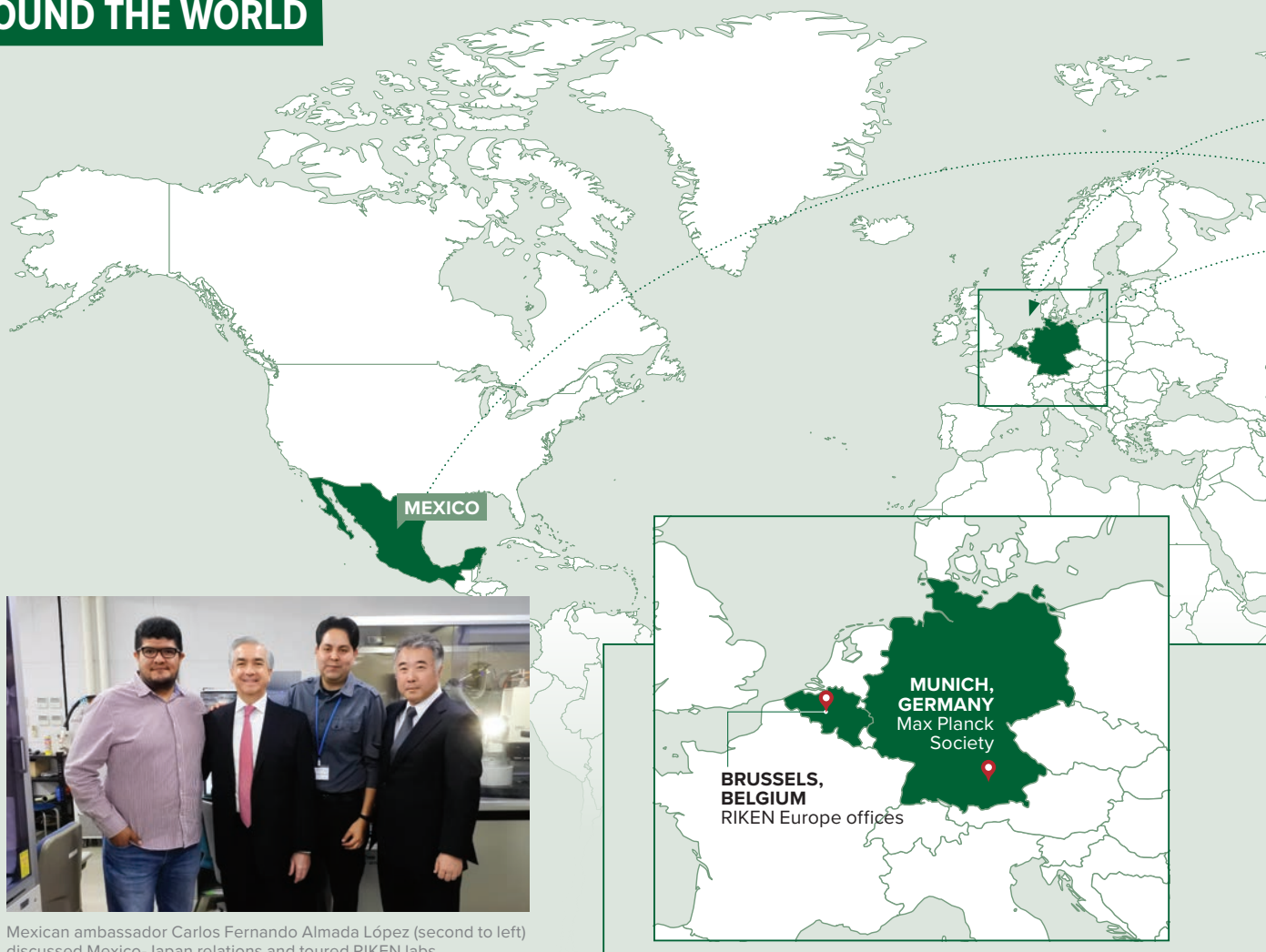
E-mail: pr@riken.jp

AROUND THE WORLD



Mexican ambassador Carlos Fernando Almada López (second to left) discussed Mexico-Japan relations and toured RIKEN labs.

Mexican ambassador visits Wako campus

On 25 October 2018, Mexico's ambassador to Japan, Carlos Fernando Almada López, visited RIKEN's Wako campus. He met with RIKEN President Hiroshi Matsumoto and RIKEN Executive Director Shigeo Koyasu to discuss the institute's relationship with Mexico and to consider ways to increase the presence of Mexican researchers in Japan and how to spread knowledge about RIKEN in Mexico.

The ambassador and his staff were given tours of three laboratories, including two that have Mexican researchers among their staff.

http://www.riken.jp/en/pr/topics/2018/20181030_1/

RIKEN's third overseas office opened in Brussels, Belgium, in 2018.

Brussels sprouts new RIKEN office

RIKEN has established collaborative research agreements with 275 institutions in 43 countries around the world. Of these partnerships, 84 are with institutions in 19 European countries. To further strengthen links there, on 1 November 2018, RIKEN established a new overseas office in Brussels, Belgium. The new office's mission is to enhance RIKEN's access to European research resources, collaborations and personnel exchanges, as well as to strengthen links with government and funding agencies in Europe and the European Union (EU).

This is RIKEN's third overseas office, following office openings in Singapore in 2006 and Beijing in 2010.

Many prominent research figures attended the opening ceremony, including Kazuo Kodama, ambassador from the Japanese government's Mission of Japan to the European Union, Jean-Eric Paquet, director general of the EU's Directorate-General for Research and Innovation, and Jean-Pierre Bourguignon, president of the European Research Council.

http://www.riken.jp/en/pr/topics/2018/20181207_1/

Delegates at the RIKEN–MPG Administrative Roundtable Meeting on best practices in academic administration.

Exchange with the Max Planck Society

In November 2018, six people from the Max Planck Society (MPG) in Germany came to Japan for the 2nd RIKEN–MPG Administrative Roundtable Meeting on academic administration best practice.

RIKEN and MPG have been conducting collaborative research for more than 30 years, and the administrative roundtable started last year. The first meeting was held at the MPG's headquarters in Munich, Germany.

The roundtable covered a wide range of areas, including governance, human resource management, communications and collaboration with external partners. Representatives of a number of administrative departments from each institute gave presentations about their responsibilities and systems, and the participants actively discussed each topic over two days.

http://www.riken.jp/en/pr/topics/2018/20181030_1/

Leading the Graph500 for four years straight

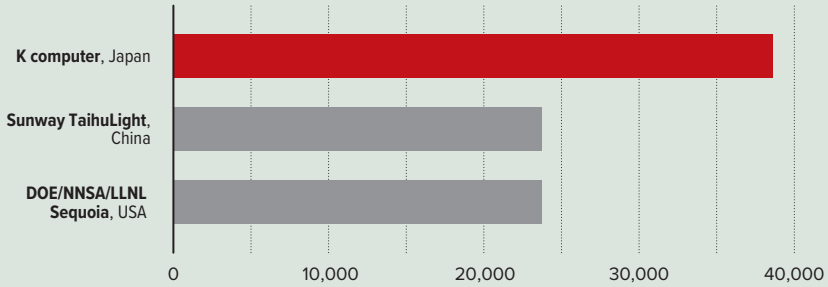
For the eighth time in a row, the K computer has taken the top spot on the biannual Graph500 ranking. The Graph500 benchmark gauges the ability of supercomputers to process data-intensive loads rather than looking at simple speed, which is measured by the better known Top500 ranking.

Graph500's goal is to improve computing involving complex data problems in Big Data areas such as cybersecurity, medical informatics, data enrichment, social networks, symbolic networks and modeling neural circuits in the brain.

The top rank was won this time through the collaborative efforts of RIKEN, Kyushu University, Tokyo Institute of Technology, the Barcelona Supercomputing Center, Fujitsu, and Fixstars Corporation. To benchmark the supercomputer, the group used 82,944 of K computer's 88,128 compute nodes. They used these nodes to solve a breadth-first search of an extremely large graph containing 1 trillion nodes and 16 trillion edges in 0.45 of a second; it gave the team a score of 38,621 giga TEPS.

http://www.riken.jp/en/pr/topics/2018/20181114_1/

TOP 3 SUPERCOMPUTERS COMPARED



Twenty highly cited researchers

Twenty RIKEN researchers—12 with primary affiliations to RIKEN—made Clarivate Analytics' 2018 list of highly cited researchers. The list is a tally of the world's most influential scientists and social scientists, "who have demonstrated significant influence through publication of multiple highly cited papers during the last decade." More than 4,000 scientists were chosen, 90 from Japan. This year, a new area called Cross-Field was added to recognize researchers working in interdisciplinary areas. The Cross-Field category was used to identify some 2,000 researchers and was a response to concerns that prominent researchers were publishing papers in several fields, but not enough in any one to make the list.

https://hcr.clarivate.com/

http://www.riken.jp/en/pr/topics/2019/20190108_2/

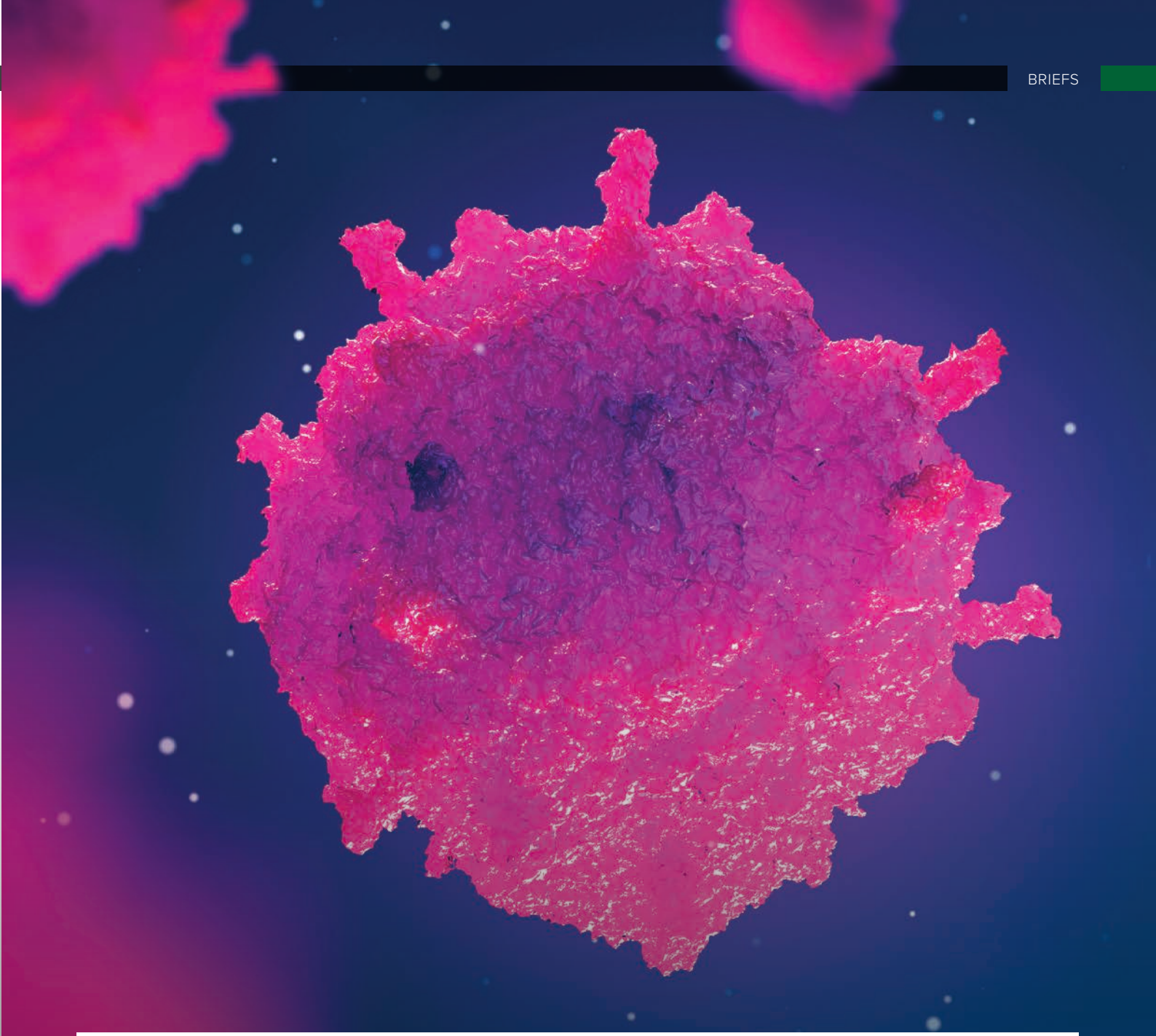
CLARIVATE ANALYTICS' HIGHLY CITED RESEARCHERS AT RIKEN

PRIMARY RIKEN AFFILIATION

- **Piero Carninci,** RIKEN Cross-Field
- **Yuji Kamiya,** RIKEN Plant & Animal Science
- **Mikiko Kojima,** RIKEN Plant & Animal Science
- **Sadamichi Maekawa,** RIKEN Cross-Field
- **Naoto Nagaosa,** RIKEN/University of Tokyo (UTokyo) Physics
- **Franco Nori,** RIKEN/University of Michigan Physics
- **Motoaki Seki,** RIKEN/Yokohama City University Plant & Animal Science
- **Mitsunori Seo,** RIKEN Plant & Animal Science
- **Kazuo Shinozaki,** RIKEN/Nagoya University Plant & Animal Science
- **Ken Shirasu,** RIKEN Plant & Animal Science
- **Yoshinori Tokura,** RIKEN/UTokyo Physics
- **Lam-Son Phan Tran,** RIKEN Plant & Animal Science

SECONDARY RIKEN AFFILIATION

- **Takuzo Aida,** UTokyo/RIKEN Cross-Field
- **Ryotaro Arita,** UTokyo/RIKEN Cross-Field
- **Kenya Honda,** Keio University/RIKEN Immunology
- **Yoshihiro Iwasa,** UTokyo/RIKEN Cross-Field
- **Kazuki Saito,** Chiba University/RIKEN Plant & Animal Science
- **Hitoshi Sakakibara,** Nagoya University/RIKEN Plant & Animal Science
- **Takao Someya,** UTokyo/RIKEN Cross-Field
- **Kazuo Takimiya,** Tohoku University/RIKEN Cross-Field



The Single Cell Science Symposium

Eleven speakers addressed more than 200 delegates in Tokyo at the Single Cell Science Symposium 2018, organized by the RIKEN Center for Integrative Medical Sciences.

The Single Cell Science Symposium is a series of meetings that began in 2017 to address advanced technologies used in single-cell analysis in genomics, to bring together scientific leaders in single-cell biology, and to introduce new projects of the Human Cell Atlas Japan.

