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FALL 2020

RESEARCH

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HIGH TIME

Atomic clocks
chime with Einstein

MAPPING MARMOSSET MINDS

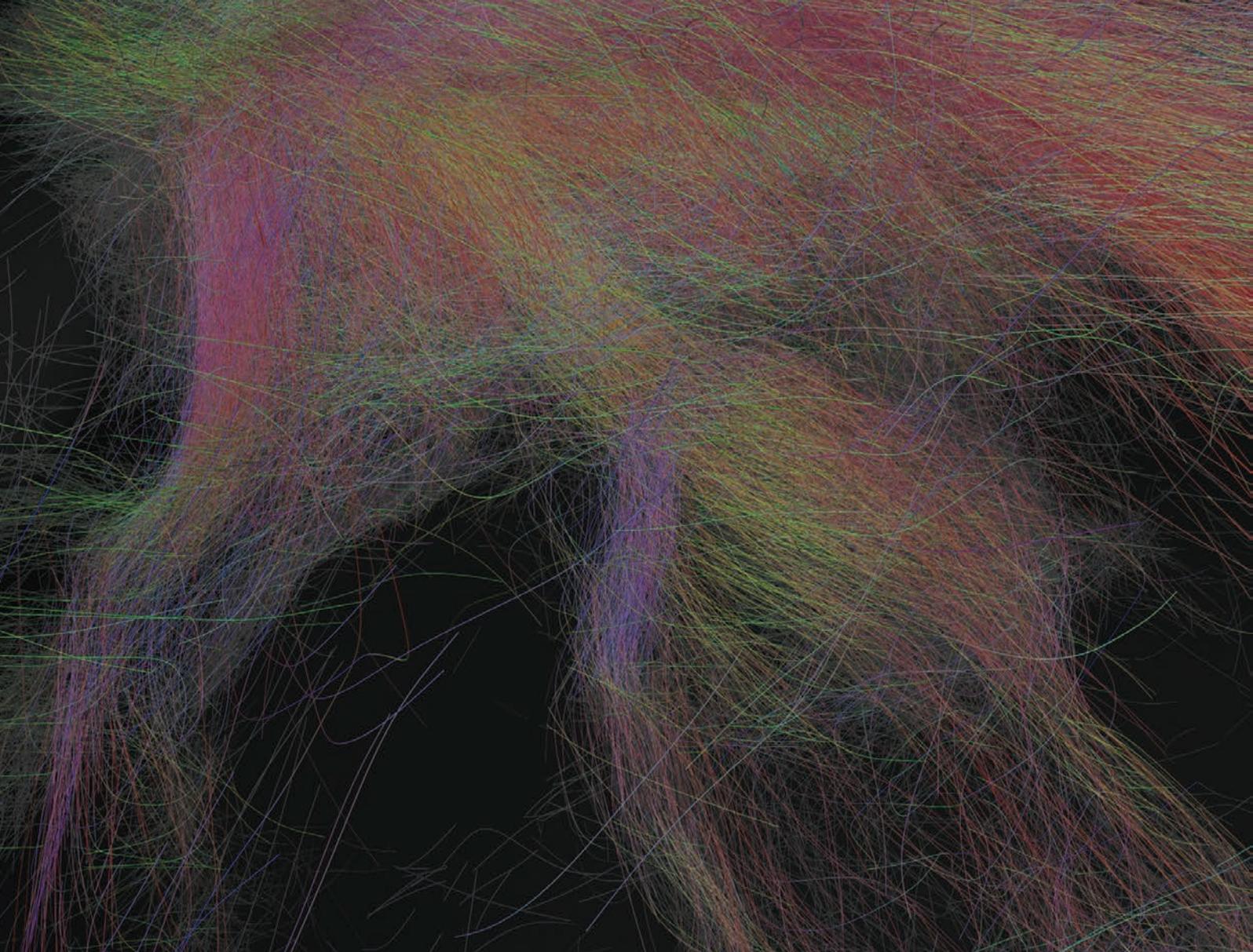
What primates
can teach us
about cognition

BRAVING THE ELEMENTS

Seeking an island
of stability

CATCHING WAVES

Uncovering
the source of
deep sleep



▲ Marmoset magic

Marmosets are social, fecund and age more quickly than bigger monkeys, so they speed up studies on age-related and developmental diseases. Their brains are also less furrowed and more easily imaged than the commonly studied macaque. Enthusiasm for mapping marmoset brains (pictured) has grown rapidly since 2009, when a Japanese team showed that they pass a genetic modification onto offspring in their sperm and eggs, a first for primates. That team is now helping the RIKEN-led Brain/MINDS project use marmosets to understand the brain (see page 26).

RIKEN RESEARCH

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

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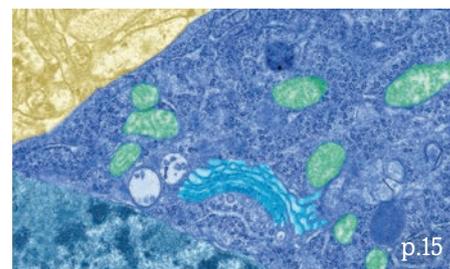
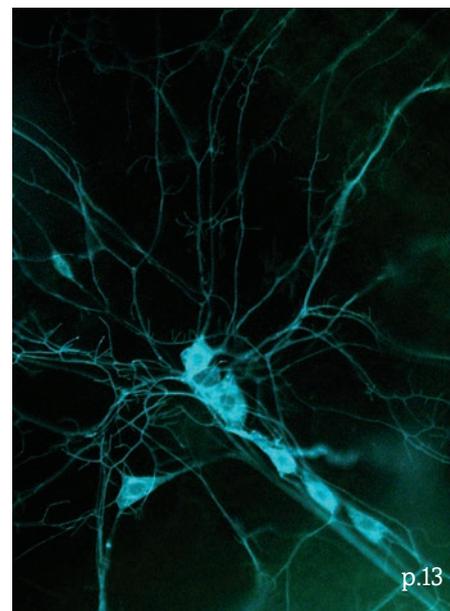
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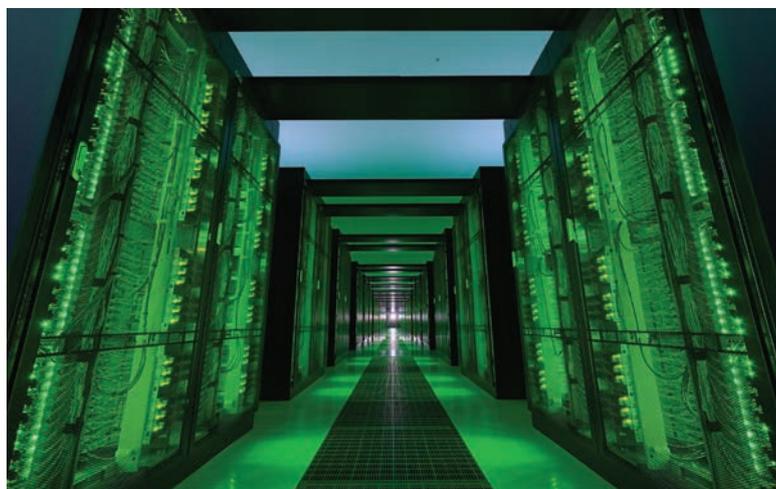
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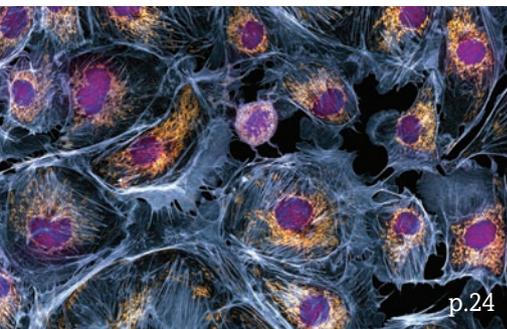
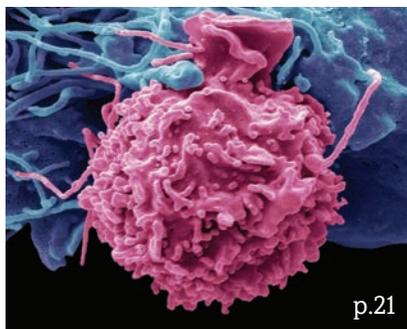


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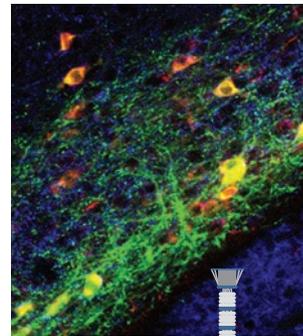
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A new star in the supercomputing world



Michihiko Minoh
Executive Director, RIKEN

Although the world is still struggling with the COVID-19 pandemic, we have some good news in these troubled times. In June, Japan's new supercomputer, Fugaku, ranked top in all four major global rankings of supercomputer performance, including the LINPAC benchmark used for the Top500 ranking. However, although the awards are a great encouragement, Fugaku was not built to win awards, but rather to do new, high-level computing.

There are three things I think make Fugaku unique. First, it was developed using a process called co-design, in which we worked with partners (including application specialists) to make sure that the computer is geared toward high-performance applications. Second, we adopted Arm technology used in smartphones. This means that, potentially, applications developed for Fugaku could one day be used on our smartphones. And third, we envision that Fugaku will be used to aid cloud-based services. Furthermore, the A64FX processor that Fujitsu created for our system will be used internationally in systems built by Hewlett Packard supercomputing subsidiary, Cray. This is very significant, as Japanese chips have long found it difficult to find a place in markets overseas.

I should also note that the benchmarks were run before Fugaku was fully installed. I think that a great deal of credit has to go to the engineers who worked tirelessly to tune the system under difficult conditions.