This year, the symposium expanded its single-cell scope to clinically relevant human tissues and computational approaches to single-cell data, to help meet the needs of medical communities in Japan.

http://www.ims.riken.jp/?p=3539

Speakers and guests at the symposium. Piero Carninci (6th from right) leads the RIKEN Single Cell Project and spearheads Asia's Human Cell Atlas effort.

QUANTUM COMPUTING

Combining the best of both qubits

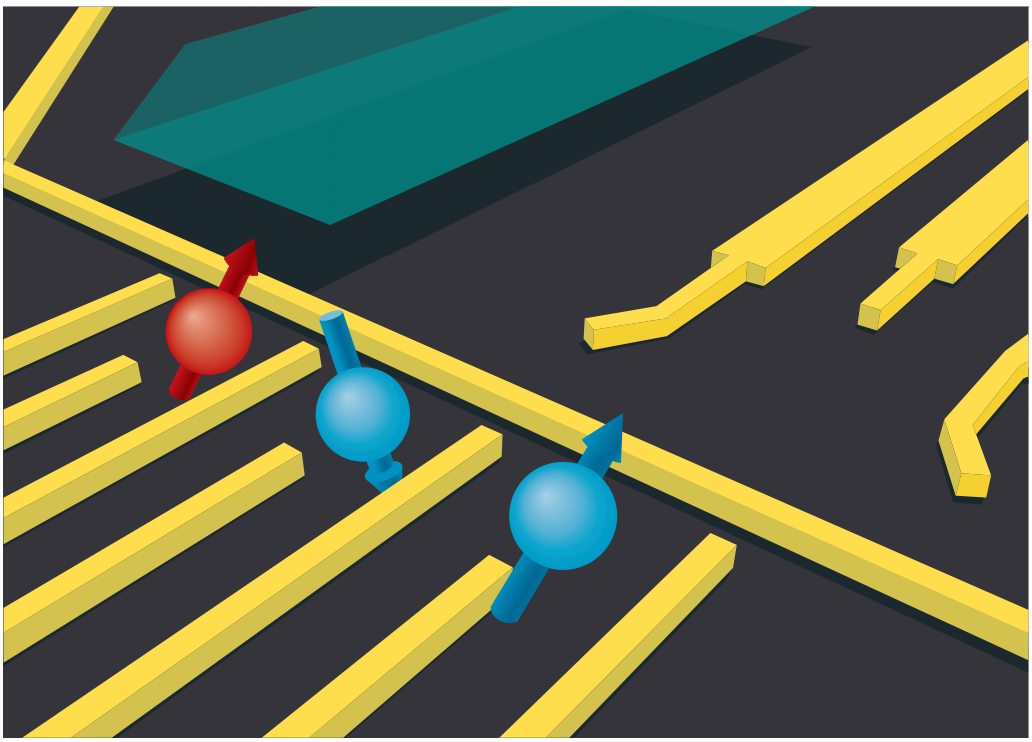
Using two kinds of quantum information units promises to speed up data processing in quantum computers

A hybrid quantum computer that employs two types of qubit—the fundamental computing element of quantum computers—has been demonstrated by RIKEN researchers[1]. This device could help scale up quantum computers.

Quantum computers based on a property of electrons known as spin have the potential to solve difficult mathematical problems that are unsolvable by conventional computers. But it has been difficult to scale them up to the size required to perform real-world calculations.

Back in 1998, Daniel Loss of the University of Basel, who is also a team leader at the RIKEN Center for Emergent Matter Science, and David DiVincenzo of IBM, proposed building a quantum computer based on the spin of electrons in quantum dots—a small particle that behaves like an atom and can be manipulated.

Since then, Loss and collaborators have endeavored to build practical quantum computer devices that are sufficiently fast, but there are three barriers to realizing this. First, the device needs to be quickly initialized—the process of putting a qubit into a certain state. Second, it must maintain coherence long enough to make a measurement. Coherence refers to the entanglement between two quantum states, which is used to make the measurement; if qubits lose their coherence due to noise in their environment, for example, they cannot be used for calculations. And finally, it must be possible to quickly read out the final state of the qubit.



A quantum computer that uses the electron spins (indicated by arrows in the image) of two kinds of qubits has been demonstrated by RIKEN researchers.

RIKEN-led teams have combined two types of qubits in a single device

Now, the RIKEN-led teams headed by Seigo Tarucha and Daniel Loss have combined two types of qubits in a single device (see image).

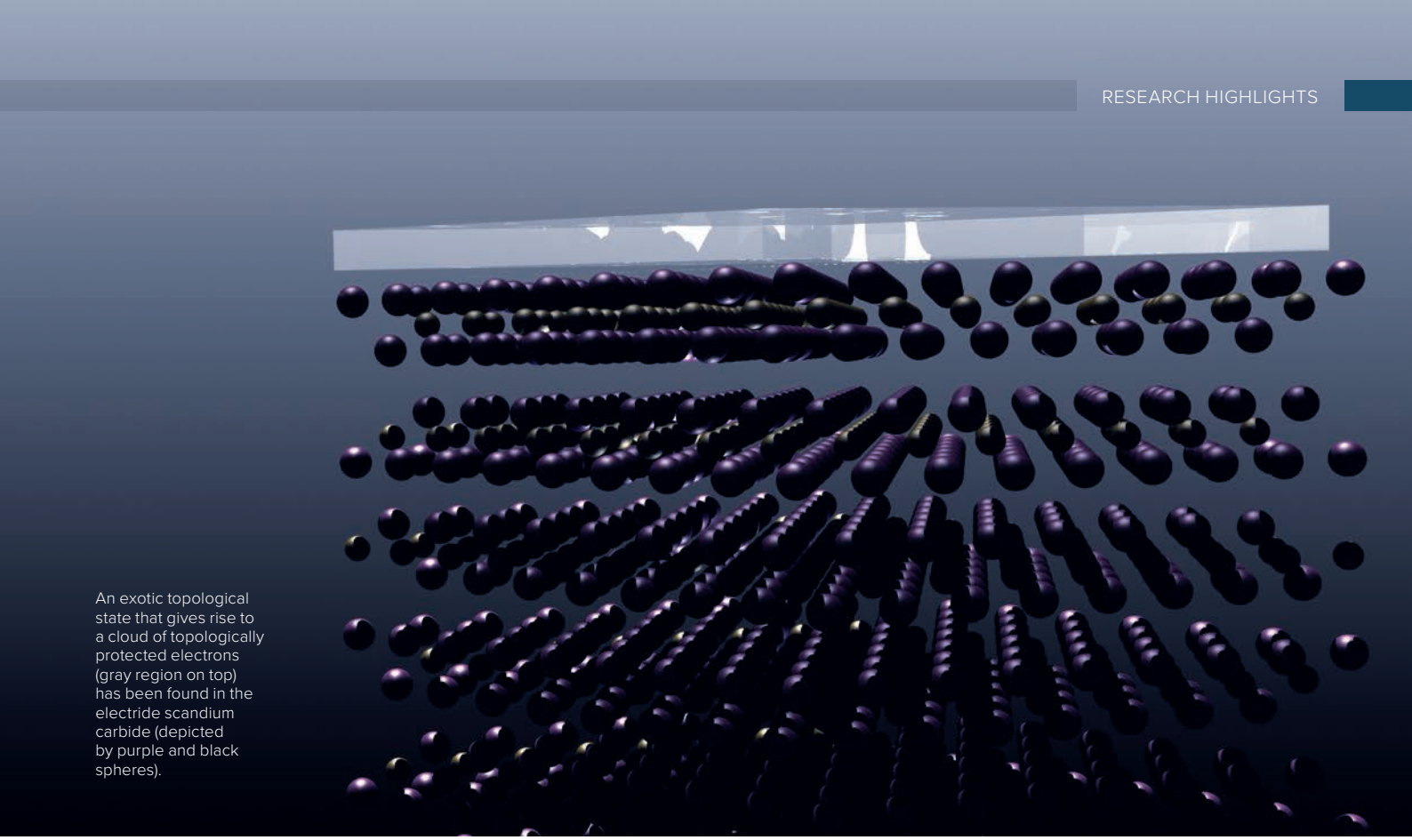
The first qubit has a very high fidelity—meaning that it is in a clear state, making it ideal for calculations. It also remains coherent for a long time, so that it will stay in a given state for a relatively long period before losing its signal to the environment. Unfortunately, these qubits cannot be quickly initialized or read out. In contrast, the second type of qubit can be quickly initialized and read out, but it rapidly loses its coherence.

The scientists combined the two types of qubit with a type of quantum gate that allowed spin states to be entangled between the qubits fast enough to maintain the coherence. This allowed the state of the first kind of qubit to be read out by measuring the second kind of qubit.

"With this study, we've demonstrated that different types of quantum dots can be combined on a single device to overcome their respective limitations," says Akito Noiri, the lead author of the study. "This offers important insights that can contribute to the scalability of quantum computers." ●

Reference

1. Noiri, A., Nakajima, T., Yoneda, J., Delbecq, M. R., Stano, P., Otsuka, T., Takeda, K., Amaha, S., Allison, G., Kawasaki, K. *et al.* A fast quantum interface between different spin qubit encodings. *Nature Communications* **9,** 5066 (2018).



An exotic topological state that gives rise to a cloud of topologically protected electrons (gray region on top) has been found in the electride scandium carbide (depicted by purple and black spheres).

TOPOLOGICAL MATERIALS

Electrides in a twist

Calculations point to a new source of electronically unique materials

A new class of materials could be employed in electronic devices because of their useful surface properties[1]. Electrides may harbor exotic topological states, according to calculations by RIKEN scientists.

Topology is an area of mathematics that describes an object in terms of those physical properties that remain the same even when the shape of the object changes. It has been an important theoretical concept in quantum and particle physics for decades, but the last few years has seen the emergence of materials that exhibit extraordinary properties due to topology.

Many types of topological materials have been identified, including topological insulators and topological semimetals. In topological insulators, electrons can scud across the material's surface but cannot travel below the surface. That is because the surface electrons exist in a quantum mechanical state that is geometrically 'twisted'.

This special topology protects surface states, imparting them with remarkable resilience to impurities and imperfections in the material. This robustness makes topological matter an exciting prospect for a new generation of information processing devices.

To date, the search for new topological materials has largely been limited to matter that includes heavy elements with intrinsic magnetic properties, such as bismuth. This greatly narrows the choice of potentially useful materials. Now, Motoaki Hirayama from the RIKEN Center for Emergent Matter Science and his colleagues have shown that an entirely different class of materials, known as electrides, can also exhibit topological properties.

Like common table salt (sodium chloride), electrides are ionic crystals—ordered arrays of positively charged cations and negatively charged anions. But in electrides, the anions are electrons rather than ions. Some of the electrons prefer to sit between the atomic nuclei in the crystal structure. This means they are less influenced by the nuclei's electric fields and so are weakly bound to the atomic lattice. Hirayama and co-workers theoretically modeled the behavior of these electrons in various electride materials using so-called first-principles calculations.

"For example, we found an exotic topological state in the electride scandium carbide," says Hirayama. "Thanks to its nontrivial topology and electride properties, its topological charges float on the material's surface."

The team found that electrides can support various topological phases, including both topological insulating and topological semimetal phases. And they suggest that these effects could be observed using commonly used experimental techniques, such as scanning tunneling microscopy and angle-resolved photoelectron spectroscopy.

"The next step is to further investigate the physical properties of these topological electrides," says Hirayama. "We expect them to be a rich source of physics."

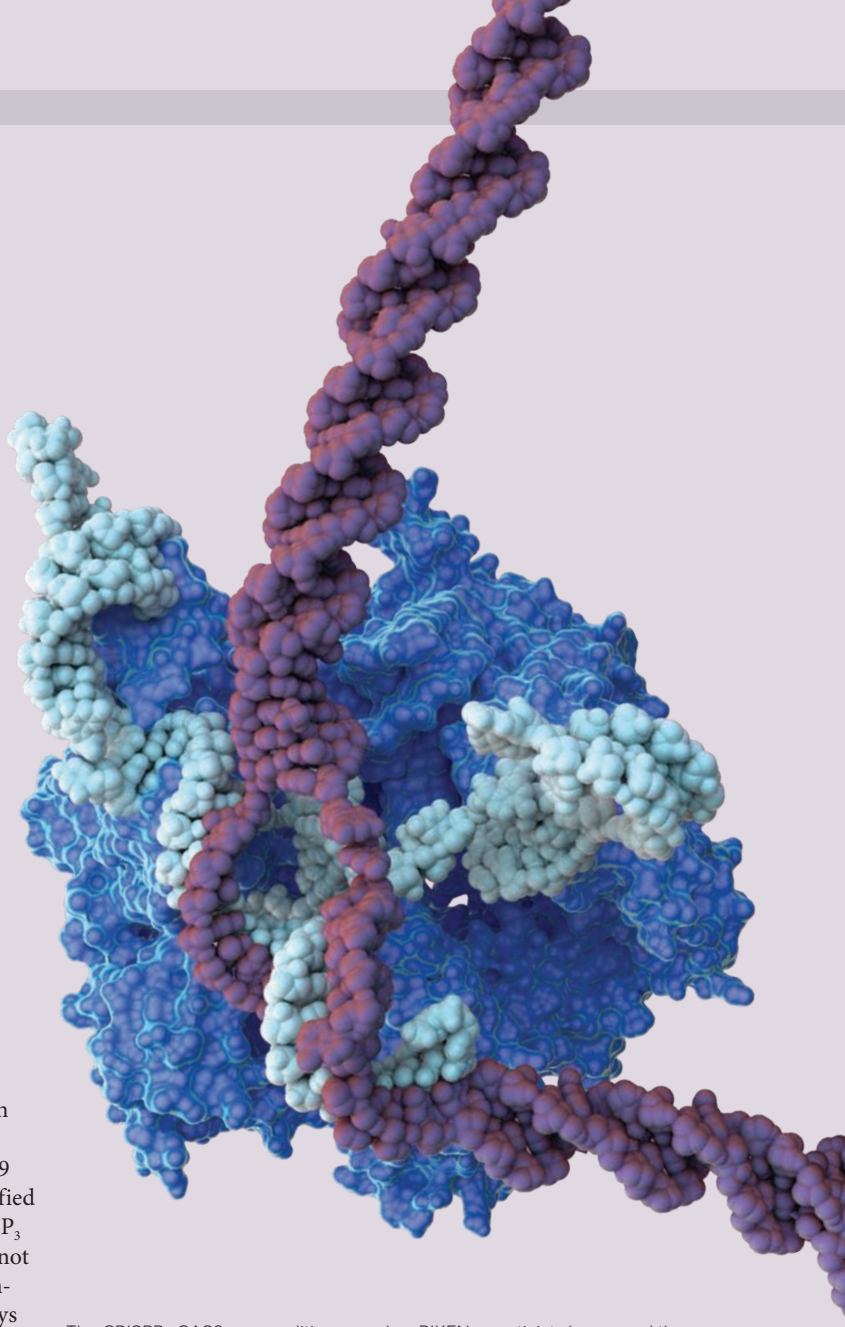
Reference

1. Hirayama, M., Matsuishi, S., Hosono, H. & Murakami, S. Electrides as a new platform of topological materials. *Physical Review X* **8,** 031067 (2018).