But again, going beyond awards, we look forward to seeing what Fugaku will accomplish. It will be used for a wide range of applications with strong social implications, such as drug discovery, big-data analysis, and even artificial-intelligence applications. For example, in April this year we announced that Fugaku would be used for research aimed at stemming the COVID-19 pandemic, looking onto areas such as diagnostics, therapeutic development, and big-data analysis of the virus spread (see more on page 9).

I'd like to emphasize above all that Fugaku is available to researchers, and we plan to make it available to a wide range of users, so I would like to encourage our partners globally to talk to us about how we can make this a truly valuable resource.



COVER STORY:

RIKEN researchers are using lasers to create transportable, hyper precise optical lattice clocks. These can help measure a very, very slight change in the speed of time high above the ground.
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Masataka Sasabe

Keep up to date



What really drives animal behavior?

Asuka Takeishi

RIKEN Hakubi Team Leader

Neural Circuit of Multisensory Integration RIKEN Hakubi Research Team, RIKEN Cluster for Pioneering Research/RIKEN Center for Brain Science

▣ Please describe your role at RIKEN.

I am the first Hakubi fellow to be part of the Kato-Sechi program and I lead a neuroscience lab studying animal behavior. As a recipient of a very competitive fellowship, I also feel I have a role in the promotion of gender diversity at RIKEN, especially as a working mom.

▣ Describe your current research.

Animals are exposed to continuously changing environmental stimuli, such as temperature, odor, light



and sound. We are interested in how animals integrate all this information within the brain and make behavioral decisions.

Many brain disorders are associated with behavioral problems, and we hope our research can contribute to understanding the fundamental mechanisms underlying these disorders.

▣ What do you think has been the most interesting discovery in your field in the last few years?

Research in 2014 on fruit flies found that fruit fly sensitivity and taste preferences are controlled by 'feeding state'—fed or starved. It was an elegant series of experiments that showed that a regulatory mechanism of the nervous system was linked to a feedback mechanism based on the internal fed-state of the animal.

We tend to think of problems in complicated ways. However, I learned from this and other important studies that the fundamental mechanism of nature can be simple. This was a great example of a beautiful experiment.

▣ My research is important for society because...

Knowledge obtained from studies using simple animals, such as nematode worm *Caenorhabditis elegans*, can reveal fundamental mechanisms that are universal. The mechanisms underlying behavioral decisions have been some of the biggest mysteries of neuroscience, although many neurological disorders are known to accompany behavior abnormalities. Ultimately, I hope our research can help us understand human behavior.

▣ How did you become interested in your current field of research?

I'm interested in how an animal responds to stimuli. It's still a mystery how or why animals make certain decisions. I became interested in this because I wanted to work in natural conditions as much as possible, and found state/environment-dependent behavior dynamics research very attractive.

▣ How has being at RIKEN helped your research?

Aside from the wonderful environment RIKEN provides, contact with the other talented personnel is most important to me. I am very lucky that I can interact and discuss science with high-level scientists. It was also very helpful that I could communicate and discuss my lab setup with skillful assistants, even before I joined.

Thanks to the help of some RIKEN assistants, the promotion office, facilities section, other researchers at the RIKEN Center for Brain Science and the Hakubi budget, our rooms were renovated and supplied with all the reagents and machines needed to start experiments much sooner than I expected.

“ *The mechanisms underlying behavioral decisions have been some of the biggest mysteries of neuroscience.* ”

▣ What are some technologies that you use for your research?

Sequencing services and fluorescent microscopes are a must for our research. It is incredibly helpful that we have the RIKEN BSI-Olympus Collaboration Center supplied with advanced confocal microscopes and advanced techniques for obtaining high-quality images.

▣ What are your professional and personal goals?

My professional goal is to understand our brain mechanisms at a level that will help scientifically and reasonably explain or predict an individual's behavior. ■

The magnetic field of spin-orbitronics

Collins Ashu Akosa

Postdoctoral Researcher
Spin Physics Theory Research Team,
RIKEN Center for Emergent Matter Science

Describe your role at RIKEN.

I'm a postdoctoral researcher in the Spin Physics Theory Research Team at the RIKEN Center for Emergent Matter Science (CEMS), led by Professor Gen Tatara. I seek to theoretically explore new directions in an emerging field called spin-orbitronics, in which scientists seek to exploit the interplay of electron charge and spin in the presence of 'spin-orbit interactions', the results of which could have potential applications to microelectronic devices.

I'm fascinated by the prospect of utilizing spin-orbit interaction... to create high-density and low power-consuming data storage.

What sparked your interest in your field?

I have been fascinated by magnets since high school. However, I chose to pursue my undergraduate studies in mathematics with a minor in computer science at the University of Buea in Cameroon, located at the foot of the beautiful 4,040 meter-high Mount Cameroon. This decision was motivated partly due to my love for mathematics as well as the fact that it would keep me open to varied career options. However, I took about 85% of my elective courses in physics. I was introduced to the concept spintronics during my days as graduate student in Theoretical Physics at the African

University of Science and Technology, Abuja, Nigeria.

Describe your current research.

I use mathematical equations to explain the behavior of tiny magnets and magnetic heterostructures at very short length and time scales.

In particular, I employ 'spin gauge field theory' to investigate how the interplay of spin-orbit interactions, charge and the spin of electrons influence transport in novel magnetic textures, such as domain walls and skyrmions. I'm also interested in the nature of magnetization dissipation in anti-ferromagnetic systems with broken inversion symmetry.

One fascinating prospect is the use of spin-orbit interaction (and related effects) to manipulate magnetic states at very short lengths to create smart, high-density, high-efficiency and low power-consuming data storage and memory technologies. Even more enchanting is the possibility of incorporating naturally abundant antiferromagnets—characterized by ultrafast dynamics—into these technologies to govern aspects such as transport properties.

When did you join RIKEN?

I joined RIKEN in April 2017, a few

months after the completion of my PhD. During my studies, I had read a lot of interesting research papers by Professor Tatara. I contacted him a couple of months before my PhD defense to express a desire to join his group. I was extremely impressed with the humility and simplicity of his response.

What has been your most memorable experience at RIKEN?

My first attendance of a CEMS weekly group meeting focused on skyrmions. Walking into a 100-capacity room filled with leaders in spintronics discussing fundamental concepts and their latest experimental observations was one of the most intimidating, yet motivating, experiences I've had. ■

Careers at RIKEN

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FUGAKU, FASTEST SUPERCOMPUTER IN THE WORLD

RIKEN's Fugaku is the first supercomputer in history to take the top spot in all three major global computing power rankings.

Supercomputer Fugaku has placed first on all the major global rankings, the Top500, HPCG, HPL-AI and Graph500 rankings simultaneously, an achievement that was announced in June.

The Top500 is the most widely known of these lists and ranks supercomputers based on speed. HPCG is intended to rank efficiency at running real-world applications. HPL-AI ranks a supercomputer's capabilities at tasks typically used in artificial intelligence applications, and Graph500 ranks systems based on their ability to process data-intensive loads.

This is the first time Fugaku, which is based at the RIKEN Center for Computational Science (R-CCS) in Kobe, has entered and it is still being developed by RIKEN and Fujitsu Limited using advanced Advanced Reduced instruction set computing Machine (Arm®) technology.

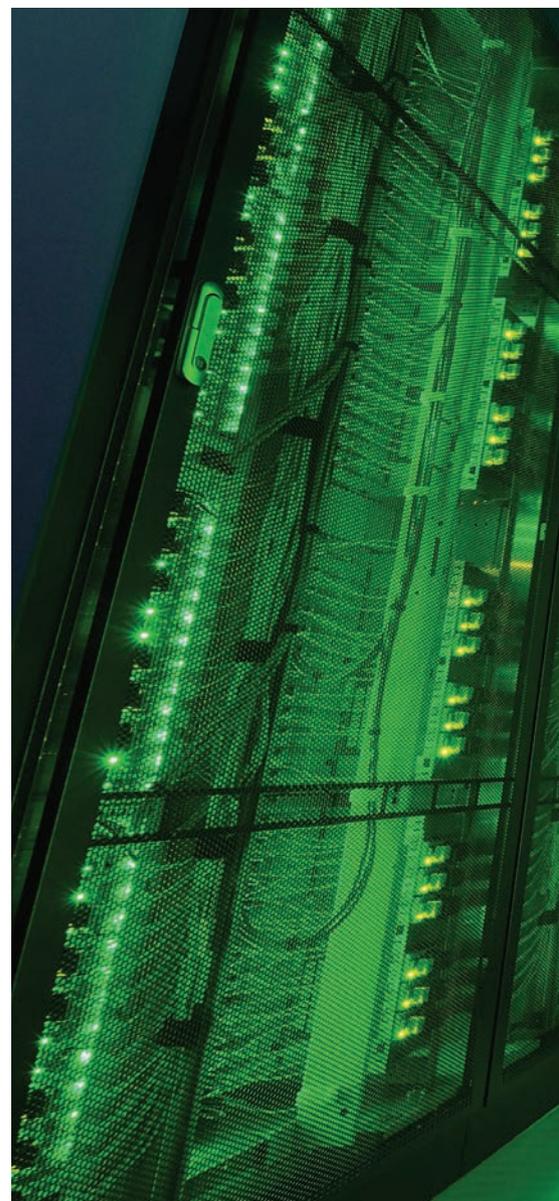
For the Top500, Fugaku achieved a LINPACK score of 415.53 petaflops using only 152,064 of its eventual 158,976 nodes. This was 266.93 petaflops more than its nearest competitor, the Summit supercomputer based at Oak Ridge National Laboratory in the United States. It marks the first time a Japanese system has taken the top ranking since June 2011, when the K computer—Fugaku's predecessor—took first place.

On the HPCG list, Fugaku scored 13,400 teraflops using 138,240 nodes. On HPL-AI Fugaku gained a score of 1.421 exaflops—the first time a computer has even earned an exascale rating on any list—using 126,720 nodes. The top ranking on Graph500 was achieved via the efforts of a collaboration involving RIKEN, Kyushu University,

Fixstars Corporation and Fujitsu Limited. Using 92,160 nodes, it solved a breadth-first search of an enormous graph with 1.1 trillion nodes and 17.6 trillion edges in approximately 0.25 seconds, earning it a score of 70,980 gigaTEPS, more than doubling the score of 31,302 gigaTEPS the K computer and far surpassing China's Sunway TaihuLight, which is currently second on the list, with 23,756 gigaTEPS.

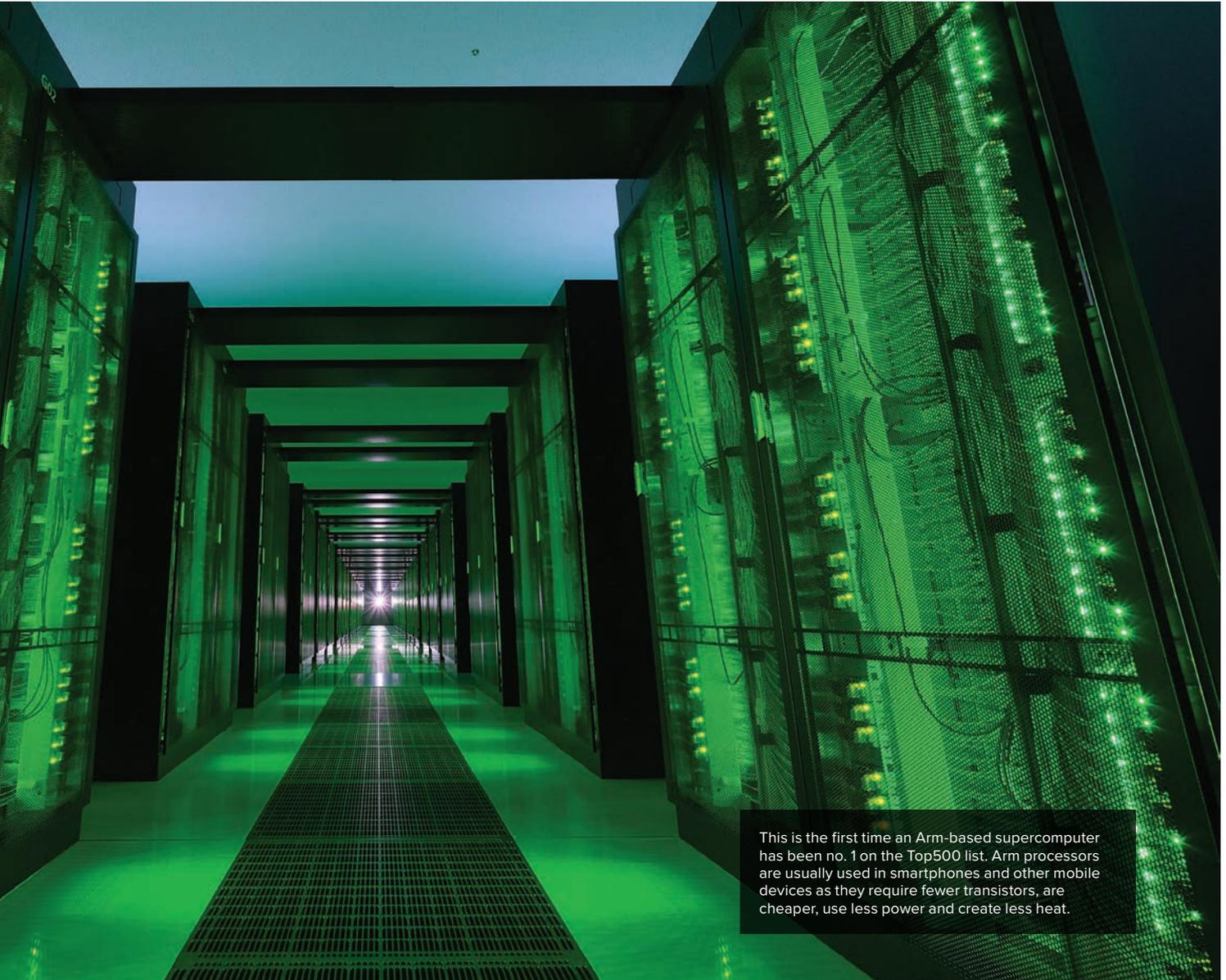
Fugaku is being developed to one day carry out a wide range of applications that will address high-priority social and scientific issues. It will be put to use running applications in areas such as drug discovery; personalized and preventive medicine; simulations of natural disasters; weather and climate forecasting; energy creation, storage and use; development of clean energy; new material development; new design and production processes; and—as a purely scientific endeavor—elucidation of the fundamental laws and evolution of the Universe. In addition, Fugaku is currently being used on an experimental basis for research on COVID-19, including on therapeutics and simulations of the spread of the virus. The new supercomputer is scheduled to begin full operation in 2021.

According to Satoshi Matsuoka, director of RIKEN R-CCS, "Fugaku was developed based on the idea of achieving high performance on a variety of applications of great public interest...and we are very happy that it has shown itself to be outstanding on all the major supercomputer benchmarks. In addition to its use as a supercomputer, I hope that the leading-edge IT developed for it will contribute to major advances on difficult social challenges such as COVID-19."



According to Naoki Shinjo, Corporate Executive Officer of Fujitsu Limited, "I believe that our decision to use a co-design process for Fugaku, which involved working with RIKEN and other parties to create the system, was a key to our winning the top position on a number of rankings. I am particularly proud that we were able to do this just one month after the delivery of the system was finished, even during the COVID-19 crisis."

Rene Haas, President, IP Products Group (IPG) for Arm, added that "the supercomputer Fugaku illustrates a dramatic shift. For



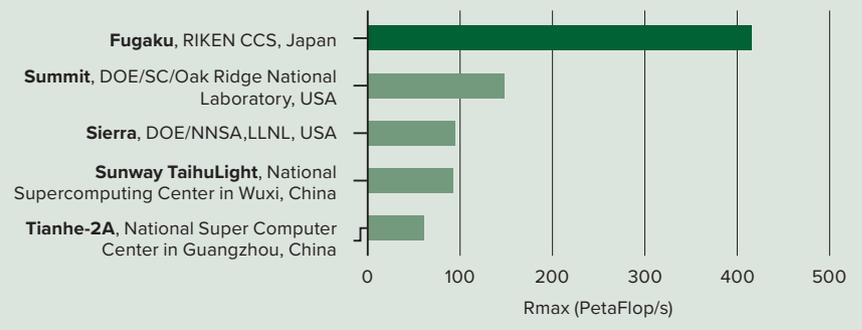
This is the first time an Arm-based supercomputer has been no. 1 on the Top500 list. Arm processors are usually used in smartphones and other mobile devices as they require fewer transistors, are cheaper, use less power and create less heat.

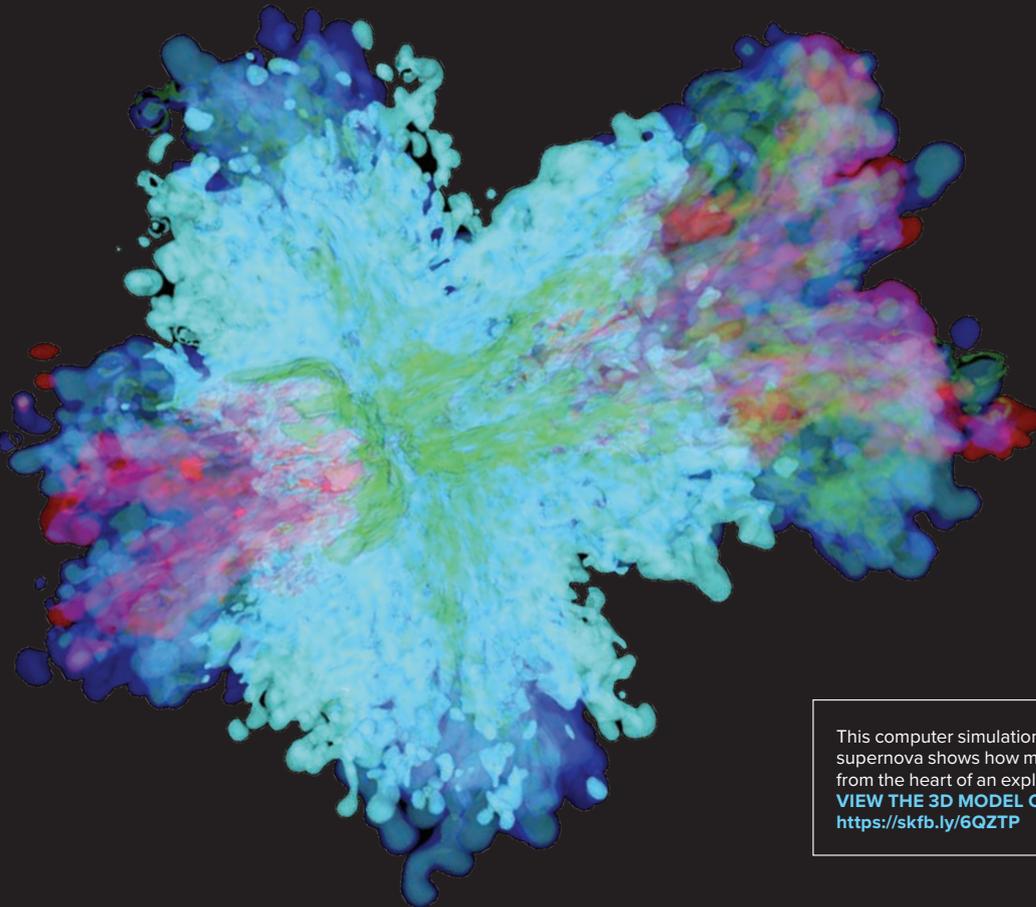
Arm, this achievement showcases the power efficiency, performance and scalability of our compute platform, which spans from smartphones to the world's fastest supercomputer. We congratulate RIKEN and Fujitsu Limited for challenging the status quo and showing the world what is possible in Arm-based high-performance computing.”