GENETIC DISORDERS

How mutations cause a movement disorder

Mutant genes upset the normal function of calcium in neurons in the brain region responsible for walking



The CRISPR–CAS9 gene-editing complex. RIKEN geneticists have used the gene-editing technique to investigate how mutations cause one form of the movement disorders known as spinocerebellar ataxias.

RIKEN geneticists have discovered how mutations related to a group of movement disorders produce their effects[1]. This will aid scientists to find ways to treat these disorders.

Degenerative movement disorders called spinocerebellar ataxias are caused by dysfunctions in the cerebellum brain region, which is responsible for smooth, coordinated movements such as walking and speaking.

Different spinocerebellar ataxias have different genetic origins. Recently, the spinocerebellar ataxia SCA29 was found to be associated with mutations that affect the protein receptor IP_3R1, which is especially common in neurons in the cerebellum.

These findings will help the quest to develop effective treatments

Now, Katsuhiko Mikoshiba's team at the RIKEN Center for Brain Science has determined how the many different mutations related to SCA29 affect IP_3R1 function within cells.

Studying mutations in IP_3Rs is difficult because nearly all cells have one or more of three types. Other researchers have made cells lines in which all three types have been deleted, but introducing mutant genes into them takes time.

Mikoshiba's team used CRISPR genome-editing technology to create cells in which all three IP_3R genes were disrupted. Introducing mutant or wild-type IP_3Rs into these cells could be done very efficiently, allowing them to complete the study much quicker than normal.

The team examined over ten mutations related to SCA29. "Surprisingly, all of the SCA29 pathological mutations identified within or near the place that IP_3 attaches to IP_3R1 completely (not partially) blocked the calcium-releasing activity of IP_3R1," says first author Hideaki Ando.

Calcium is crucial for signaling between neurons and is stored in cells when not being used. When IP_3 attaches to IP_3R1, it allows calcium to pass through so that it can be released from storage when needed. By blocking calcium release, the SCA29 mutations prevent calcium from doing its job.

The team did further tests to determine how the different mutations disrupted calcium release and found that in 9 of 12 mutations near the binding region, IP_3 was prevented from binding to the receptor.

Two other mutants indirectly affected IP_3R1 activity through mutations affecting the binding site of another protein known as CA8. Calcium release is normally suppressed when CA8 binds to the receptor, but calcium release was higher than normal in the mutants. CA8 mutations have also been identified in people with congenital ataxia and intellectual disabilities. The team found that these mutations also prevented normal suppression of calcium release.

These findings will help the quest to develop effective treatments. "Now we know that spinocerebellar ataxias can result from both suppressed or enhanced calcium release though the IP_3 type 1 receptor," Ando explains. "Therefore, drug development that enhances or inhibits IP_3R1 activity may lead to effective treatments for these disorders." ●

Reference

1. Ando, H., Hirose, M. & Mikoshiba, K. Aberrant IP_3 receptor activities revealed by comprehensive analysis of pathological mutations causing spinocerebellar ataxia 29. *Proceedings of the National Academy of Sciences of the USA* **115,** 12259–12264 (2018).

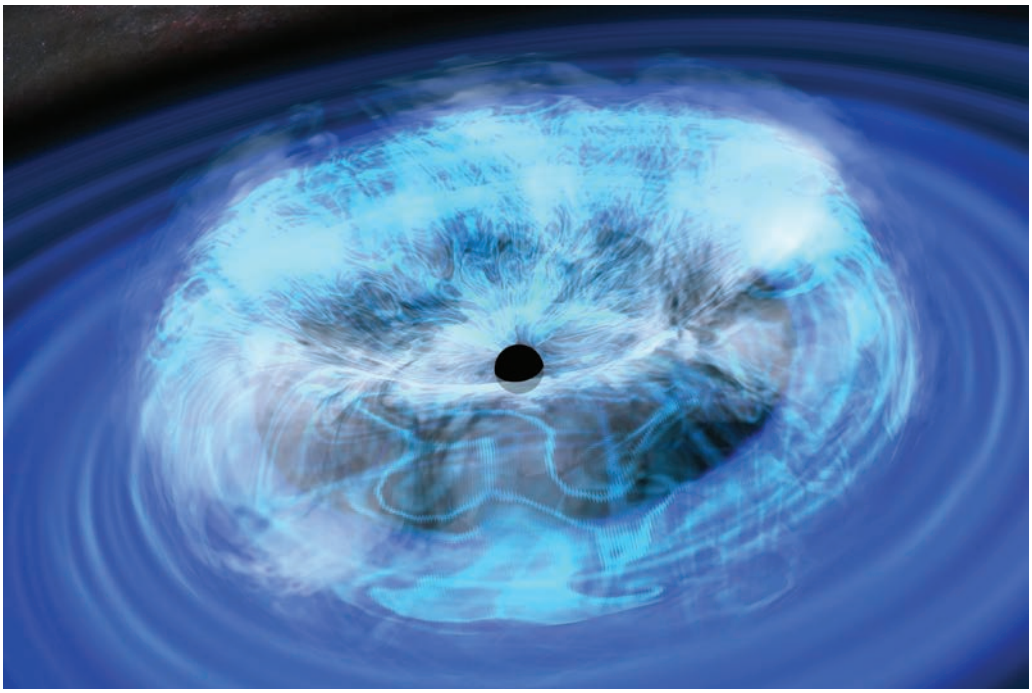
BLACK HOLES

Magnetic heating ruled out for supermassive black holes

Measurements using radio telescopes reveal that the magnetic fields around supermassive black holes are too weak to heat the superheated plasma that surrounds them

The strength of magnetic fields near two supermassive black holes at the centers of an important type of active galaxy has been measured by RIKEN researchers using the ALMA radio telescope in Chile[1]. Surprisingly, the magnetic fields appear to be too weak to power the clouds of superheated plasma that encompass the black holes.

Like the Sun, supermassive black holes at the centers of galaxies are surrounded by coronae of superheated plasma (see image). The coronae of such black holes can be heated to temperatures of about a billion degrees Celsius. These phenomenal temperatures have long been assumed to be sustained by magnetic fields, but this had not been confirmed since these magnetic fields had not been measured.



An artist's impression of the corona around a supermassive black hole.

The researchers had previously predicted that electrons in the plasma surrounding black holes would emit synchrotron radiation—the radiation emitted when charged particles traveling close to the speed of light are accelerated in a direction perpendicular to their path—as they exist together with the magnetic forces in the coronae. Specifically, this type of radiation would be long-wavelength electromagnetic radiation in the form of radio waves.

The team set out to measure these fields from two 'nearby' active galactic nuclei: IC 4329A (about 200 million light-years away) and NGC 985 (about 580 million light-years away). They compared measurements from the ALMA observatory in Chile with those from two other radio telescopes, which measure slightly different frequency bands. The team found that there was an excess of radio emission originating from synchrotron radiation, in addition to emissions from the jets cast out by the black holes.

The team deduced that the coronae were about 40 Schwarzschild radii in size (where 1 Schwarzschild radius is the radius within which light cannot escape from a black hole) and had a magnetic field strength of about 10 gauss, which is stronger than Earth's magnetic field at ground level but considerably weaker than that of a typical fridge magnet.

"The surprise is that, although we confirmed the emission of radio synchrotron radiation from the corona in both objects, it turns out that the magnetic field we measured is much too weak to be able to drive the intense heating of the coronae around these black holes," says Yoshiyuki Inoue of the RIKEN Interdisciplinary Theoretical and Mathematical Sciences Program. He also notes that both galaxies exhibited the same phenomenon, suggesting it could be general.

The group now plans to look for signs of powerful gamma-rays that should accompany the radio emissions, to further understand what is happening in the environment near supermassive black holes. ●

Reference

1. Inoue, Y. & Doi, A. Detection of coronal magnetic activity in nearby active supermassive black holes. *The Astrophysical Journal* **869,** 114 (2018).

Plants wilt when they do not get sufficient water, but recover when water is supplied again. RIKEN researchers have gained new insights into the complex biological process that enables plants to rehydrate.

PLANT GENETICS

How plants bounce back after drought

Researchers have discovered how a key plant hormone that enables plants to rehydrate after drought accumulates when water is in short supply

The development of drought-resistant plants could be boosted by a genetic analysis by RIKEN scientists that has revealed how a protein controls the transcription of a gene that allows plants to survive after periods of drought[1].

If you neglect to water your plants for a week or two, they usually recover once you give them water again. This rehydration is driven by a complex biological process that depends on a plant hormone called ABA. For plants to rehydrate, ABA must accumulate during the early stages of dehydration, but not much was known about how dehydration stress causes ABA to accumulate.

To investigate this, Hikaru Sato of the Gene Discovery Research Group (PI Kazuo Shinozaki), RIKEN Center for Sustainable Resource Science, and collaborators screened a library of 1,670 transgenic plant lines and performed a series of experiments. "We used a library of plant lines that was created with chimeric repressor silencing technology," explains Sato. "This special technique is used for identifying novel transcription factors in plant genetic science."

Looking for plants with characteristics similar to ABA-deficient mutants, the team found a plant line in which overexpression of NGA with a chimeric repressor domain resulted in reduced levels of the enzyme NCED3 during dehydration stress. This was promising since plants need NCED3 to make ABA. The scientists hypothesized that NGA was a transcription factor that could control the production of NCED3, and ultimately the biosynthesis of ABA.

It turns out there is a whole family of NGA proteins, and the team found that all of them bind to the region of the *NCED3* gene that triggers its transcription.

But the story is not that simple. The team created transgenic plants for each member of the NGA family and found that NGA proteins are naturally found in different parts of plants and show different expression patterns during dehydration stress. Some were expressed in the roots and others in the leaves. The timing of NGA expression also varied between different lines. It is thus unlikely that they all respond in the same way to drought stress.

To determine which NGA proteins are important for natural ABA synthesis, the team created knockout mutants for each. All the plants grew normally when water was available, but only the NGA1 mutants could not be revived by rehydration after water had been withheld until the plants withered.

Improving drought tolerance is a top priority for plant scientists. "Several studies have shown that increasing ABA levels can improve drought tolerance in plants," notes Sato. "Our finding that NGA1 is necessary for ABA biosynthesis will thus likely be helpful for developing new ways to increase drought-stress tolerance."

Reference

1. Sato, H., Takasaki, H., Takahashi, F., Suzuki, T., Iuchi, S., Mitsuda, N., Ohme-Takagi, M., Ikeda, M., Seo, M., Yamaguchi-Shinozaki, K. *et al. Arabidopsis thaliana* NGATHA1 transcription factor induces ABA biosynthesis by activating *NCED3* gene during dehydration stress. *Proceedings of the National Academy of Sciences USA* **115,** E11178–E11187 (2018).

EVOLUTIONARY DEVELOPMENT

Lamprey shines a light into ears

An analysis of how the inner ear develops in jawless fish casts light on its evolution

Cyclostome embryos have provided a new insight into how the inner ear of all vertebrates evolved[1].

Comparing organs among related animals is helpful for better understanding both evolutionary development and ultimately the processes by which organs develop.

Jawed vertebrates including humans have inner ears with three semicircular canals, which allow them to sense their position and three-dimensional acceleration as well as stay balanced. The fossil record shows that a group of jawless fish from the Paleozoic era had only two semicircular canals. To understand the evolutionary changes that led to three canals, the researchers looked at the only two types of jawless vertebrates (cyclostomes) that still exist on Earth: lampreys and hagfish.

Although lampreys have two semicircular canals and hagfish have only one, hagfish are not thought to be more primitive than lampreys. Shigeru Kuratani at the RIKEN Center for Biosystems Dynamics and colleagues performed comparative embryological analyses and a series of molecular biological experiments to explore why this was so.

Analysis of the regulatory genes that control the development of the semicircular canals showed that all vertebrates, including lampreys and hagfish, have a similar basic pattern for inner-ear development. Key genes, such as *Tbx1* and *Patched*, were expressed at the same places with the same timing across lampreys and hagfish as well as jawed vertebrates.

The anterior and posterior canals in jawed vertebrates appear to be genetically homologous to the anterior and posterior parts of the lamprey canal, while the pattern for the single hagfish canal was shown to represent a derived condition rather than a primitive one.

By studying two jawless fish—lamprey (shown here) and hagfish—researchers have gained new insights into how the inner ear evolved.

This provides a new story for inner-ear evolution

Jawed and jawless fish differ in that jawed fish have a common crus, a structure that connects the anterior and posterior canals in jawed vertebrates. The current study could not determine whether the common crus is something that jawed vertebrates gained or jawless vertebrates lost.

Further analysis focused on the *Otx1* gene, the gene needed for the proper development of the lateral canal, the third canal that is unique to jawed vertebrates. The researchers found that despite lacking a lateral canal, lampreys and hagfish both expressed *Otx1* in the proper location during development. This was surprising since its expression was thought to have led to the evolution of the lateral canal. Instead, it appears that *Otx1* expression in the otic vesicle is an ancient feature of all vertebrates.

The researchers anticipate that studying an animal that represents the lineages before jawed and jawless vertebrates diverged will lead to greater clarification of evolutionary pathways. ●

Reference

1. Higuchi, S., Sugahara, F., Pascual-Anaya, J., Takagi, W., Oisi, Y. & Kuratani, S. Inner ear development in cyclostomes and evolution of the vertebrate semicircular canals. *Nature* **565,** 347–350 (2019).