The rankings were announced on June 22 at the ISC High Performance 2020 Digital, an international high-performance computing conference.

www.riken.jp/en/news_pubs/news/2020/20200623_1/

TOP500 RANKINGS 1-5, JUNE 2020





This computer simulation of a supernova shows how matter is ejected from the heart of an exploding star.
VIEW THE 3D MODEL ONLINE:
<https://skfb.ly/6QZTP>

Star merger leads to supernova

Two stars in a nearby galaxy came together to form a blue supergiant, which subsequently exploded as a supernova, simulations by RIKEN astrophysicists suggest.

A core-collapse supernova occurs when the core of a massive star can no longer withstand its own gravity. The core collapses, triggering a violent explosion that blasts away the star's outer layers, leaving behind a neutron star or black hole.

In 1987, a star exploded in the Large Magellanic Cloud, one of our galaxy's closest neighbors.

Observations have revealed that in this case the progenitor was a compact blue supergiant, not the usual red supergiant.

"It's been a mystery why the progenitor star was a blue supergiant," says Masaomi Ono, who studies supernovas at the RIKEN Astrophysical Big Bang Laboratory.

Ono's team simulated asymmetric core-collapse supernova explosions of four progenitor stars and compared them with observations.

The closest match involved a blue supergiant progenitor formed by

a merger between two stars: a red supergiant and main-sequence star. During the merger, the larger star would have stripped matter from its smaller companion, which spiralled inwards until it was completely absorbed, forming a rapidly rotating blue supergiant.

The simulation may provide hints for where to look for the neutron star birthed in this stellar cataclysm, which has not been located despite 30 years of searching.

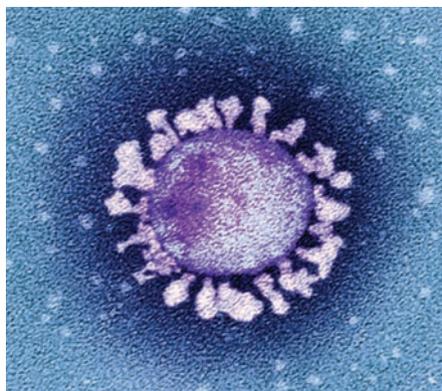
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Fugaku joins league of extraordinary supercomputers studying COVID-19

In June, RIKEN joined forces with the COVID-19 High Performance Computing Consortium, a high-profile international network aiming to coordinate supercomputer research on countermeasures to the COVID-19 pandemic; all members volunteer and donate free 'compute time'.

RIKEN's participation will center on the supercomputer Fugaku, currently the fastest supercomputer in the world (see page 6), operated by the RIKEN Center for Computational Sciences (R-CCS) in Kobe.

Fugaku, Japan's flagship high-performance computing system, was already being used for research and modeling of COVID-19 under a program run by Japan's Ministry of Education, Culture, Sports, Science and Technology (MEXT). As a consortium member, R-CCS will now also collaborate with MEXT to provide computational and data resources



The Fugaku supercomputer will donate time to global research teams as a member of the COVID-19 High Performance Computing Consortium.

to researchers around the world and to help disseminate the results of the group's research.

The original consortium was set up by IBM and the United States federal

government, but has since consolidated many of the important players in compute power, as well as major cloud providers, and more than 56 research teams.

Other members include Google Cloud, Microsoft, Nvidia, Intel, the Massachusetts Institute of Technology, Oak Ridge National Laboratory, Lawrence Berkeley National Laboratory, NASA, the Swiss National Supercomputing Centre's Piz Daint supercomputer team and many more. The joint effort is working on everything from looking for a complete vaccine and therapeutic treatments, to modeling how the virus spreads.

RIKEN joined in the wake of a commitment in May by Science and Technology Ministers of the G7 economic forum to strengthen high-performance computing-based research on COVID-19.

www.riken.jp/en/news_pubs/news/2020/20200623_5/index.html

Light detectors realized using organic liquid crystals

A response to light usually seen only in inorganic compounds has been realized in organic liquid crystals by an all-RIKEN team, opening the way to highly responsive photodetectors.

Conventional solar cells and light detectors are based on the photovoltaic effect. But another effect, called the bulk photovoltaic effect (BPVE), can generate currents in simpler structures than the photovoltaic effect. It also responds very rapidly to light and generates a highly constant current. These advantages could lead to a new generation of solar cells and light detectors.

The BPVE has been mainly studied in inorganic material, but organic compounds offer advantages such as flexibility and wavelength tunability. Previously, Daigo Miyajima of the RIKEN Center for

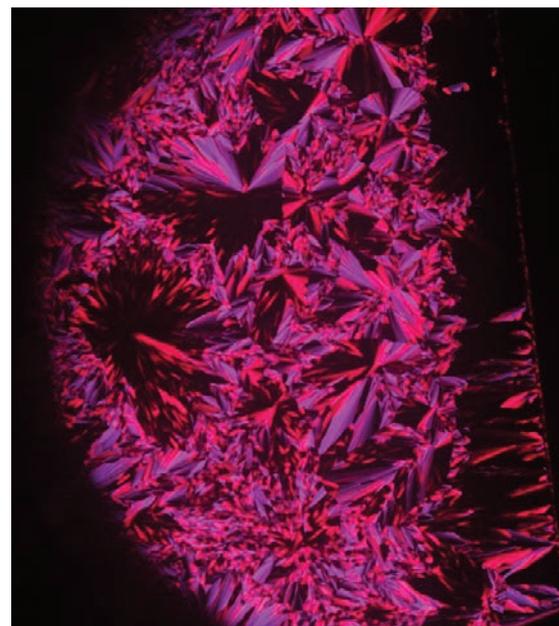
Emergent Matter Science and co-workers had studied the BPVE in a liquid-crystal column consisting of fan-shaped molecules stacked on top of each other. But it absorbed light only in the ultraviolet range.

Now, by tinkering with the base molecule's composition, they have observed the BPVE in the columnar liquid crystal over a wide wavelength range, which extends to red wavelengths.

By applying an electric field, the current in the liquid crystal jumped by about 6,600 times when light was shone on it—similar to the response of conventional light detectors, but it was realized in a device with a much simpler structure.

The team is seeking to make devices on flexible substrates.

www.riken.jp/en/news_pubs/research_news/rr/20200605_1/index.html



A polarized optical microscopy image of the columnar liquid crystals sandwiched between two crossed polarizers with and without (pictured) an electric field. This suggests that applying an electric field breaks the symmetry of the liquid crystals.

SKYRMIONS

Sound waves cause magnetic spins to whirl

Nanoscale magnetic whirlpools can be formed in a film by applying sound waves

The path to developing energy-saving memory devices is a little clearer, thanks to physicists at RIKEN. They have used sound waves to create tiny magnetic swirls known as skyrmions in a magnetic film in a way that promises to be more energy efficient than conventional methods¹.

It has only been about a decade since skyrmions were first observed in experiments, but research into them has exploded since then. Typically just several nanometers in diameter, skyrmions are highly stable and can be shunted around using extremely low electrical currents. All of this makes them ideal for realizing highly energy efficient data-storage devices that are smaller and faster than current devices.

This is analogous to the creation of a particle and its antiparticle in particle physics

Skyrmions are usually created by applying a short electrical pulse to a thin magnetic film, but the high current densities involved can cause heating, which squanders energy. “To realize energy-saving skyrmion-based devices, we need to find an efficient method to create skyrmions,” says Tomoyuki Yokouchi of the

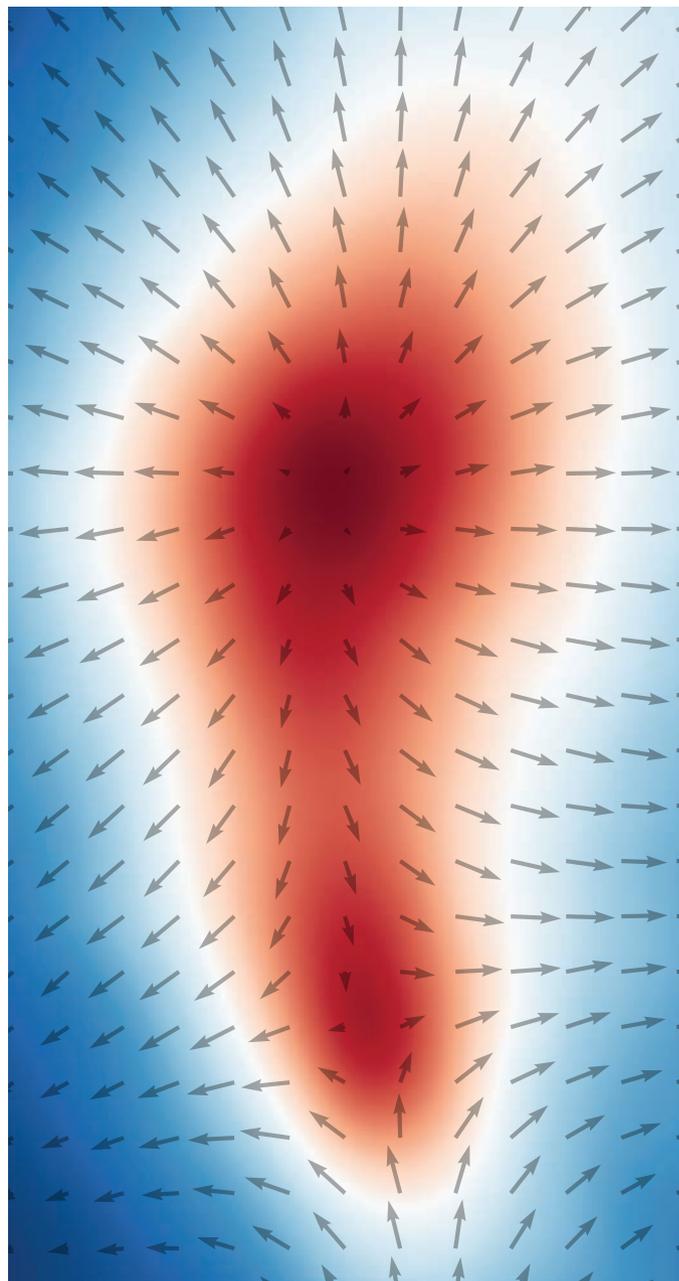
RIKEN Center for Emergent Matter Science (CEMS). “Current pulses can form skyrmions but require a sizeable current density, which is likely to cause significant heating. Hence, we need to find another way that doesn’t cause heating.”

Now, Yokouchi and colleague Yoshichika Otani, also at CEMS, and their co-workers have created skyrmions in a magnetic film by applying a special sound wave that travels on the surface of the film. The sound wave causes the atoms in the films to move, which in turn induces changes in the direction of the electron spins.

This method causes much less heating than applying an electrical pulse. It also has the advantage of being able to generate multiple skyrmions over a wide area. In contrast, electrical currents can only create skyrmions in specific narrow regions on a film.

To discover more about how the skyrmions were being made, the team performed a computer simulation. They found that two skyrmions actually form—a skyrmion and an anti-skyrmion (see image)—but the anti-skyrmion then disappears because it is less stable. “This is analogous to the creation of a particle and its antiparticle in particle physics,” says Yokouchi. “We were surprised that the creation process of skyrmions by sound waves included such a step.”

The team is now performing experiments to find out how fast skyrmions form by this process.



Numerical simulations of the formation of skyrmions by sound waves revealed that a skyrmion (top, larger red structure) and an anti-skyrmion (bottom, smaller red structure) form, but the anti-skyrmion subsequently annihilates.

They are also investigating whether sound waves can be used to move skyrmions around in the film. “We hope this work will deepen the basic science of skyrmion physics and contribute to the development of next-generation, energy-saving memory devices that are based on skyrmions,” says Otani. ●

Reference

1. Yokouchi, T., Sugimoto, S., Rana, B., Seki, S., Ogawa, N., Kasai, S. & Otani, Y. Creation of magnetic skyrmions by surface acoustic waves. *Nature Nanotechnology* **15**, 361–366 (2020).

GLASS TRANSITION

Scattered x-rays cast light on enigmatic transition

Synchrotron-generated x-rays can be used to probe what happens when liquids solidify into disordered solids, a process that has puzzled physicists for decades

The potential of an x-ray spectroscopy technique to shed light on the mysterious phenomena that occur when a liquid nears a glass-like state has been demonstrated by four RIKEN physicists¹.

On cooling, many liquids undergo a sharp switch at their freezing points, snapping into crystalline solids. The most famous example is water, with a freezing point of 0 degrees Celsius.

In contrast, many liquid polymers and other materials go through a more graceful transition known as the glass transition. The solids they form have structures closer to the random order of a liquid than the ordered structure of crystalline solids such as ice and metals. Glass is a classic example: it is a solid at room temperature but its molecules are arranged in a disordered manner.

There are many unanswered questions about the glass transition. “The phenomenon of glass transition is one of the biggest mysteries of soft-matter physics,” notes Taiki Hoshino of the RIKEN SPring-8 Center. “Some scientists even question whether the glass transition is really a transition or if it just looks like one.”

One key that may help unlock the mysteries about the glass transition is the concept of dynamical heterogeneity—fluctuations in space and time in the local dynamic behavior of molecules. “Many researchers believe that the glass transition can be explained in terms of dynamical heterogeneity,” says Hoshino.



On cooling, glass changes from a liquid to a solid. Despite intensive research, many aspects of this transition remain unknown. A study by RIKEN researchers demonstrates the potential of x-ray photon correlation spectroscopy to provide new clues into the glass transition.

Now, Hoshino and three RIKEN SPring-8 Center colleagues have used synchrotron-generated x-rays to measure dynamical heterogeneity in a liquid polymer near its glass-transition temperature.

During the measurements, the polymer was squeezed between a stationary cylindrical rod and a moving substrate. Liquid closer to the substrate moved faster than liquid near the rod, resulting in a velocity gradient across the liquid. The team found that the dynamical heterogeneity decreased as the velocity gradient was increased. This confirmed the predictions of a molecular

dynamics simulation published more than 20 years ago.

The researchers used a technique called x-ray photon correlation spectroscopy (XPCS). Because the light waves that make up a laser beam all peak and trough in sync with each other, laser light scattered from an object generates a speckle pattern on a screen. XPCS uses the speckle pattern generated by x-rays to obtain information about a sample. “If the scatterers in the sample move, the scattering pattern changes,” explains Hoshino. “These fluctuations reveal information about the motion of the scatterers.”

Hoshino notes that XPCS has not enjoyed as much popularity among soft-matter physicists as other techniques. However, he hopes this study will convince others of its potential. “Our results show that XPCS is a powerful technique for studying the glass transition,” he comments. ●

Reference

1. Hoshino, T., Fujinami, S., Nakatani, T. & Kohmura, Y. Dynamical heterogeneity near glass transition temperature under shear conditions. *Physical Review Letters* **124**, 118004 (2020).

NUCLEAR REACTIONS

Charting a course to the island of stability

Physicists propose a way to boost their chances of synthesizing new superheavy elements that will open up the eighth period of the periodic table

Measurements of collisions between small and large atomic nuclei by RIKEN physicists will inform the quest to produce new elements and could lead to new chemistry involving superheavy elements¹.

Two tantalizing goals lie nearly within the grasp of experimental nuclear physicists. One is to break into the eighth row of the periodic table. Scientists have made all the elements in the first seven rows—from hydrogen (one proton) to oganesson (118 protons). Thus, synthesizing heavier elements will open up new ground.

The other goal is to locate the ‘island of stability’ in the sea of superheavy nuclei; nuclei with fewer or more protons than nuclei in this island are unstable. Superheavy elements generally become more unstable the more protons they contain. For example, the most stable isotope of nihonium (113 protons) has a half-life of nearly 8 seconds, whereas that of oganesson is a mere 0.7 milliseconds. But theorists think this trend will change for nuclei lying just beyond oganesson. They conjecture that a particularly stable nucleus exists that is ‘doubly magic’, having

magic numbers (that is, stable full shells) of both protons and neutrons. Long-lived superheavy elements will open up a new type of chemistry, which involves more protracted reactions.

To realize these goals, experimentalists need to determine how to maximize their chances of producing superheavy nuclei since it is estimated to take more than three months to synthesize a single atom. To do this, they need to know the repulsive force two nuclei experience when they approach each other due to the attractive force of the nuclear potential.

Now, Taiki Tanaka of the RIKEN Nishina Center for Accelerator-Based Science and co-workers have measured this repulsion by firing small nuclei (neon, magnesium and calcium)

at large ones (curium and uranium) and measuring how they scattered.

They discovered that the repulsive barrier is mostly affected by the deformation of the larger nucleus, which is shaped like a rugby ball. Comparison with the excitation functions for producing known superheavy elements suggests that firing the smaller nucleus such that it approaches the side of the deformed larger nucleus will be the most effective strategy for producing new superheavy nuclei.

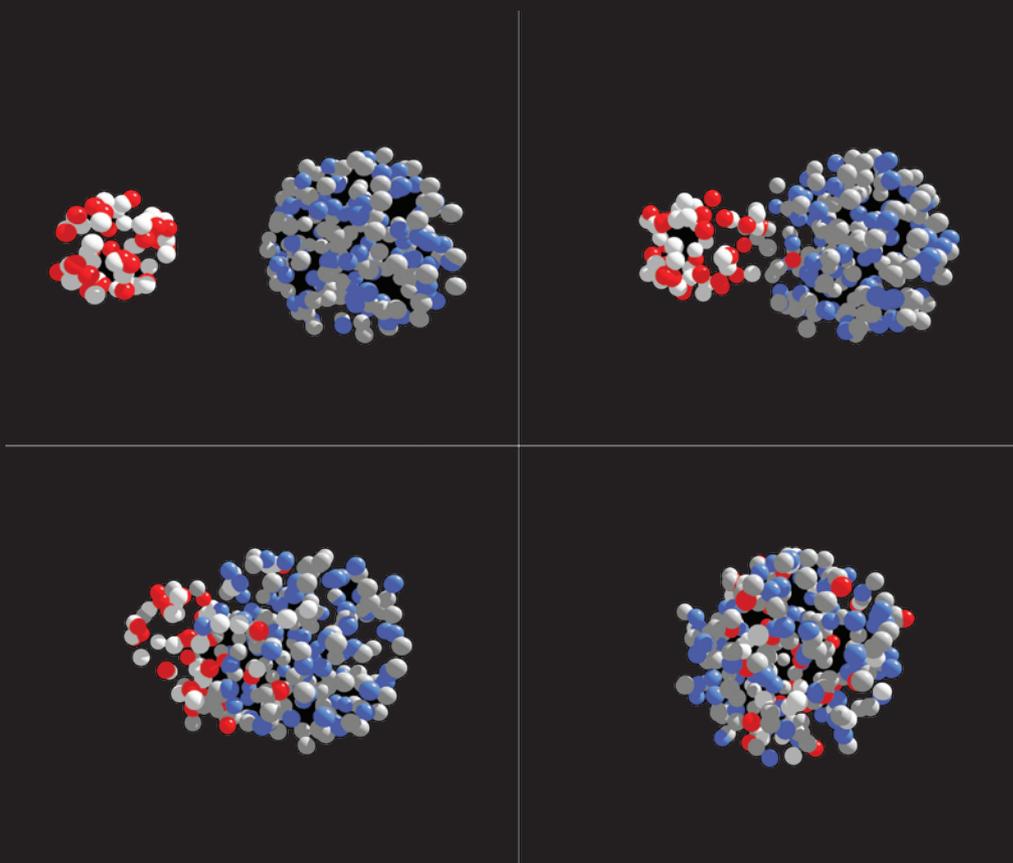
If this trend holds for heavier nuclei then the optimum energy of the smaller nucleus can be determined just by measuring the repulsive barrier of the larger nucleus, which only takes about a day. “From this systematic study, we’ve proposed a new method to

estimate the optimum incident energy to synthesize a new element,” says Tanaka.