ARTIFICIAL INTELLIGENCE

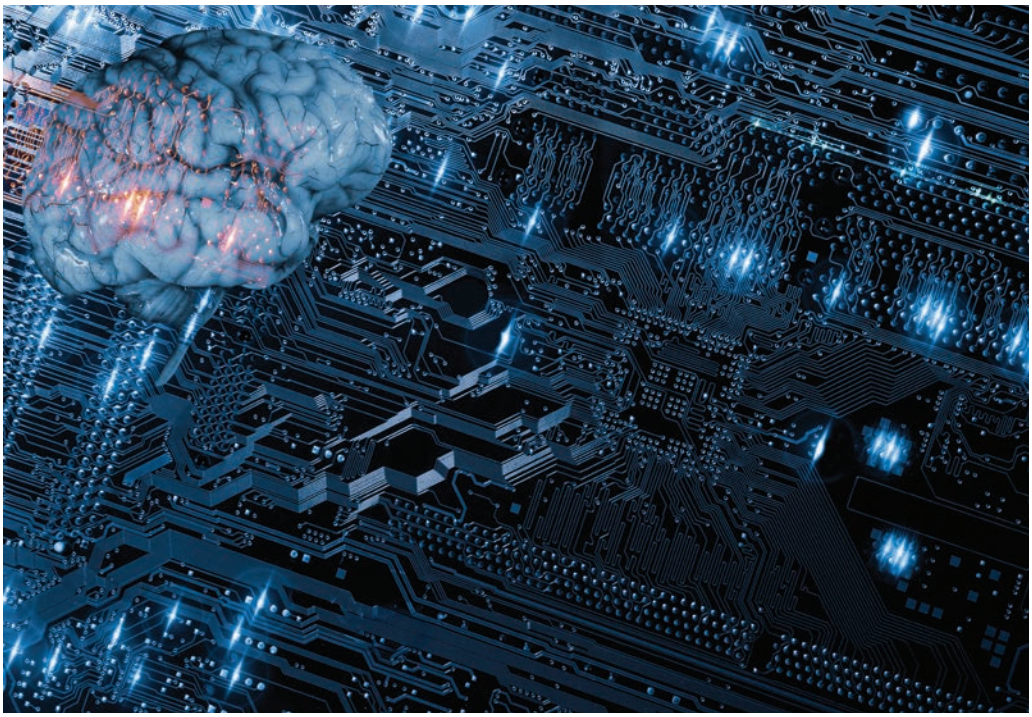
Machines equipped with confidence

Classification that harnesses the power of artificial intelligence has become more versatile

A machine learning method that allows artificial intelligence (AI) to classify things into two categories even when important data is lacking has been developed by RIKEN researchers[1]. This approach could lead to wider application of AI to various classification tasks.

Classifying things is critical for our daily lives. For example, we have to detect objects and faces. When using AI, such tasks are based on classification technology in machine learning—having the computer learn using the boundary that separates so-called positive and negative data. However, the learning process needs both kinds of data, and negative data are often not available.

For example, a retailer wanting to predict who will purchase their products can easily find data on customers who have purchased from them (positive data) but cannot obtain data on customers who did not (negative data) since they lack access to their competitors' data.



RIKEN researchers have used artificial intelligence to enhance the versatility of classification technology.

"Our classification technology could be used in new situations where only positive data can be gathered"

"Previous classification methods couldn't cope with situations where negative data were not available, but we have made it possible for computers to learn with only positive data, as long as we have a confidence score for our positive data, constructed from information such as buying intention or the active rate of app users," explains Takashi Ishida of the RIKEN Center for Advanced Intelligence Project. "Using our new method, we can let computers learn a classifier only from positive data equipped with confidence."

Ishida proposed letting computers learn by adding a confidence score, which corresponds mathematically to the probability of whether the data belongs to a positive class. His team developed a method that enables computers to learn a classification boundary only from positive data and information on its confidence (positive reliability) for classification problems of machine learning that divide data positively and negatively.

The team tested their method on photos containing various fashion items. For example, they chose T-shirt photos as the positive class and sandal photos as the negative class. The researchers attached confidence scores to the T-shirt photos. They found that, in some cases, their method, which did not access the negative data (that is, sandal photos), was just as effective as a method that uses both kinds of data.

"This discovery could expand the range of applications where classification technology can be used," says Ishida. "Even in fields where machine learning has been actively used, our classification technology could be used in new situations where only positive data can be gathered due to data regulation or business constraints. In the near future, we hope to put our technology to use in various research fields, such as natural language processing, computer vision, robotics and bioinformatics." ●

Reference

1. Ishida, T., Niu, G. & Sugiyama, M. Binary classification from positive-confidence data. *Preproceedings of 32nd Conference on Advances in Neural Information Processing Systems* (2018).

An enormous halo of hot gas surrounds the Milky Way. Stellar explosions called core-collapse supernova may be feeding it with fresh gas.

ASTROPHYSICS

The Milky Way's hot spotty halo

Observations from Suzaku observatory reveal that core-collapse supernovae have fed the gas cloud that surrounds our galaxy

A halo of hot gas that surrounds the Milky Way has been mapped by RIKEN researchers, revealing how exploding stars have helped to shape this blazing shroud[1].

The Milky Way is a spiral galaxy up to 100,000 light years across, and our Sun is just one of hundreds of billions of stars within it. The galaxy has a halo, which is partly made up of gas accumulated from the vast expanses of intergalactic space, but it is also molded and supplemented by matter ejected from the galaxy's stars. The balance between these two sources is not fully understood, and there is ongoing debate about the halo's size and shape.

To help resolve these questions, a team of scientists that included Shinya Nakashima of the RIKEN High Energy Astrophysics Laboratory and Yoshiyuki Inoue of the RIKEN Interdisciplinary Theoretical and Mathematical Sciences (iTHEMS) Program used observations from the Suzaku telescope, which operated in orbit until 2015, to study x-rays coming from the mysterious halo.

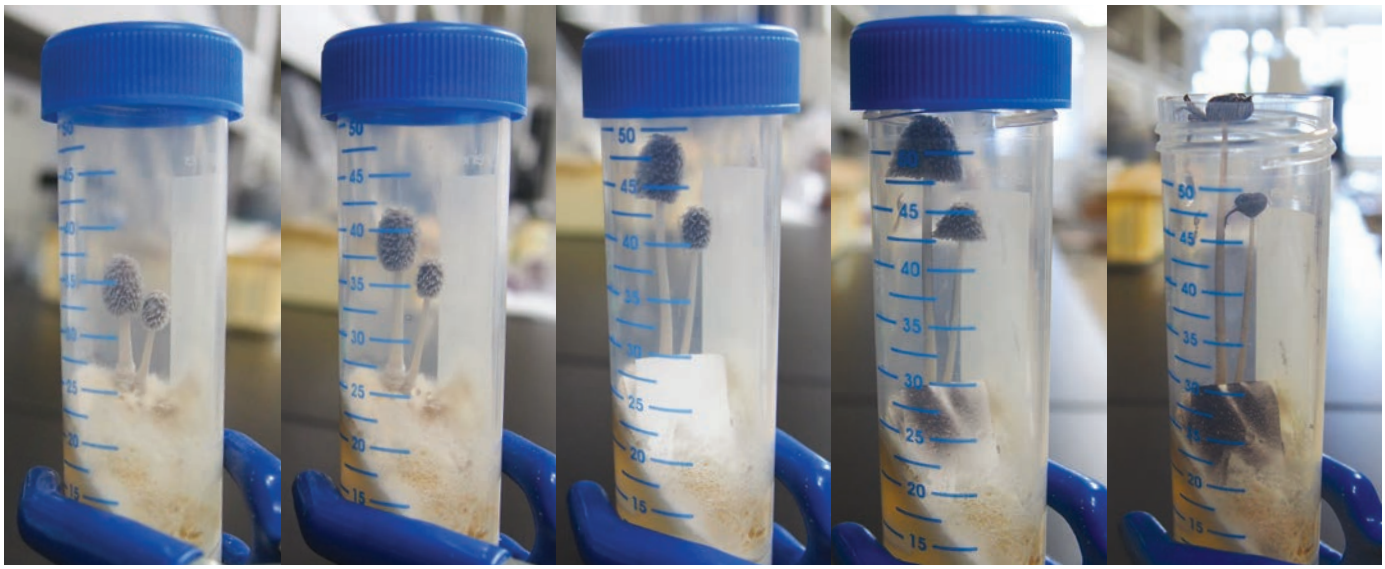
The researchers found that the halo has a median temperature of about 3 million degrees Celsius. They also tracked how the density of gas in the disk gradually drops off with distance from the center. By comparing their observations with gas distribution models, the researchers concluded that most of the x-rays are emitted by a disk of hot gas with a mass equivalent to roughly 50 million Suns. The halo also includes a larger, spherical ball containing the mass of a billion Suns, but its lower density means that it emits relatively few x-rays.

The researchers also discovered that the disk has quite a high ratio of oxygen to iron, which is characteristic of a type of stellar explosion called a core-collapse supernova. They conjecture that these explosions may have been responsible for supplying much of the gas in the disk, an idea supported by the presence of randomly distributed hotspots in the halo (see image). "Core-collapse supernovae occur at the end of the lives of massive stars," says Nakashima. "They provide fresh, hot gas that contains elements synthesized by the supernova."

The team now hopes to more precisely measure the ratio of oxygen to iron in the halo using a future x-ray observatory, XRISM, which is scheduled to be launched in 2021 by the Japan Aerospace Exploration Agency (JAXA) and NASA. "We would then like to search for hot gaseous halos in other galaxies with another future x-ray observatory, Athena, to be launched in the early 2030s by the European Space Agency," adds Nakashima. ●

Reference

1. Nakashima, S., Inoue, Y., Yamasaki, N., Sofue, Y., Kataoka, J. & Sakai, K. Spatial distribution of the Milky Way hot gaseous halo constrained by Suzaku X-ray observations. *The Astrophysical Journal* **862,** 34 (2018).



Growth of the inky cap mushroom and subsequent chemical disintegration (right frame) for analysis of its secondary metabolites, which were found to exhibit anticancer and antimalarial activity.

FUNGAL SECONDARY METABOLITES

Looking for treasure in a toadstool

Molecules in a mushroom could lead to new antimalarial and anticancer drugs

Both cancer and malaria could be combatted by molecules found in a common mushroom by an all-RIKEN team[1].

The mushroom *Coprinopsis cinerea*, also known as inky cap (see image), is often used in molecular biology research because it is easy to grow in the lab. However, little is known about its secondary metabolites—species-specific molecules synthesized from metabolites that are essential for survival, such as glucose and amino acids.

"This common mushroom is unexplored as a natural source of chemicals," comments Junnosuke Otaka at the RIKEN Center for Sustainable Resource Science. "Our work is like a treasure hunt." The hidden treasure may include lead compounds for drug research—chemicals whose initial promise stimulates investigation of modifications to create new drugs.

Compounds known as cuparene sesquiterpenoids are potential sources of lead compounds, and they have been reported in a variety of organisms, including fungi and plants. In particular, in previous studies, two related compounds had been isolated from another mushroom, which has a different appearance and habitat from *C. cinerea*.

Based on these chemical studies, the researchers predicted that *C. cinerea* produces specific sesquiterpenoids with unusual chemical structures. They obtained three particularly interesting target compounds. Determining their stereochemistry was challenging, but the team confirmed their results by synthesizing one of the compounds and analyzing it using x-ray crystallography.

The team then looked for significant biological activities, partly motivated by the fact that some similar compounds are potent antimicrobials. But they got more than they had bargained for. "We didn't expect to find activity against human leukemia cells or the malaria parasite," says Otaka. This surprise may open up new avenues in anticancer and antimalarial research.

The most effective compound in the biological activity tests, which has been named hitoyopodin A after the Japanese name for *C. cinerea*, has a three-ring chemical structure composed of aromatic rings and an oxygen atom. Otaka speculates that the rigidity of this unusual ring structure may be crucial for bestowing the antileukemia and antimalarial activity. He emphasizes, however, that more research is needed to test that idea and to gain clearer understanding of the mechanisms involved.

Further studies could include identifying the molecules that hitoyopodin A interacts with to bring about medically useful effects. The team will also investigate why the molecules they have discovered are made by the mushrooms. "We want to identify their ecological role in nature," Otaka explains. This will include testing hypothesized involvement in generating other secondary metabolites. ●

Reference

1. Otaka, J., Shimizu, T., Futamura, Y., Hashizume, D. & Osada, H. Structures and synthesis of hitoyopodins: bioactive aromatic sesquiterpenoids produced by the mushroom *Coprinopsis cinerea*. *Organic Letters* **20,** 6294–6297 (2018).

ELECTROACTIVE MATERIALS

Watching iron work

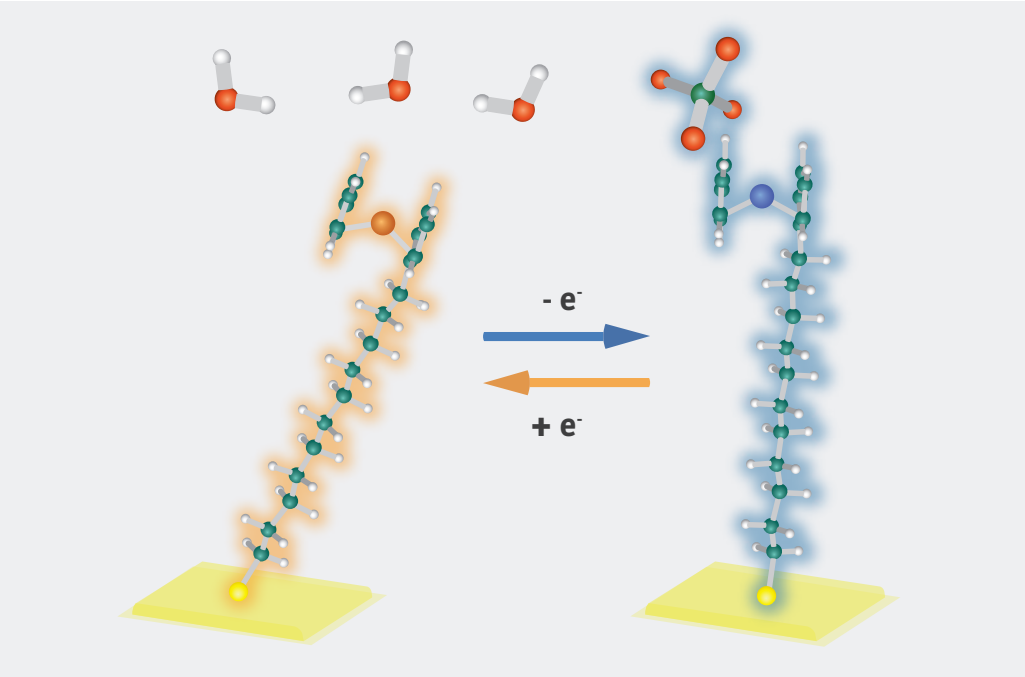
A powerful method can analyze the properties of a single layer of iron-tipped molecules

A new analytical technique developed by researchers at RIKEN could see self-assembled electrochemically active materials deployed in applications such as biosensors, molecular electronics and energy-storage devices. They used photoelectron spectroscopy to detect changes in the electroactive materials under different electrochemical conditions[1]. New insights generated by the technique should spark significant progress toward real-world applications for these promising materials.

Researchers often create self-assembled electroactive structures by exploiting the strong chemical bond that forms between sulfur atoms and gold. Coating an electrode with gold and submerging it in a solution of molecules with a sulfur group at one end creates a bristling forest of these molecules across the electrode as the sulfur atoms grab onto the gold surface.

Useful functionality can emerge if the other tip of the molecules on this self-assembled surface bears an electrochemically active substituent, such as ferrocene, which consists of an iron atom sandwiched between two five-membered carbon rings. By varying the applied electrical potential, the iron atoms will gain or shed electrons in a process known as redox, altering the surface's chemical and physical properties.

The challenge has been observing that functionality in action, explains Raymond Wong of the RIKEN Surface and Interface Science Laboratory.