The team plans to use this insight to make new superheavy elements. “In the short term, we’ll try to make new elements such as elements 119 or 120,” says Tanaka. “In a decade or two, we want to reach the island of stability.” ●

Reference

1. Tanaka, T., Morita, K., Morimoto, K., Kaji, D., Haba, H., Boll, R. A., Brewer, N. T., Van Cleve, S., Dean, D. J., Ishizawa, S. *et al.* Study of quasielastic barrier distributions as a step towards the synthesis of superheavy elements with hot fusion reactions. *Physical Review Letters* **124**, 052502 (2020).



Simulation showing a smaller nucleus (nickel in this case) fusing with a larger one (gold). Nuclear physicists at RIKEN have proposed a new way to estimate the optimum incident energy for synthesizing new superheavy elements that will open up the eighth period of the periodic table.

NEURON DEVELOPMENT

Atypical myosin affects where neurons branch out

A well-known actin motor protein is found to play an important role in the branching of neurons

The long-sought medical goal of repairing damaged neurons may be a little closer after RIKEN scientists made an unexpected discovery about the role of Myosin6, a well-known actin motor protein in neuron branching¹. The discovery was made by combining approaches from molecular genetics, cell imaging, artificial learning and animal behavior studies. Branch-like structures known as dendrites on neurons gather and process information from other neurons. The shape these dendrites adopt greatly affects how a neuron functions in neural circuits, and disruptions to the branching process can lead to intellectual disability and psychiatric disorders.

But little is known about the molecular processes that drive the neuron patterning. “We’ve known for a long time that a genetic blueprint determines the shape of a neuron,” says Adrian Moore of the RIKEN Center for Brain Science (CBS). “But we’re a long way from being able to read that blueprint—it’s still a black box.”

Knowing the processes involved in neuron branching could lead to practical benefits in the future. “If we can understand how neurons grow, we could repurpose some of these programs to help neurons regenerate after damage,” notes Moore.

Myosins act as miniature motors, causing muscles to contract and cells to move. Now, Moore and colleagues have discovered that the Myosin6 protein plays a key role in determining the position of primary neural branches. “We weren’t expecting

to find that Myosin6, a well-known actin motor protein, affects neural branching,” says Moore.

To make this discovery, the team combined two technologies: time-lapse imaging of developing neurons in living fruit flies and machine learning, which quantified the dendritic patterns in the images. They then compared the imaging parameters obtained with the behavior of molecules within the growing neuron.

“Much progress has been made in imaging neuron formation in living flies. We’re now able to follow a neuron from birth

to maturity,” says Moore. “At the same time, the ability of computers to analyze images has been rapidly improving. We married those two technologies in this study.”

In their analysis of neuron development and branching, the team employed a tool from animal behavioral studies—ethograms, which quantitatively catalogue animal behavior. “I’m a molecular biologist by training, but through interacting with my neuroscience colleagues at CBS who focus on behavior, I’ve come to realize that cells exhibit behavior just like animals do,” says Moore. “In this study, we

looked at neurons in the same way as we would look at animals or populations and asked how they behave and what underlines that behavior.”

“This work is important in showing how new approaches like the one we have adopted could be used to advance biomedical research,” Moore adds. ●

Reference

1. Yoong, L.-F., Lim, H.-K., Tran, H., Lackner, S., Zheng, Z., Hong, P. & Moore, A. W. Atypical myosin tunes dendrite arbor subdivision. *Neuron* **106**, 452–467 (2020).

A fluorescence micrograph of the dendrites of a fruit-fly neuron. RIKEN researchers have discovered that the protein called Myosin6 plays a key role in the development of these branches.

MOTT INSULATORS

Why a conducting material acts as an insulator

Physics textbooks couldn't explain why tantalum disulfide was insulating instead of conducting until its 'Mottness' was tested

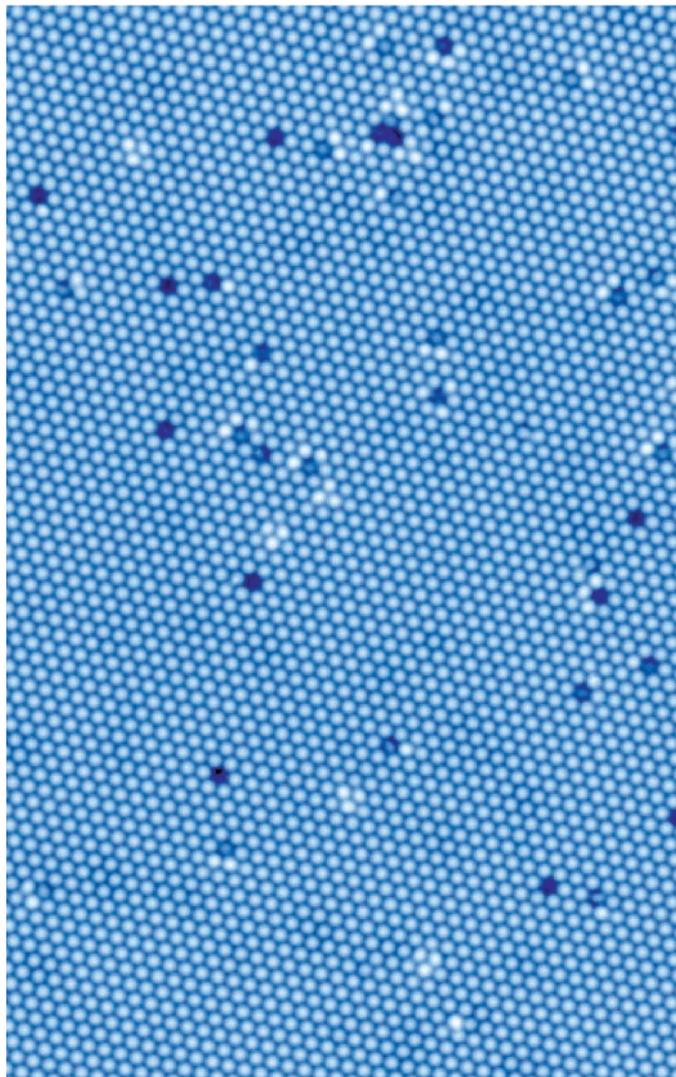
According to physics textbooks, tantalum disulfide should be an electrical conductor, but every test showed it acting as an insulator. Now four RIKEN scientists have explained why¹. In addition to resolving a long-standing controversy in solid-state physics, this finding could aid the search for high-temperature superconductors.

Crystalline materials should be good conductors when they have an odd number of electrons in each repeating cell of their structure, and poor conductors when they have an even number. However, sometimes this formula breaks down.

One example is 'Mottness', so called because the property is based on the work of Sir Nevill Mott. According to that theory, when electrons in the structure strongly repel each other, they cannot move around freely to generate an electric current.

To complicate matters, in some situations electrons in different layers of a 3D structure can pair up to create a bilayer structure with an even number of electrons. Some physicists have suggested that this pairing of electrons could restore the textbook understanding of the insulator, making it unnecessary to invoke Mottness as an explanation.

Now, Christopher Butler and Tetsuo Hanaguri and two co-workers, all at the RIKEN Center for Emergent Matter Science, have looked at tantalum disulfide. Since it has 13 electrons in its repeating structure, it should be a conductor, but it behaves as an insulator. There has been



A scanning tunneling microscopy image of a cleaved surface of tantalum disulfide.

controversy over whether this is caused by its Mottness or by a pairing structure.

The team looked at ultraclean surfaces of tantalum disulfide crystals using a scanning tunneling microscope (see image), which can sense where electrons are in a

material and their degree of conduction behavior.

They found the crystal layers were stacked into pairs. Sometimes the crystals cleaved between two pairs of layers, and sometimes through a pair, breaking it. Spectroscopy measurements on the paired and

unpaired layers revealed that even the unpaired ones were insulating, leaving Mottness as the only explanation.