A ferrocene-tipped molecule attached to a gold surface changes its orientation as it gains an electron (when near water molecules; left) or loses an electron (when near ClO_4^- ions; right).

"Conventional characterization typically employs electrochemical methods such as cyclic voltammetry. But that only tells you the material's overall current response as a function of electrical potential," explains Wong. "Our work is motivated by the desire to obtain complementary information on the electronic and structural details that accompany redox."

Wong and his colleagues developed a way to probe those details using x-ray and ultraviolet photoelectron spectroscopy (XPS/UPS). They designed an experiment in which an electrochemical cell was coupled to an XPS/UPS chamber by a gate valve.

The researchers tested this setup using a ferrocene-tipped self-assembled monolayer as a model system. As the iron atoms switched between neutral ferrocene and the positively charged ferrocenium state, the team observed changes in the orientation of the molecules (see image), the thickness of the monolayer and the formation of ion pairs.

To perform the XPS/UPS analysis, the sample had to be transferred from the electrochemical solution to a vacuum chamber via the gate valve. The fact that the self-assembled monolayer retained its structure under vacuum opens up many new possibilities. "This means that we can potentially use other vacuum techniques, including scanning probe microscopy, for real-space observations of the local changes induced by electrochemical redox," Wong predicts. ●

Reference

1. Wong, R. A., Yokota, Y., Wakisaka, M., Inukai, J. & Kim, Y. Discerning the redox-dependent electronic and interfacial structures in electroactive self-assembled monolayers. *Journal of the American Chemical Society* **140,** 13672–13679 (2018).

CATALYSIS

Open sandwich opens opportunities

New catalyst shows potential for industrial applications by creating chiral silicon–carbon molecules in only left- or right-handed forms

A catalyst that could meet the need that new pharmaceuticals and novel materials have for silane molecules with their carbon–silicon bonds has been developed by RIKEN researchers[1]. The catalyst has an 'open sandwich' structure and is able to attach silicon to a wide variety of carbon-based molecules, while controlling the stereochemistry of the newly formed carbon–silicon bond, forming left- or right-handed molecules to order.

"We will continue to explore the potential of this novel class of catalysts"

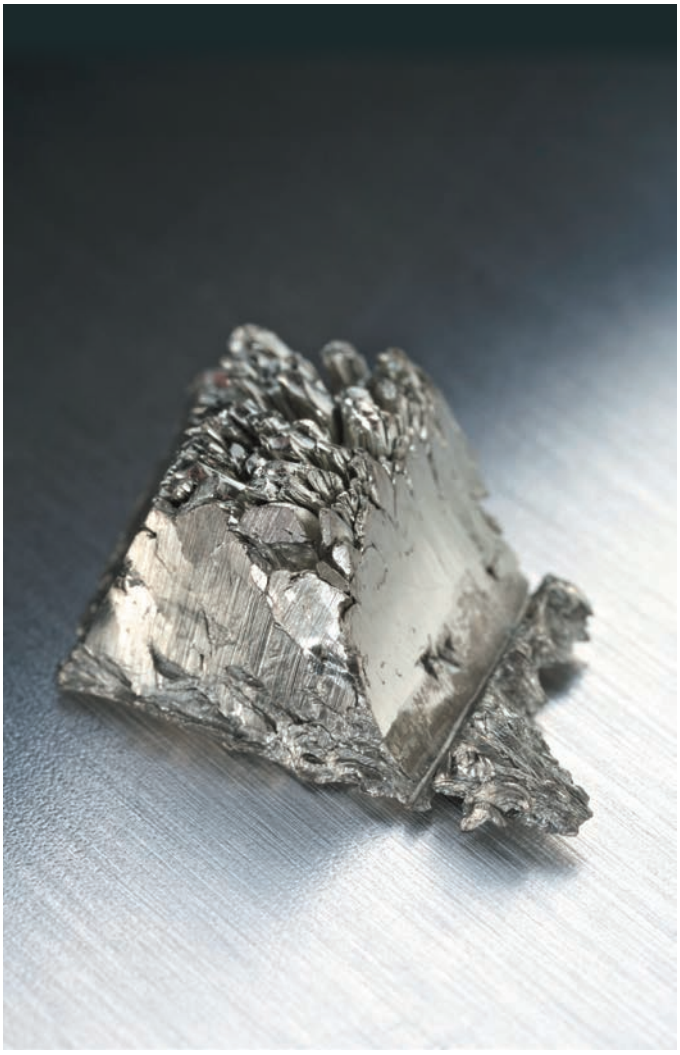
As silicon is readily availably, being the second-most abundant element in the Earth's crust, there is a great deal of interest in putting it to use, says Zhaomin Hou from the RIKEN Center for Sustainable Resource Science, who led the research. Silicon is a close chemical relative of carbon—it sits directly below carbon in the periodic table—and can readily be incorporated into carbon-based organic molecules in a reaction called a hydrosilylation. However, forming this new carbon–silicon bond often creates a molecule that can exist in left- and right-handed forms, which are called enantiomers. When the mirror-image molecules have silicon at their heart, they are known as silicon stereogenic.

For most applications, researchers need a single enantiomer in pure form. "There has been a lack of an efficient and general route or catalyst for synthesizing silicon-stereogenic silanes of just one enantiomer," Hou says. "We recently found that chiral, half-sandwich catalysts containing rare-earth metals can show unique activity and selectivity in a number of asymmetric transformations. This prompted us to study the synthesis of silicon-stereogenic silanes by using these catalysts," he says.

The 'meat' of the chiral open sandwich complex is a scandium ion that catalyzes the hydrosilylation reaction. The 'bread' is a large molecular side unit, known as a ligand, that hangs off one side of the metal, forcing the formation of a new carbon–silicon bond on the other side. The team tried ligands of several shapes and sizes before finding one that was just right, controlling how the two reacting molecules come together and greatly favoring the formation of one enantiomer over the other.

The catalyst proved to be chemically versatile. "It shows high activity for the hydrosilylation of a wide range of aliphatic and aromatic alkenes with both cyclic and non-cyclic silanes," Hou says. It is also highly selective, delivering yields of up to 98% pure left or right handedness. "Chiral half-sandwich rare-earth complexes can serve as a unique platform for asymmetric catalysis."

Hou adds that the potential is huge. "It offers an efficient and general route for synthesizing silicon-stereogenic silanes from easily available starting materials. We will continue to explore the potential of this novel class of catalysts for various chemical transformations." ●



Ions of scandium (shown here in elemental form) in a chiral open-sandwich complex catalyze the stereoselective hydrosilylation reaction.

Reference

1. Zhan, G., Teng, H.-L., Luo, Y., Lou, S.-J., Nishiura, M. & Hou, Z. Enantioselective construction of silicon-stereogenic silanes by scandium-catalyzed intermolecular alkene hydrosilylation. *Angewandte Chemie International Edition* **57**, 12342–12346 (2018).

CIVIL ENGINEERING

Rapidly assessing salt in bridges

Neutrons can speed up the inspection of aging infrastructure by measuring the salt content of concrete structures without damaging them

RIKEN researchers have evaluated the use of neutrons to measure the salt content of structures such as bridges, tunnels and elevated roadways, which can suffer from degradation due to exposure to salt from seawater and other sources. This offers a faster, non-destructive way to assess the safety of old infrastructure.

The collapse of a bridge in August 2018 in Genoa, Italy, that resulted in 43 deaths has highlighted the danger posed by aging infrastructure. Like many countries, Japan faces major problems in this regard since many of its bridges and tunnels were constructed during the 1960s and 1970s and are now suffering degradation.

But the inspections needed to assess the state of infrastructure take time. For example, the salt content of cement structures is typically gauged by boring out cores, which is time consuming and can slightly damage structures.

The researchers used a device that employs a compact neutron source to produce a beam of neutrons with a wide energy range. Neutrons are an attractive way to image structures as they can penetrate quite far into metallic materials because they do not interact via the electromagnetic force and thus are unaffected by electric charge. Occasionally, they interact with nuclei in the materials they penetrate, leading to the release of gamma rays that can be detected.

In the present study, the team irradiated a series of concrete blocks with salt squeezed between them with a neutron beam and measured 'prompt' gamma rays—gamma rays that are emitted immediately upon irradiation by neutrons—using high-energy-resolution detectors.

The prompt gamma rays are emitted from the nuclei in the concrete blocks, and different elements can be detected from the energies and intensities of emitted gamma rays. For example, the energy peaks from the prompt gamma rays emitted by chlorine-35—a component of salt—were 517, 786, 788 and 1,165 kiloelectron volts, and so on.

This offers a faster, non-destructive way to assess the safety of old infrastructure

The researchers could detect the presence of salt even when it was surrounded by more than 5 centimeters of concrete, where rebar corrosion starts. Each measurement took about 10 minutes.

"This is very exciting because Japan and other countries suffer from serious infrastructure degradation, and it's impossible to predict when a major accident will happen," says Yoshie Otake of the RIKEN Center for Advanced Photonics, who led the study. "Our feasibility study has shown that neutron beams can indeed be used to measure whether the salt content of a concrete structure is within the legal limits set by the government. Our next challenge is to build a compact neutron source that is small and light enough to be readily transported to various infrastructures to conduct measurements."

Inspecting aging infrastructure can be time-consuming and arduous work. Using neutrons to assess the salt content of concrete promises to speed up some of that assessment.

CELL BIOLOGY

Ensuring cellular cargo gets delivered to the right address

The molecular mechanism that ensures cellular cargo is transported along the right track has been identified

The molecular mechanism responsible for conveying proteins along the 'trunk' of neurons has been uncovered by RIKEN researchers[1]. This finding challenges conventional thinking about how the cellular transport system works.

Neurons contain a network of filamentous proteins called microtubules (see image), which act as conveyor belts, relaying proteins, organelles and other cell components to their proper destinations. This transport occurs as a result of interactions between microtubule filaments and a superfamily of motor proteins called kinesins.

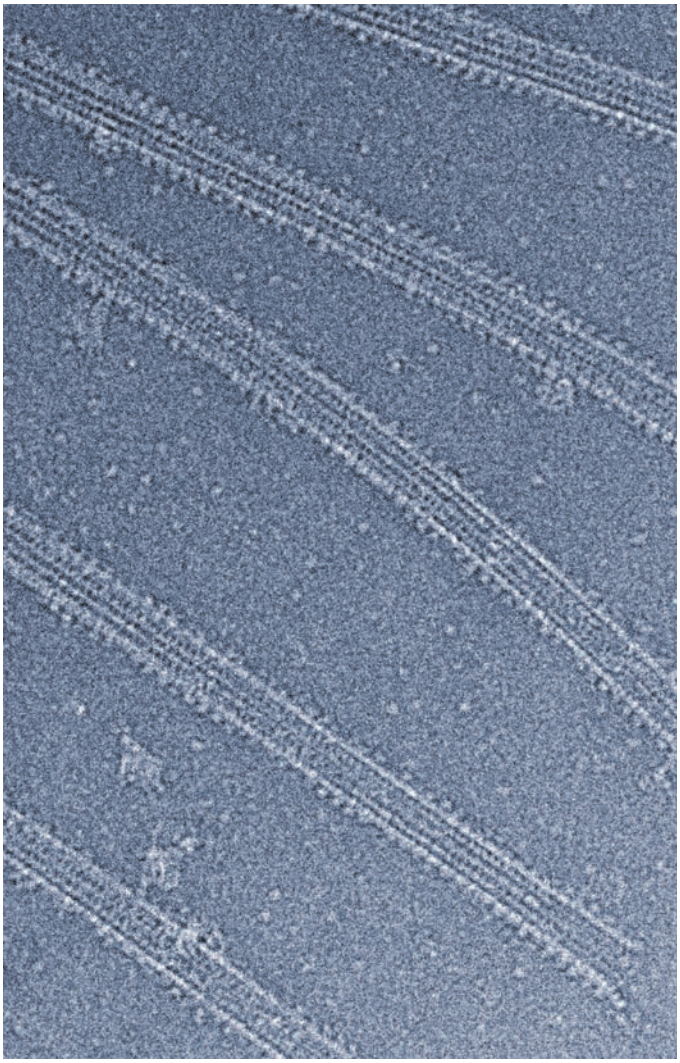
"We wanted to discover how kinesin chooses the correct track"

A neuron has a tree-like structure, with many branches, or dendrites, but just one trunk—the axon. Among the thousands of microtubules that run from the neuron body, less than a few per cent go to the axon. However, some kinesins transport their cargo just to the axon, and it had been unclear how they pick out just the few microtubules that go there.

"We wanted to discover how kinesin chooses the correct track," says Yasushi Okada of the RIKEN Center for Biosystems Dynamics Research. "We had previously proposed that the microtubule itself acts as a road sign." Okada and co-workers have now shown experimentally that their proposal is correct.

The researchers looked at how the road signs are organized in the cell and were surprised to find that when kinesin-1, a member of the kinesin superfamily, binds to a microtubule, the microtubule changes into a state that has a high affinity for kinesin-1. As a result, the microtubule recruits more kinesin-1 molecules.

Okada's team, in collaboration with Nobutaka Hirokawa at the University of Tokyo, then explored the structural basis behind this mechanism and found that when kinesin binds to a microtubule, it initiates a domino effect. It rotates β-tubulin (one of the two subunits that make up microtubule filaments), which pushes its neigboring α-tubulin (the other subunit of microtubules), causing it to simultaneously twist and shift. This movement pushes the next β-tubulin, and so on. In this way, the binding of just a few kinesin molecules to a microtubule can trigger global changes in its shape.



Cryo-electron micrograph of microtubules decorated with kinesin.

"This mechanism is analogous to ant pheromones," explains Okada. "Ants use pheromones to find the shortest path between their nest and food. As they walk, they place pheromones, which act as road signs to other ants, which use them to trace the same path. This is a well-known example of self-organization, and the kinesin–microtubule system uses the same principle."

The team now plans to obtain further evidence for this self-organization model and to study further regulations of microtubule shape and kinesin-based movement. ●

Reference

1. Shima, T., Morikawa, M., Kaneshiro, J., Kambara, T., Kamimura, S., Yagi, T., Iwamoto, H., Uemura, S., Shigematsu, H., Shirouzu, M. *et al.* Kinesin-binding–triggered conformation switching of microtubules contributes to polarized transport. *Journal of Cell Biology* **217,** 4164–4183 (2018).

PLANT BIOLOGY

How cesium harms plants

Cesium actively blocks the uptake of potassium by plants, starving them of the essential nutrient

Cesium in the soil disrupts plant growth mainly through restricting the ability of plants to take up potassium—a vital nutrient—RIKEN scientists have discovered[1]. This finding will inform strategies to clean up cesium-contaminated soil and to protect plants from the harmful effects of contamination.

Radioactive cesium often contaminates land after nuclear disasters such as the one at the Fukushima Daiichi Nuclear Power Plant in 2011. Since plants readily take up cesium from contaminated soil, cesium-tolerant plants could be used to clean up contaminated regions. But producing such plants first requires understanding how cesium affects normal plants.