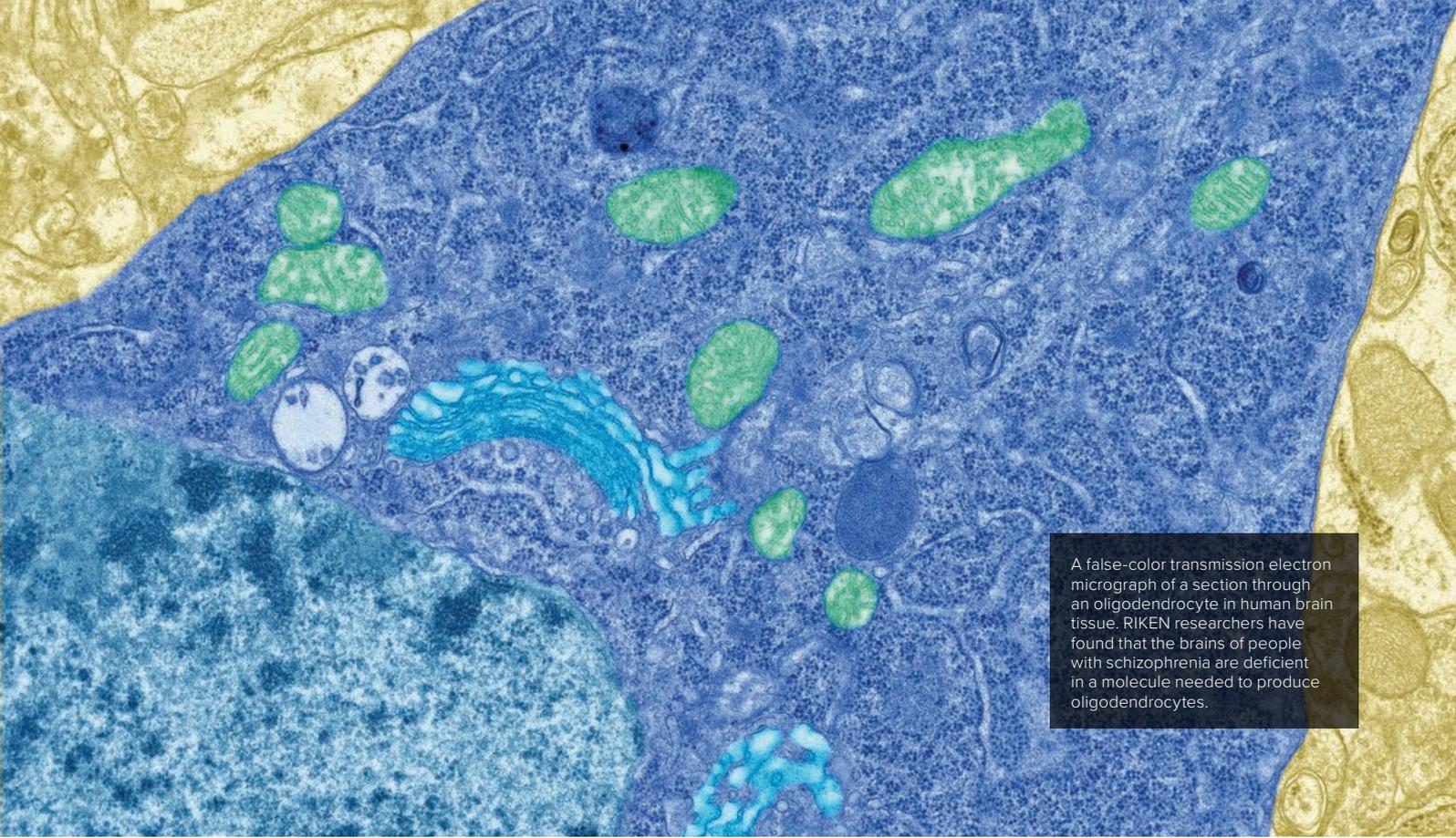
"The exact nature of the insulating state and of the phase transitions in tantalum disulfide have been long-standing mysteries, and it was very exciting to find that Mottness is a key player, aside from the pairing of the layers," says Butler. "This is because theorists suspect that a Mott state could set the stage for an interesting phase of matter known as a quantum spin liquid."

It was very exciting to find that Mottness is a key player

"The question of what makes this material move between insulating to conducting phases has long been a puzzle for physicists, and I am very satisfied we have been able to put a new piece into the puzzle," says Tetsuo Hanaguri. "Future work may help us to find new interesting and useful phenomena emerging from Mottness, such as high-temperature superconductivity." ●

Reference

- Butler, C. J., Yoshida, M., Hanaguri, T. & Iwasa, Y. Mottness versus unit-cell doubling as the driver of the insulating state in 1T-TaS₂. *Nature Communications* **11**, 2477 (2020).



A false-color transmission electron micrograph of a section through an oligodendrocyte in human brain tissue. RIKEN researchers have found that the brains of people with schizophrenia are deficient in a molecule needed to produce oligodendrocytes.

SCHIZOPHRENIA

White-matter deficiency opens up new opportunity

A deficiency in the white matter of schizophrenia sufferers points to a new direction for therapies

The white matter in the brains of people with schizophrenia is deficient in a certain fatty molecule, RIKEN researchers have discovered¹. This finding promises to provide a much-needed stimulus for developing drugs that can treat the neural disorder.

Most of the drugs currently available for treating schizophrenia are based on dopamine, but they are ineffective in about one third of patients. “Because we don’t have another angle on what causes schizophrenia, many pharmaceutical companies are pulling out of schizophrenia-related drug development,” says Takeo Yoshikawa of the RIKEN Center for Brain Science (CBS). “Hopefully, our findings can provide the new angle with a new target for drug development.”

While much remains unknown about how schizophrenia

affects the brain, the brains of schizophrenia sufferers are known to have less white matter than average brains. White matter in the brain is made from oligodendrocytes, special cells that wrap around the parts of neurons that carry outgoing signals, which help them to communicate with each other. Abnormalities in the white matter may lead to irregular communication between neurons and could be behind characteristic symptoms of schizophrenia such as hallucinations and the inability to distinguish reality from thoughts.

Yoshikawa’s team investigated sphingolipids, a group of lipids that have some functions related to white matter. Postmortem analysis of the large white-matter tract that connects the left and right sides of the brain showed a severe deficiency in

SIP, a sphingolipid needed in the production of oligodendrocytes.

Further tests showed that although normal amounts of SIP had been produced, it was metabolized and degraded when it should not have been. “Drugs that prevent SIP degradation could be particularly effective in treating schizophrenia,” says Kayoko Esaki, also of CBS.

The researchers also examined postmortem brains of people with bipolar disorder or major depressive disorder, but did not find SIP levels that differed from those in unaffected brains. This indicates that the problem is not a common feature of mental disorders but is specific for schizophrenia.

Measuring SIP levels in postmortem brains was challenging, requiring interdisciplinary expertise in mass spectrometry, which

Esaki provided. “This was the first psychiatric study of the postmortem brain to use mass-spectroscopic analysis,” notes Yoshikawa.

Animal studies are needed before schizophrenia-specific clinical trials can begin. “The next important step is to determine precisely which SIP receptor-acting drugs are effective in experimental animals,” says Yoshikawa. ●

Reference

1. Esaki, K., Balan, S., Iwayama, Y., Shimamoto-Mitsuyama, C., Hirabayashi, Y., Dean, B. & Yoshikawa, T. Evidence for altered metabolism of sphingosine-1-phosphate in the corpus callosum of patients with schizophrenia. *Schizophrenia Bulletin* sbaa052 (2020).

RAMAN SPECTROSCOPY

A sprinkle of salt

A thin substrate of sodium chloride aids the spectroscopic investigation of single-molecule vibrations

Scientists at RIKEN have been able to detect vibrations of a single molecule, allowing them to produce different maps of the molecule for different vibrations¹. This technique is promising for probing the chemical properties of materials on a single-molecule level and for discovering new nanomaterials.

Raman spectroscopy is commonly used to study the vibrations of molecules, but its resolution is limited by the wavelength of the light used to irradiate the sample. This becomes problematic for the study of very small systems such as single molecules.

Tip-enhanced Raman spectroscopy (TERS) overcomes this problem by using the tip of a scanning tunneling microscope (STM) to enhance the resolution. But this method has its own limitations—it enhances molecular vibrations that are parallel to the tip much more than those perpendicular to the tip and it can alter the chemical properties of the sample.

Now, Yousoo Kim and Rafael Jaculbia from the RIKEN Surface and Interface Science Laboratory and their co-workers have overcome both these limitations of STM-TERS.

They did this by adding a thin layer of sodium chloride between a silver substrate and the sample—in this case, an isolated molecule of copper

naphthalocyanine (see image). By scanning the tip across the molecule, the team could obtain maps of the molecule that differed depending on the molecular vibration used to produce the map.

We are looking forward to seeing our technique be used to identify new molecules

In this technique, because the molecule is not in direct contact with the silver surface, vibrations that are perpendicular to the tip could be detected just as well as those parallel to

the tip. In addition, since the sodium chloride layer physically separated the sample and the silver substrate, the chemical properties of the sample remained unchanged.

“We didn’t need to perturb the system to get the maps; our results showed that the molecule remains in its original electronic state by keeping the tip farther from the molecule,” explains Jaculbia. “With this strategy, we are able to keep the molecule’s intrinsic properties, which is useful for investigating the unperturbed properties of a single molecule.”

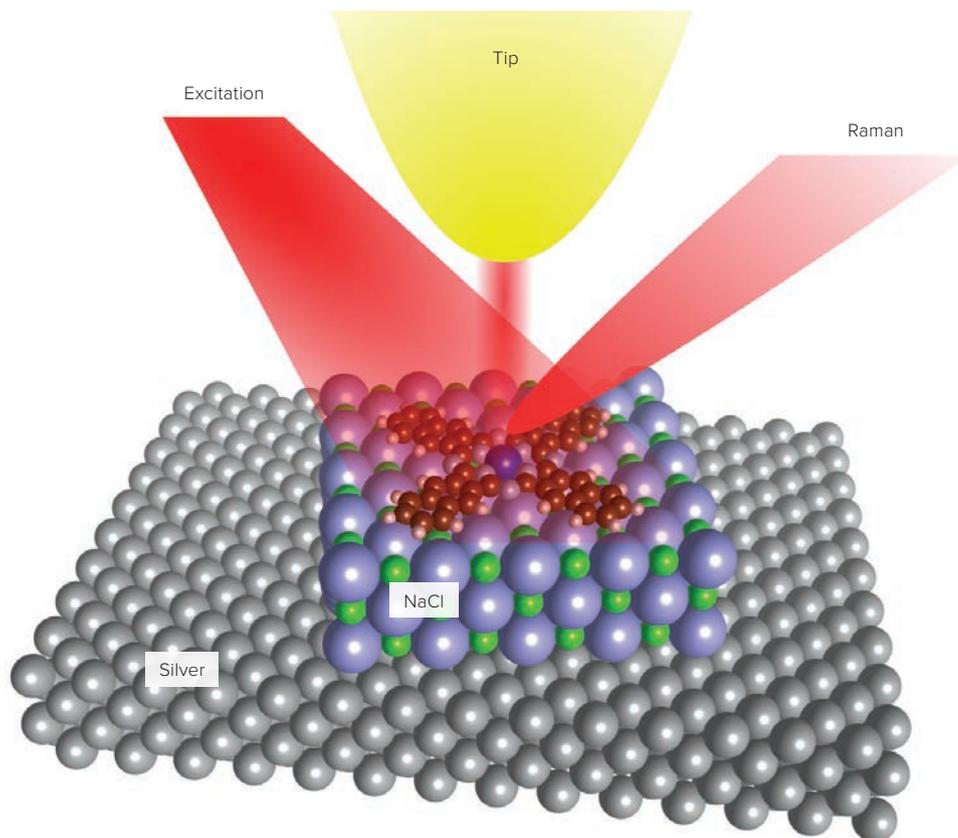
“Our technique is a truly non-invasive probe with the capabilities of both high chemical sensitivity and nanoscale spatial resolution,” comments Kim. “Such

a technique is indispensable for discovering new nanoscale materials and investigating the intrinsic chemical properties of materials.”