Part of the reason why cesium is bad for plants is because it is chemically similar to potassium, so that plants growing in cesium-contaminated soils can become deficient in potassium. But plant scientists have long suspected that cesium does more than just starve plants of potassium through competing with it—cesium also actively interferes with biological processes involving potassium.

They found that plants lacking the AKT1 channel were highly sensitive to cesium

Now, Ryoung Shin and Eri Adams at the RIKEN Center for Sustainable Resource Science and their co-workers have found that cesium blocks the uptake of potassium by the roots.

The team tweaked the genome of the model plant *Arabidopsis* to disrupt the functioning of two key proteins, AKT1 and HAK5, which transport potassium across cell membranes. They found that plants lacking the AKT1 channel were highly sensitive to cesium and that their growth was severely stunted compared to that of control plants with fully functioning transporters. For example, the roots of AKT1 channels treated with cesium were about half as long as those of control plants when potassium was abundant.

When cesium was absent, the mutant plants accumulated only a third of the potassium of the control plants and suffered further potassium reductions when treated with cesium. In contrast, plants lacking the HAK5 transporter accumulated potassium and grew as well as control plants.

These results indicate that the AKT1 potassium channel is indispensable for the healthy growth of plants in the presence of cesium. The functions of other potassium transporters such as HAK5 seem to be redundant or are compensated when cesium is present, but the same is not true of AKT1—the absence of a single component of the AKT1 potassium channel leads to a hypersensitive response to cesium.

"These findings confirm that cesium-induced growth inhibition in plants occurs primarily through reduction of potassium accumulation and that this reduction happens because cesium blocks potassium influx through a major potassium channel," says Adams. "Our findings will help scientists understand how to use plants to clean up radiocesium-contaminated lands." ●

The nuclear disaster at Fukushima nuclear power plant resulted in vast areas of land being contaminated with radiocesium and other radioisotopes. Cesium-tolerant plants could be used as part of efforts to remediate such areas.

Reference

1. Adams, E., Miyazaki, T., Saito, S., Uozumi, N. & Shin, R. Cesium inhibits plant growth primarily through reduction of potassium influx and accumulation in Arabidopsis. *Plant and Cell Physiology* **60,** 63–76 (2019).

EVOLUTIONARY GENOMICS

Shark genomes yield long-held secrets

The genomes of three sharks reveal the genetic basis of their unique lifestyles

By analyzing the genomes of sharks and comparing them with those of other vertebrates, RIKEN scientists have gained fresh glimpses into the unique life histories and evolutionary paths of sharks. To do this, they decoded the whole genomes of two shark species and improved the whale shark genome sequences released previously[1].

Advances in genome sequencing have made it possible to compare genomes from different species, giving us insights into their evolutionary histories and characteristics. But genome sequencing for sharks has been hampered by their huge genomes, which are even larger than the human genome.

Sharks have many unique characteristics, including their body structures, reproductive systems, sensing mechanism and extreme longevity. Fully decoded shark genomes will be a tremendous boon to research aimed at discovering the molecular bases for these characteristics.

With this ultimate goal in mind, a team led by Shigehiro Kuraku at the RIKEN Center for Biosystems Dynamics Research analyzed shark genomes using cutting-edge DNA sequencing technologies and comparative bioinformatics that could handle gigabase-scale sequences. They chose two primary species—the brownbanded bamboo shark and the cloudy catshark—because they lay eggs and can be raised in aquariums, making it relatively easy to obtain live specimens. The researchers also more completely assembled the entire whale shark genome, which had been previously released.

RIKEN genomicists have released genome sequences of the brownbanded bamboo shark (pictured) and the cloudy catshark for the first time as well as improved publicly available genome sequences of the whale shark.

"Our results will fill a long-standing gap in the genome biology of animals"

One puzzle about sharks is why their genomes are so large. The team found that the large genome size is due to massive insertions of repetitive elements. At the same time, shark genomes have been evolving slowly, which means that they have kept many ancestral gene repertoires and can be thought of as 'living fossils' in a genomic sense.

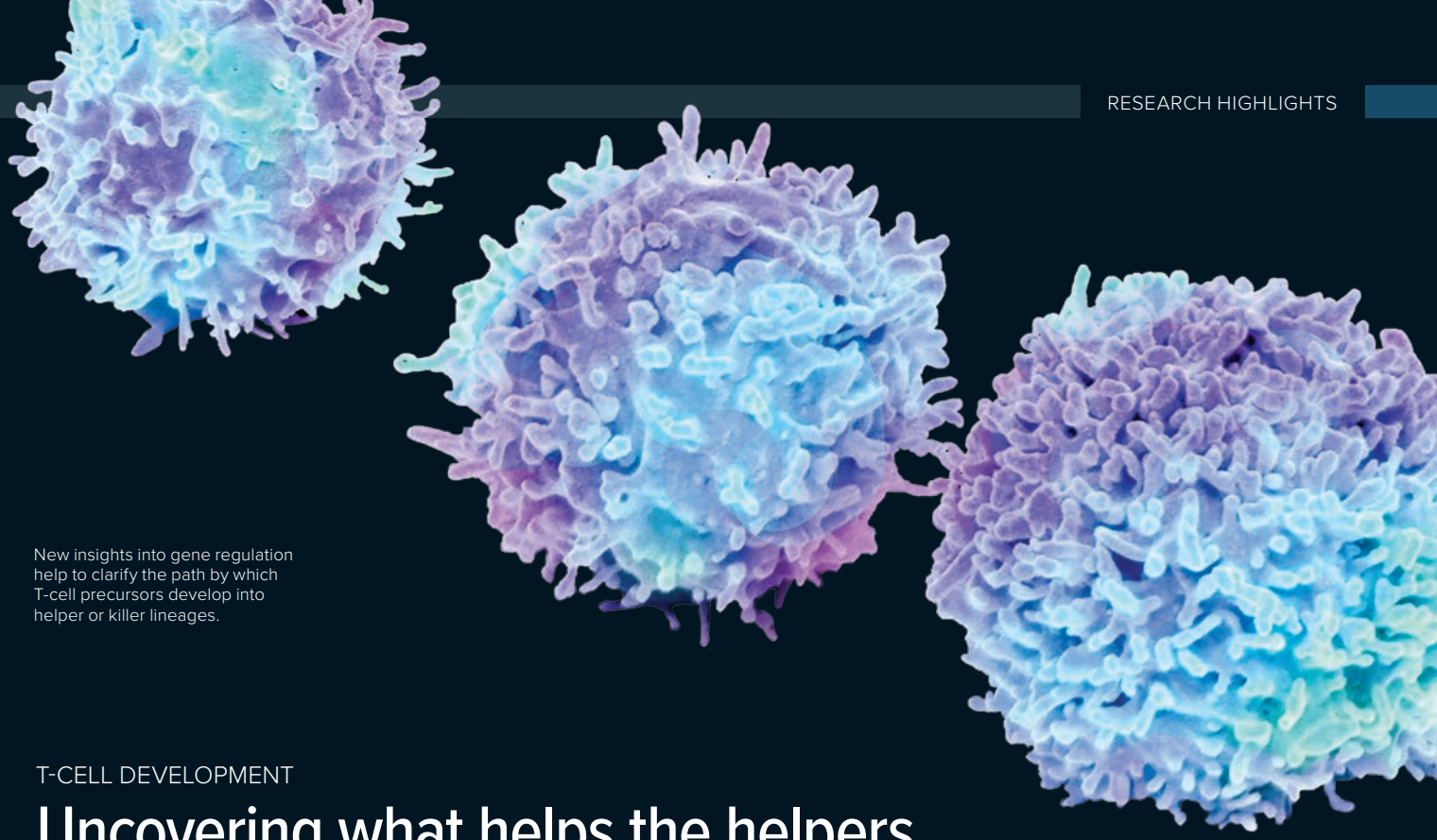
The team found that sharks have counterparts of human genes that produce endocrine hormones and receptors regulating growth, reproduction and homeostasis, such as obesity, appetite and sleep. This finding suggests that components of our molecular machinery for basic physiology have existed for more than 450 million years, in the common ancestor of sharks and humans.

The newly decoded shark genomes have already provided several insights. For example, the team showed that all three shark species have relatively few olfactory receptor genes, implying that they depend on other systems, such as sensing electromagnetic fields, for navigation.

"Our results will fill a long-standing gap in the genome biology of animals and will also help us gain greater understanding about metabolism, reproductive cycle and health monitoring of sharks," says one of their collaborators, Keiichi Sato, deputy director of Okinawa Churaumi Aquarium. "Such understanding should contribute to the conservation of marine environments as well as to sustainable husbandry and exhibitions at aquariums that allow everyone to experience biodiversity up close." ●

Reference

1. Hara, Y., Yamaguchi, K., Onimaru, K., Kadota, M., Koyanagi, M., Keeley, S. D., Tatsumi, K., Tanaka, K., Motone, F., Kageyama, Y. *et al.* Shark genomes provide insights into elasmobranch evolution and the origin of vertebrates. *Nature Ecology & Evolution* **2,** 1761–1771 (2018).



New insights into gene regulation help to clarify the path by which T-cell precursors develop into helper or killer lineages.

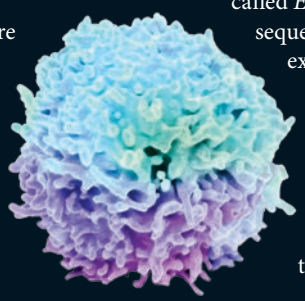
T-CELL DEVELOPMENT

Uncovering what helps the helpers

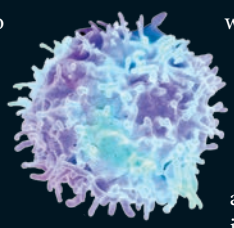
A study of helper T-cell development reveals unexpected complexity in the expression of a well-studied gene

The gene that encodes for a protein found on the surfaces of certain immune cells has been scrutinized by an all-RIKEN team[1]. This analysis has uncovered some surprising insights into how these immune cells develop.

The helper T-cells that coordinate the body's immune response to pathogens all sport a protein called CD4 on their surfaces. Early in development, precursors of T-cells become either CD4-expressing helper T-cells or CD8-expressing killer T-cells, resulting in exclusive expression of the *Cd4* or *Cd8* gene, respectively. The *Cd4* gene has been well studied as a general model for gene regulation, where expression is regulated through the coordinated effects of a 'promoter' sequence known as *P4* and an 'enhancer' sequence known as *E4p*.



But research to date has strongly hinted at the presence of an additional enhancer that had yet to be discovered. Ichiro Taniuchi, Satoshi Kojo and colleagues at the RIKEN Center for Integrative Medical Sciences set out to identify this sequence.



"It was essential to identify this last piece in order to establish this locus as a complete model gene," comments Kojo.

The researchers homed in on this second enhancer, called *E4m*, through gene sequence analysis and experimentation. Previous studies had shown that mice can produce low levels of CD4-positive T-cells at the late stage of their development even in the absence of the *E4p* enhancer. This indicates that the additional enhancer must be able to single-handedly drive some degree of helper T-cell maturation. But when both *E4p* and *E4m* were absent, CD4 expression was completely eliminated, confirming that Kojo and colleagues had indeed identified the missing sequence.

There were also some unexpected findings. For example, the *Cd4* gene contains a 'silencer' element, which inhibits the activity of *E4p* by recruiting a repressor protein called Runx. The team anticipated that the same silencer might also regulate *E4m* activity, but this turned out not to be the case.

"Our genetic approach revealed that *E4m* activity is repressed in killer T-cells by additional mechanisms," says Kojo. "Runx could bind to the *E4m* region and is still involved in *E4m* repression, even in the absence of this silencer element." This suggests the presence of direct repression of *E4m* by Runx for this gene, and a previously unknown mode of action for Runx-mediated gene inhibition.

A second surprising finding is that another regulatory protein, called ThPOK, apparently collaborates with Runx to inhibit *E4m*—despite the fact that ThPOK also helps relieve silencing of *E4p*. Kojo and his colleagues intend to explore the basis and implications of these seemingly contradictory effects on *Cd4* expression in future research.

Reference

1. Kojo, S., Yasmin, N., Muroi, S., Tenno, M. & Taniuchi, I. Runx-dependent and silencer-independent repression of a maturation enhancer in the *Cd4* gene. *Nature Communications* **9,** 3593 (2018).

BREAST CANCER

Five-minute probe improves breast-conserving surgery

A minor misunderstanding led to a fluorescent probe for tissue samples that rapidly shows breast-cancer surgeons where to cut

Katsunori Tanaka was surprised when a small, smelly chemical led his team to a tissue sample probe to help guide a surgeon's scalpel around cancerous breast tissue. Typically, tissue sample analysis during breast-conserving surgery takes 40–60 minutes, but RIKEN's new fluorescence method only takes 5 minutes.

Tanaka is an organic chemist who heads the RIKEN Biofunctional Synthetic Chemistry Laboratory, and he is fascinated by acrolein—a diminutive molecule made up of a mere eight atoms: three carbons, an oxygen and four hydrogens.

He says that its smallness has sometimes meant acrolein is neglected. "Many chemists think small molecules are too simple and prefer to investigate bigger, more complex molecules," he explains.

However, acrolein's small size belies its importance in a wide range of biological processes. A colorless liquid with an acrid odor, it is present in cigarette smoke and is given off by rotting fish and heated milk. Critically, acrolein is produced by 'oxidatively stressed' cells such as cancer cells, whose metabolism has gone awry so that they produce highly reactive and damaging oxygen species.

A SMALL (MOLECULE) MISUNDERSTANDING

Tanaka's latest discovery began with a minor miscommunication with a Russian student. RIKEN has a long-standing collaboration with Kazan Federal University in Russia, and Tanaka heads a joint laboratory between the university and RIKEN. One day he asked a Russian student to react acrolein with an amine, a nitrogen containing compound. "But she misheard me and trotted off to the lab to create a reaction between acrolein and another nitrogen-containing compound, azide," Tanaka recounts. "Remarkably, the reaction happened!"

> The team was able to get the same information from breast tissue samples... but in a fraction of the time—about 5 minutes

Initially, Tanaka was not particularly excited, because the reaction turned out to be a 'click reaction'—a very rapid and specific reaction that joins two functional groups. "Many chemists use click reactions, so I thought it probably wasn't that significant," he says.

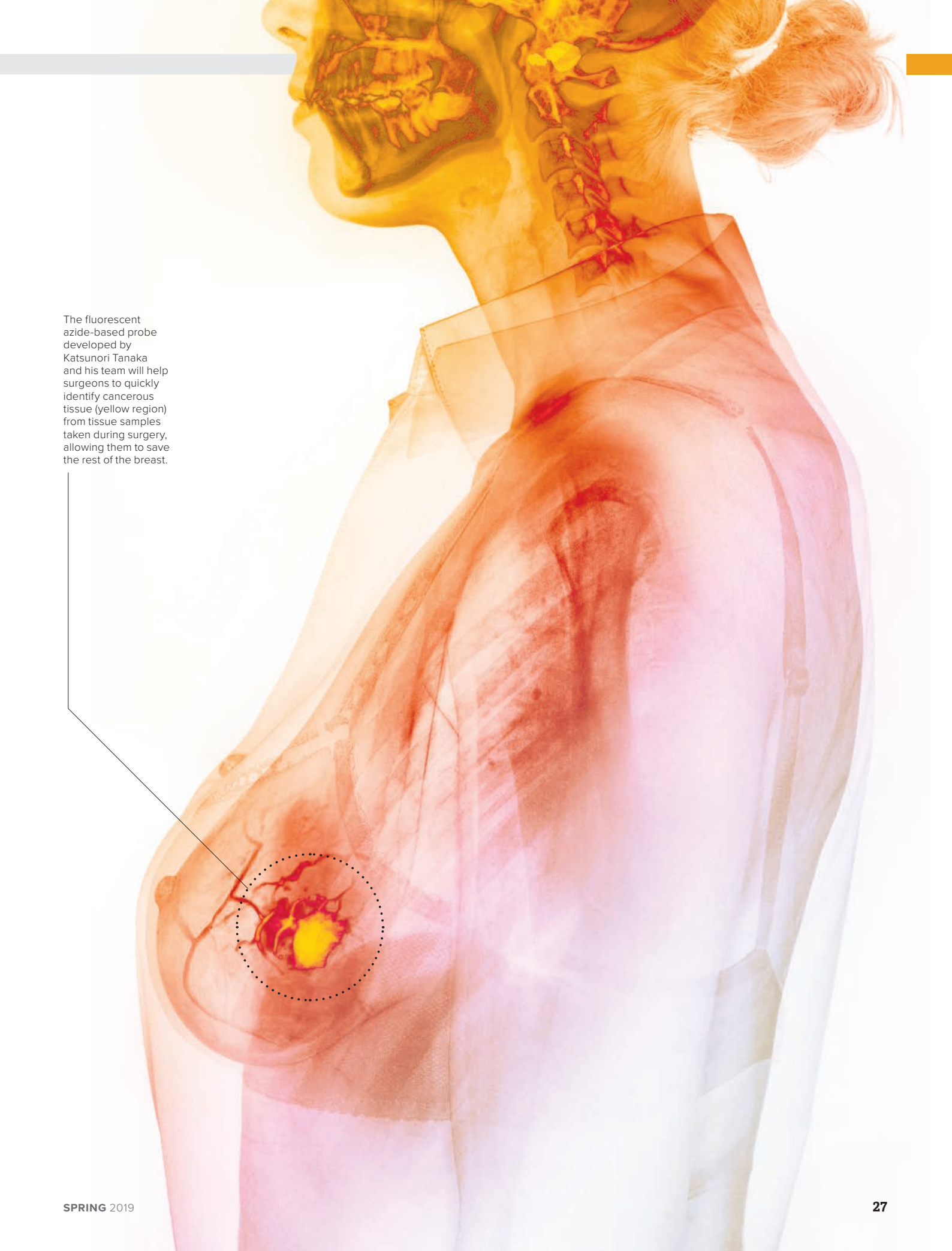
But Ambara Pradipta, a member of Tanaka's laboratory, recognized the reaction's potential when he saw oxidatively stressed cells start to fluoresce under ultraviolet light after an azide-based probe had been added. Since cancer cells are oxidatively stressed, this raised the possibility that it could be used to identify cancerous tissue. Furthermore, the reaction product remained inside these specific cells and did not stain their neighbors—a common problem with fluorescent probes that attach to cell surfaces.

RIKEN's method owes some of its effectiveness to the fact that all cancer cells produce acrolein, which was a surprise to Tanaka. "We didn't expect it, but it turns out that acrolein is found in all tumor tissues," Tanaka says. "That is a very significant discovery."

The researchers could simply add a few drops of the fluorescence-labeled phenyl azide probe to a tissue sample and it would enter the tissue's cells and react with any acrolein inside. And since the reaction product is fluorescent, acrolein-containing cells become highly visible under a fluorescence microscope.

FAST ANALYSIS TO PRESERVE BREAST TISSUE

Globally, breast cancer is the most common cancer among women and causes more female deaths than any other cancer. Surgery is usually the first form

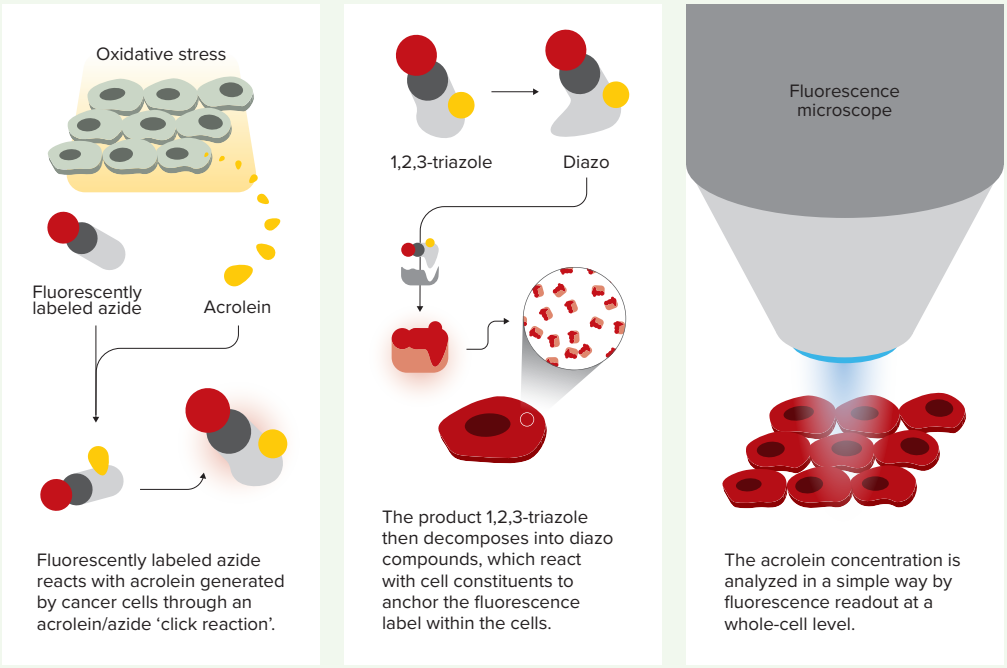


The fluorescent azide-based probe developed by Katsunori Tanaka and his team will help surgeons to quickly identify cancerous tissue (yellow region) from tissue samples taken during surgery, allowing them to save the rest of the breast.

This feature looks at the work of
KATSUNORI TANAKA

Katsunori Tanaka received his PhD (2002) from Kwansei Gakuin University, Japan, under the direction of Professor Shigeo Katsumura. After doing a post-doctoral fellowship with Professors Koji Nakanishi and Nina Berova at Columbia University (2002–2005), he joined Professor Koichi Fukase's group at Osaka University. He moved to RIKEN as an associate chief scientist in the Biofunctional Synthetic Chemistry Laboratory in 2012. Among other positions, in 2017 he was appointed group director of the Max Planck–RIKEN Joint Center for Chemical Biology Research, a deputy team leader in the GlycoTargeting Research Laboratory, which is part of the RIKEN Baton Zone Program, and a chief scientist in the RIKEN Cluster for Pioneering Research.

EVERYTHING CLICKING INTO PLACE FOR BREAST CANCER PROBE



Fluorescently labeled azide reacts with acrolein generated by cancer cells through an acrolein/azide 'click reaction'.

The product 1,2,3-triazole then decomposes into diazo compounds, which react with cell constituents to anchor the fluorescence label within the cells.

The acrolein concentration is analyzed in a simple way by fluorescence readout at a whole-cell level.

of treatment. Often the whole breast is removed in a mastectomy, but breast-conserving surgery, which removes just the cancerous tissue, is often viable and is becoming an increasingly popular option.

In breast-conserving surgery, the surgeon determines which parts of the breast to remove by taking small tissue samples, which are analyzed under a microscope by a pathologist during the operation. The results show which tissues are cancerous, and the surgeon uses this information to guide the surgery.

But since this analysis is time consuming, usually taking between 40 and 60 minutes, an effective and faster method is highly preferable. Rapid methods based on techniques such as computed tomography, magnetic resonance imaging and fluorescent probes have been developed in the lab, says Tanaka. But these methods have not been adopted in the surgical theater because they cannot distinguish finely enough between different types of cancer cells. "It's vital to emphasize that although several techniques have seemed promising in the lab, surgeons haven't been interested in them because they don't give the information they need for deciding where to cut," he points out.

Timeliness and detail is where the fluorescent azide-based probe shows its most obvious strengths. By working with physicians at Osaka University Hospital, the team was able to use the probe to get the same information from breast tissue samples as the current conventional method, including different classifications of cancer cells, but in a fraction of the time—about 5 minutes.

COMING SOON TO THEATERS

As well as being rapid, the method is very inexpensive, requiring just the azide-based probe and a fluorescence microscope. It can thus be used at small, regional hospitals. To help make this a reality sooner, Tanaka is very eager to develop a customized microscope that conforms to the strict regulations applied to surgical theater equipment, and he is currently talking to interested companies.

Tanaka says it is crucial to raise awareness of the method among surgeons, as he is convinced that they will quickly appreciate its benefits. And since acrolein is generated by all cancer cells, the azide-based probe could soon be developed further to shine a light on many other kinds of cancer tissues.

REFERENCE

Tanei, T., Pradipta, A. R., Morimoto, K., Fujii, M., Arata, M., Ito, A., Yoshida, M., Saigitbatalova, E., Kurbangalieva, A., Ikeda, J. *et al.* Cascade reaction in human live tissue allows clinically applicable diagnosis of breast cancer morphology. *Advanced Science* **6,** 1801479 (2019).

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TO EXCASCALE AND BEYOND

The post-K supercomputer will be first off the rack in the exascale era, but will have to manage a post-Moore's law world, says Satoshi Matsuoka

In the early 2020s, when RIKEN switches on its post-K supercomputer, humanity will enter the exascale era. Post-K will likely be the fastest computer in the world, the first of a new generation of supercomputers operating at computational speeds in the region of exaflops, one billion billion 'floating point operations' (FLOPS) per second.

Developed at the RIKEN Center for Computational Science (R-CCS), post-K will be two orders of magnitude faster than its predecessor, the 10-petaflop-scale K computer. Post-K will also likely be the first in a wave of exascale computers from Japan, China, the United States and Europe expected to become operational in the early 2020s. These machines will be able to tackle real-world problems that exceed the capabilities of the K computer and its petascale cohort.

For the first time, for example, we will be able to accurately model whole-city responses to natural disasters such as earthquakes. This has been difficult because there is no single scenario for planning an earthquake response; earthquakes can occur at different magnitudes and epicenters, so we have to run hundreds or thousands of scenarios to come up with realistic evacuation plans. It only becomes possible with exascale performance.

We also believe exascale computing will bring substantial breakthroughs in drug design. We will finally be able to accurately model drug interactions with whole cells rather than single proteins, and perform whole genome analyses to identify the best drugs for individual patients.

In fact, we expect that exascale computing will have applications ranging from improved climate modeling to elucidating the fundamental laws of the Universe. This will entail an era that I have dubbed the 'Cambrian explosion of computing' in which computing types will diversify immensely, a topic to which I will return.

END OF MOORE'S LAW BUILT INTO POST-K

Although post-K will be the first of the new wave of exascale machines, it will also arguably be the most advanced.

There are several strategies that contribute to what we think is a superior exascale computing design. For example, from the project's inception, 'co-design' has been key to post-K's creation. We have been actively engaging with the machine's prospective users to anticipate their future high-performance computing needs.

PRIORITY ISSUES FOR THE R-CCS

1. Innovative drug-discovery infrastructure through functional control of biomolecular systems
2. Integrated computational life science to support personalized and preventive medicine
3. Development of integrated simulation systems for hazards and disasters induced by earthquakes and tsunamis
4. Advancement of meteorological and global environmental predictions utilizing observational 'big data'
5. Development of new fundamental technologies for high-efficiency energy creation, conversion/storage and use
6. Accelerated development of innovative clean-energy systems
7. Creation of new functional devices and high-performance materials to support next-generation industries
8. Development of innovative design and production processes that lead the way for the manufacturing industry in the near future
9. Elucidation of the fundamental laws and evolution of the Universe

To further maximize real-world usability, post-K adopted and extended its ARM instruction set architecture—these chips with small sets of simple and general instructions often run computers. ARM is the most popular instruction set architecture in the world and billions of ARM chips are produced annually, ranging from very small ones in embedded controllers, to cell phone chips, to very large ones in Internet servers and supercomputers, with a vast software portfolio to match. Post-K will sit at the pinnacle of this ARM ecosystem, offering performance that we believe will best all other general central processing units in the world.

But the most crucial aspect of post-K's advantage is that it has been built with the looming end of Moore's law in mind.

Since the mid-1970s, computer-chip manufacturers have been able to double the density of transistors on a silicon chip every two years. This trend, known as Moore's law, has driven extraordinary advances in computing. Compute speeds have increased seven orders of magnitude in the last 35 years.

Today, Moore's law is tailing off. Transistors are now so small we are approaching a fundamental physical size limit. Taking the last steps toward that limit is becoming increasingly difficult. The technology company Intel, who makes the microprocessors found in most personal computers, usually transitions to a smaller transistor size every two years, but the transition from their current 14-nanometer transistor size to 7 or 10 nanometers has taken significantly longer. The vast expense and technological challenges are forcing some semiconductor manufacturers out of the game.

Moving on to nanometer and beyond will require changes in fabrication technologies. Most people anticipate Moore's law will end sometime between 2025 and 2030, before we reach the physical limits of transistors, because we can no longer afford to produce smaller transistors.

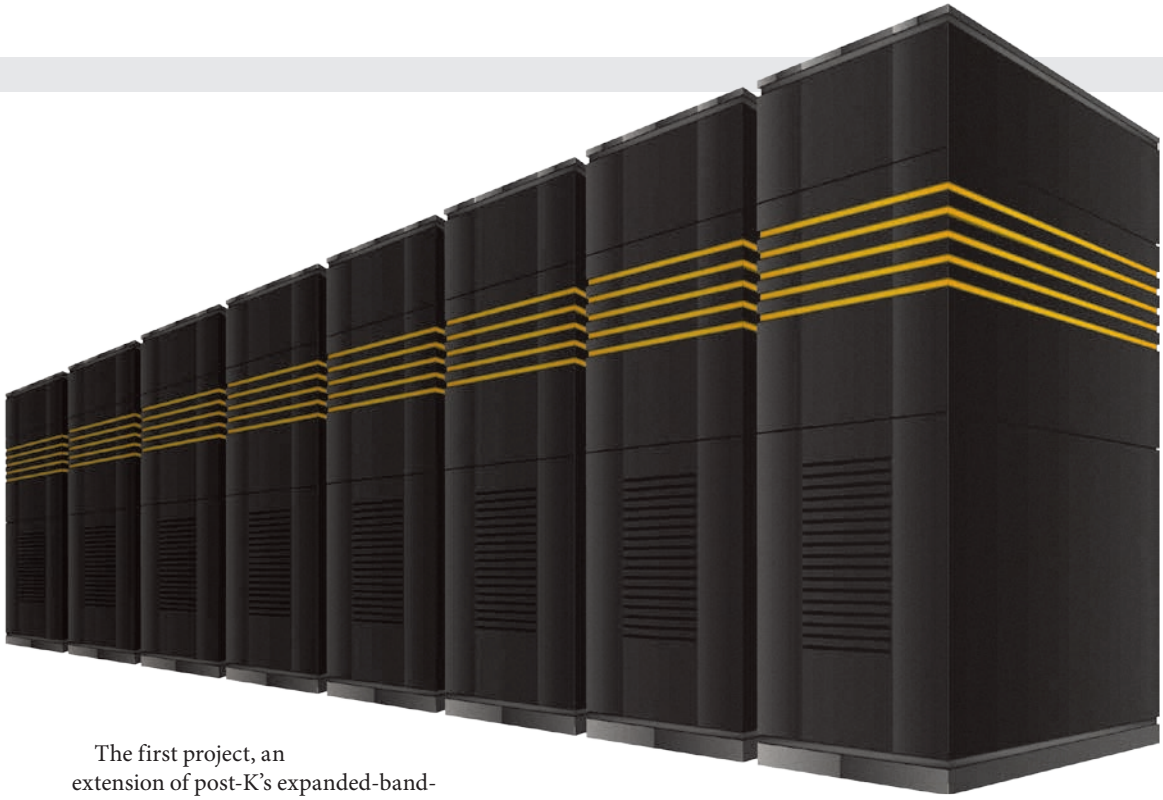
Post-K has been designed cognizant of the tailing off of Moore's law. Rather than emphasizing speed via FLOPS, post-K will therefore focus on bandwidth, the ability to move data more quickly between transistors and memory. We have concluded that most applications are already limited by bandwidth rather than FLOPS, so with post-K we are investing more into the bandwidth design to maintain a 'system balance' between compute speed and data transfer.

> We have concluded that most applications are already limited by bandwidth rather than FLOPS

A CAMBRIAN EXPLOSION OF COMPUTING

Global efforts to address the end of Moore's law have taken off in the last three or four years, as it has become evident that we are starting to experience problems that industry will not be able to address by itself. If we are to prevent supercomputer development from stagnating—and supercomputer-reliant scientific research with it—it's time to act.

At RIKEN, R-CCS-led research teams will explore two new directions, as part of four projects recently or soon to be launched.



The first project, an extension of post-K's expanded-bandwidth concept, looks at how to boost conventional computing using parameters other than extra transistors. We're looking into new technologies to move data around faster between transistors and memory—from new devices and architecture, to new algorithms and software to exploit new hardware. We can expect to increase performance from these innovations, and to keep seeing gains. In October 2018, we launched a program looking at future processors as part of this project, with a 2026/7 time frame.

Another broad area we are delving into is to move beyond conventional computing and explore alternative compute models.

Two promising fields are artificial intelligence and machine learning. Traditionally, supercomputer simulation science involves first principle physics and solving partial differential equations (PDEs), but that's not the only way to model and understand the world. Pour water in a jar and shake it, and a 3-year-old will be able to tell you what the jar contains. The child's not solving PDEs, she is recognizing empirically that the liquid moves like water.

A computer can use intelligence and deep learning to do the same thing. A good model can analyze a sequence of snapshots to anticipate what will happen next, extrapolating the next state. This approach can dramatically reduce the computational time and energy required, sometimes by four orders of magnitude. Machine learning and empirical modeling is behind the recent progress in self-driving cars, for example.

For certain research applications, empirical approaches could reasonably replace first-principles simulations. The second project of the four is a deep learning project to investigate how to accelerate machine learning, in particular deep learning, on post-K and beyond.

Other alternatives to conventional compute models involve a much more significant rethink of supercomputer hardware. Quantum computing is one area of active research; neuromorphic computing, inspired by neuroscience, is another.

In a neuromorphic computer, each compute unit connects to multiple others, across circuits that evolve over time as the machine learns, like neural circuits in the brain. We think this type of computing could be combined effectively with empirical simulation science and have started a third project on this that will involve international workshops on neuromorphic computing applications.

The fourth project will examine how to combine some of these ideas. For example, the solution to some problems may suit the neuromorphic approach, while others are solved with traditional PDE solvers, but augmented with assumptions and massive bandwidths. It's important to note that as supercomputing approaches become more varied, we will require machines that are equally heterogeneous, which presents yet another puzzle that we will also examine.

We sometimes call this heterogeneous era the 'Cambrian explosion of computing', after the dramatic diversification of life forms that characterized the Cambrian period of life on Earth. Ultimately, as in nature, Darwinian processes may kick in and we may winnow down to the most viable of these diverse designs. But right now, as we search for solutions to the end of Moore's law, it is the time to be really diverse. ●

For a full list of references, please visit the online version of this article: http://www.riken.jp/en/research/rikenresearch/perspectives/2019spring/

SATOSHI MATSUOKA
Director of RIKEN's R-CCS

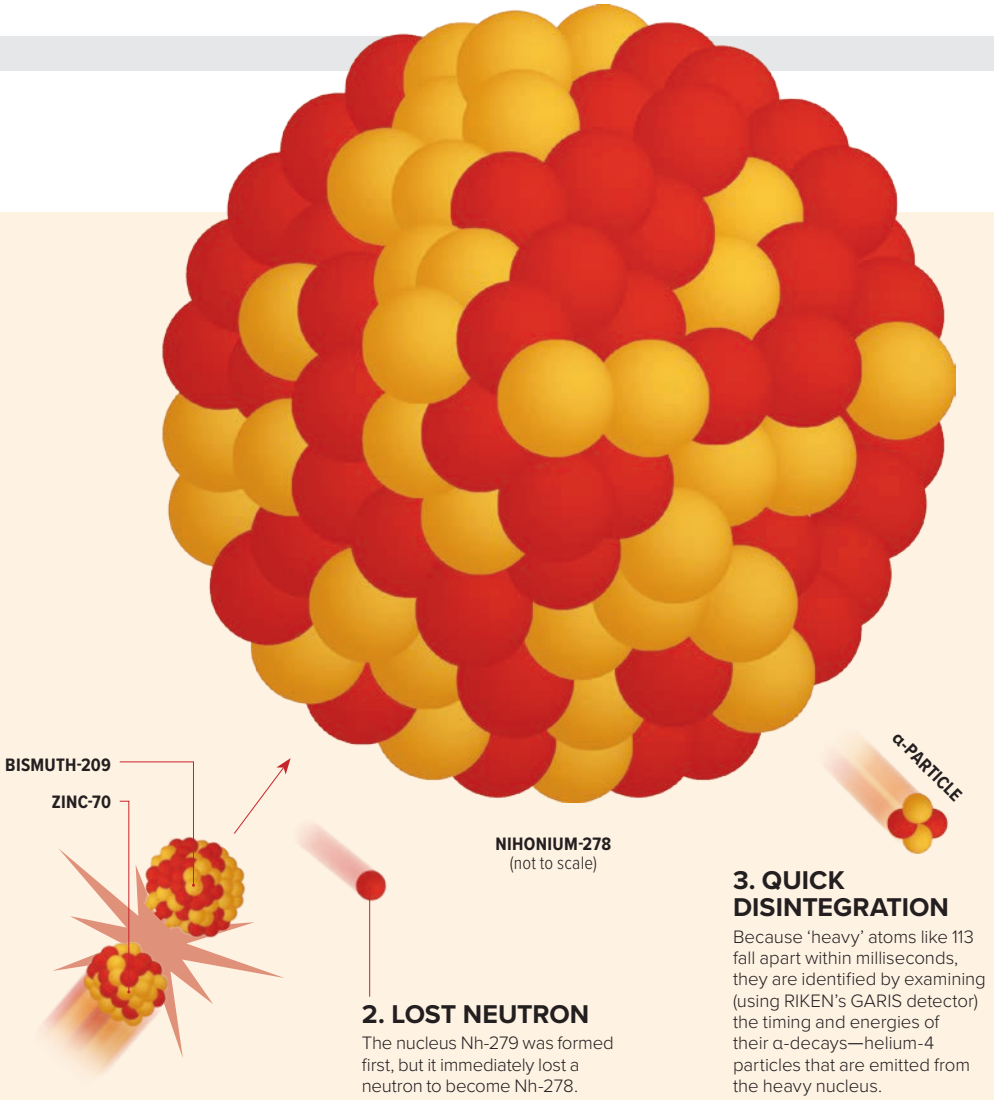
Satoshi Matsuoka became director of the RIKEN Center for Computational Science (R-CCS) in 2018. The R-CCS conducts high-performance computing (HPC) research, hosts the K computer and is developing an ARM-based 'exascale' supercomputer, the post-K machine. Previously, Matsuoka led the development of the TSUBAME series of supercomputers at the Tokyo Institute of Technology, where he still holds a professorship. He won the ACM Gordon Bell Prize in 2011 and the IEEE Sidney Fernbach Award in 2014, which are among the most prestigious awards in his field. Matsuoka was Program Chair of the IEEE/ACM Supercomputing 2013 conference, probably the world's most prominent HPC conference, and was the ACM Gordon Bell Prize selection chair in 2018.

LUCKY 113

In celebration of the United Nations General Assembly and UNESCO International Year of the Periodic Table of Chemical Elements in 2019, we look at how Kosuke Morita's team at the RIKEN Nishina Center for Accelerator-Based Science proved they had discovered element 113.

1. 83 + 30 = 113

In 2003, Morita's team began trying to synthesize element 113 by smashing together bismuth-209 (83 protons) and zinc-70 (30 protons).



2. LOST NEUTRON

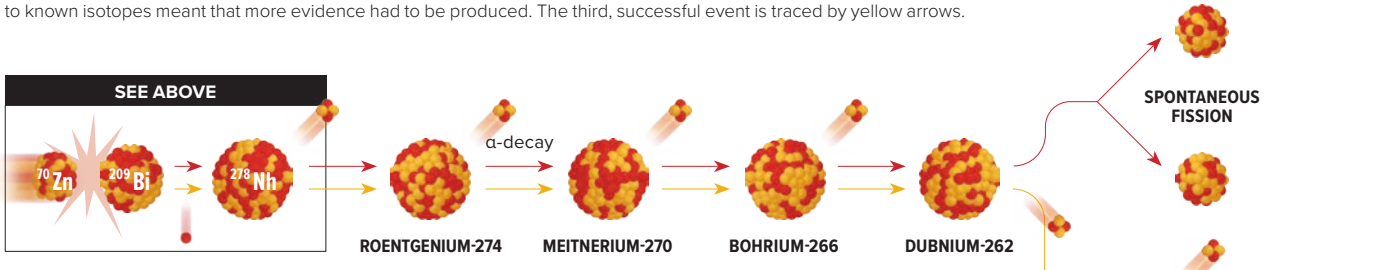
The nucleus Nh-279 was formed first, but it immediately lost a neutron to become Nh-278.

3. QUICK DISINTEGRATION

Because 'heavy' atoms like 113 fall apart within milliseconds, they are identified by examining (using RIKEN's GARIS detector) the timing and energies of their α-decays—helium-4 particles that are emitted from the heavy nucleus.

4. THIRD TIME LUCKY

When two 113 atoms were identified in 2004 and 2005, they decayed sequentially to dubnium-262 through four α-decays, indicated by red arrows below. However, according to the International Union of Pure and Applied Chemistry (IUPAC), a few inconsistencies between the decays and the fact that the nuclides reported in these chains did not correspond closely enough to known isotopes meant that more evidence had to be produced. The third, successful event is traced by yellow arrows.



EVENT 1 23 July 2004	0.344 milliseconds (ms)	9.26 ms	7.16 ms	2.47 seconds (s)	40.9 s	
EVENT 2 2 April 2005	4.93 ms	34.3 ms	1.63 s	1.31 s	0.787 s	
EVENT 3 12 August 2012	0.667 ms	9.97 ms	444 ms	5.26 s	126 s	3.78 s

SUCCESS! In 2012, the team finally saw a chain of six α-decays from an atom of element 113. It showed enough correlation to known features for IUPAC to declare the scientists the first Asian team to have discovered an element.

RIKEN'S CENTERS AND FACILITIES

across Japan and around the world

WAKO
(RIKEN's Headquarters)
- ● Interdisciplinary Theoretical and Mathematical Sciences Program (iTHEMS)
- ● Center for Brain Science (CBS)
- ● Center for Sustainable Resource Science (CSRS)
- ● Center for Emergent Matter Science (CEMS)
- ● Center for Advanced Photonics (RAP)
- ● Nishina Center for Accelerator-Based Science (RNC)
- ▲ Cluster for Science, Technology, and Innovation Hub (CSTIH)
- ▲ Cluster for Pioneering Research (CPR)
- ◆ Radio Isotope Beam Factory (RIBF)
- ▼ Head Office for Information Systems and Cybersecurity

LEGEND
- ● Strategic Research Center
- ■ Research Infrastructure Center
- ◆ Large Research Infrastructure
- ▲ Research Cluster
- ▼ Other

SENDAI
- ● Center for Advanced Photonics (RAP)

YOKOHAMA
- ● Center for Integrated Medical Sciences (IMS)
- ● Center for Biosystems Dynamics Research (BDR)
- ● Center for Sustainable Resource Science (CSRS)
- ■ SPring-8 Center (RSC)
- ▲ Cluster for Science, Technology, and Innovation Hub (CSTIH)
- ◆ Genome Sequencing
- ◆ Nuclear Magnetic Resonance (NMR)

TSUKUBA
- ■ BioResource Research Center (BRC)
- ◆ BioResource

TOKYO
- ● Center for Advanced Intelligence Project (AIP)
- ▼ Innovation Design Office

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

NAGOYA

KEIHANNA
- ● Center for Advanced Intellegence Project (AIP)
- ■ BioResource Research Center (BRC)

KOBE
- ● Center for Biosystems Dynamics Research (BDR)
- ■ Center for Computational Science (R-CCS)
- ▲ Cluster for Science, Technology, and Innovation Hub (CSTIH)
- ◆ Molecular Imaging
- ◆ K computer

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 and Malaysia. To expand our network, RIKEN works closely with researchers who have returned to their home countries or moved to another institute, with help from RIKEN's liaison offices in Singapore, Beijing and Brussels.

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