“We are looking forward to seeing our technique be used to identify new molecules based on their vibrational modes, similar to how biometric scanners process human fingerprints,” adds Jaculbia. ●

Reference

- Jaculbia, R. B., Imada, H., Miwa, K., Iwasa, T., Takenaka, M., Yang, B., Kazuma, E., Hayazawa, N., Taketsugu, T. & Kim, Y. Single-molecule resonance Raman effect in a plasmonic nanocavity. *Nature Nanotechnology* **15**, 105–110 (2020).



Schematic of the experimental set up. The sample, a molecule of copper naphthalocyanine (X-shaped structure) is adsorbed on a layer of sodium chloride (NaCl), which is deposited on a silver substrate. The tip scans the molecule and a laser beam excites the sample, the Raman spectrum of which is detected.

BRAIN AGING

Biomarker detects brain-drain problems

Scans of blood drainage from the brain could be used as a biomarker and help prevent certain cases of dementia

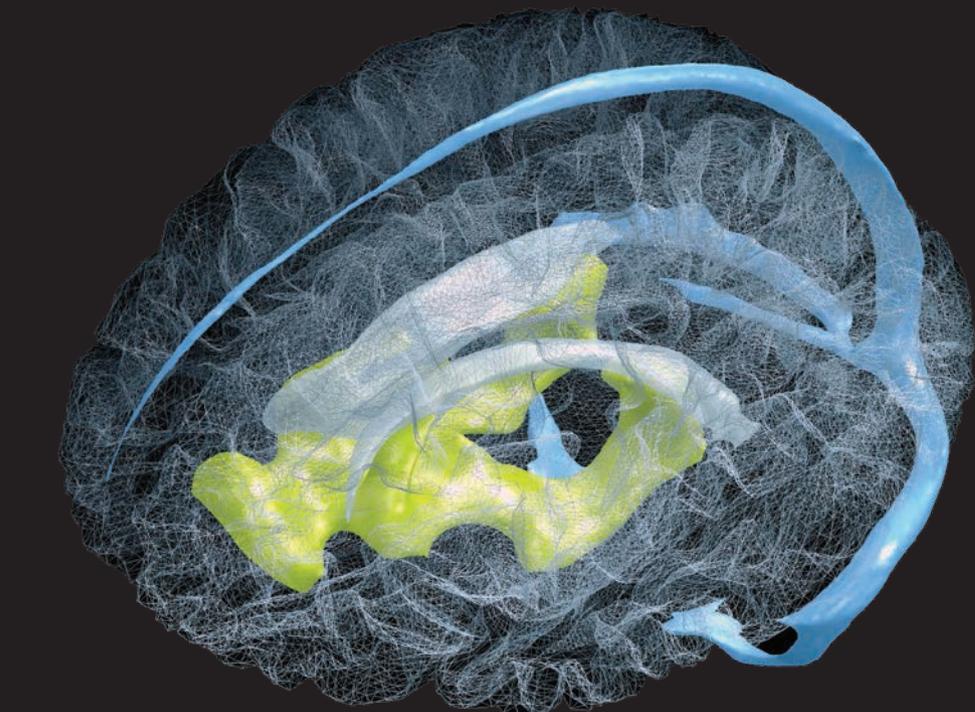
A potential biomarker for a form of dementia has been identified by researchers RIKEN after they discovered that easily detectable changes to blood circulation in the brain were predictive of a condition called ventriculomegaly¹.

After circulating through the brain, blood returns to the heart via the veins through one of two pathways: one that drains blood from regions close to the brain's surface and one that drains blood from areas deep within the brain, known as the brain's ventricles.

In young people, blood traveling either of these two paths takes roughly the same time, but by using magnetic resonance imaging (MRI) to measure blood flow changes, the team had previously found that the time it takes for blood to drain through these two pathways goes out of sync, resulting in an increasing time lag with aging.

In the present study, the researchers found that, in healthy aging, this time lag in circulation grows at almost the same rate as enlarging ventricles, but begins slightly earlier. Thus, a diagnostic MRI that measures the lag between the two drainage pathways might be a good biomarker for the aging brain and a predictor of ventriculomegaly.

"We found an age-related perfusion timing shift in the brain's venous systems whose lifespan profile was very similar to, but slightly preceded that of, ventricular enlargement," explains Toshihiko Aso of the



RIKEN researchers have found a biomarker for age-related changes in the venous drainage pattern that characterize the condition ventriculomegaly. Lower right: Three-dimensional rendering of the brain region that exhibits an upstream shift with age (yellow) located under the lateral ventricles (white). Major components of the cerebral venous system are shown in blue.

RIKEN Center for Biosystems Dynamics Research.

The researchers also examined people with traumatic brain injury because they often suffer from enlarged ventricles and have brains that appear to have aged prematurely. They found a time lag in blood drainage that was related to the disease. This effect depended on age at the time of injury, being large in people who suffered traumatic brain injury when young, but much less for those injured later in life.

"The timing asynchrony between deep and superficial

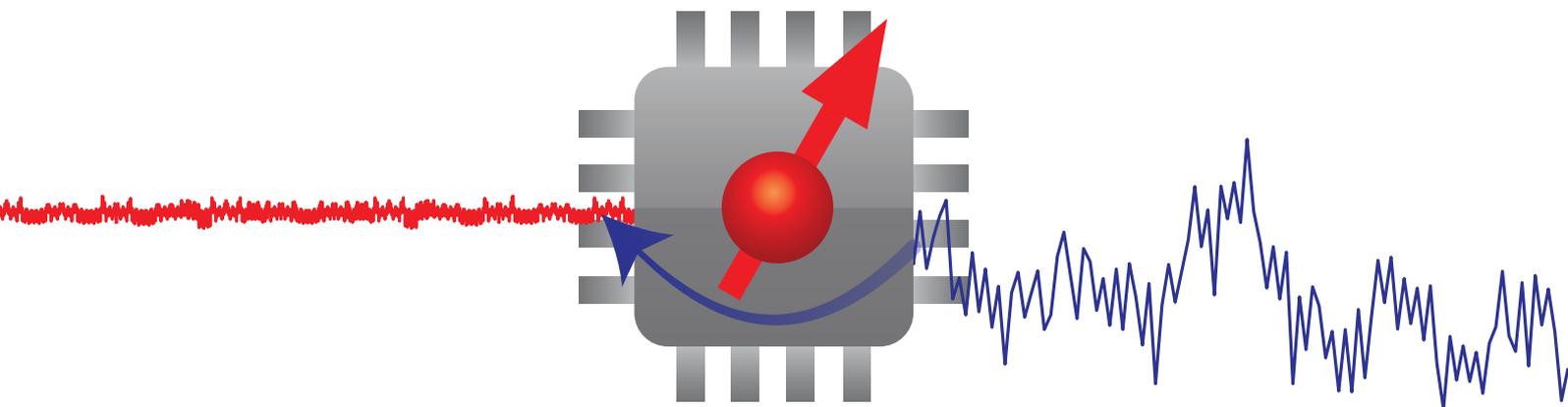
venous drainage might therefore be a common mechanism that underlies both types of ventriculomegaly," says Aso. "This new biomarker might therefore be useful for diagnosing and monitoring normal-pressure hydrocephalus (commonly known as water on the brain) that is either age related or that results from brain injury."

Early diagnosis is critical since dementia resulting from hydrocephalus can be reversed by removing the fluid buildup in the ventricles. The team is developing non-invasive applications

of this technology. "We hope that using this biomarker to monitor the aging brain becomes a part of the annual health checkup system for people in Japan," says Aso. ●

Reference

1. Aso, T., Sugihara, G., Murai, T., Ubukata, S., Urayama, S., Ueno, T., Fujimoto, G., Thuy, D. H. D., Fukuyama, H. & Ueda, K. A venous mechanism of ventriculomegaly shared between traumatic brain injury and normal ageing. *Brain* **143**, 1843–1856 (2020).



QUANTUM INFORMATION

Noise canceling on a quantum scale

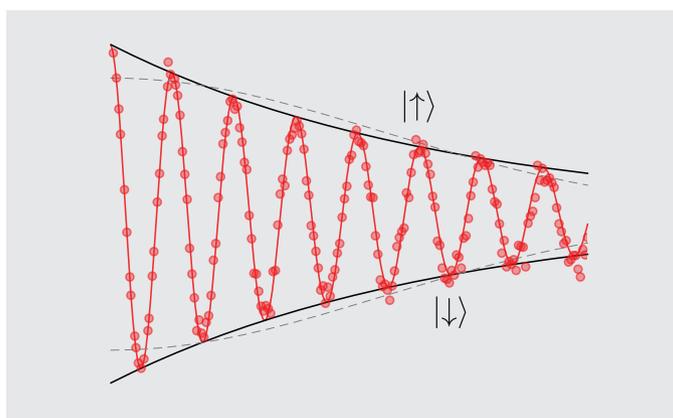
A noise-canceling experiment reveals an unexpected source of noise during quantum computations

In a finding that could help improve the accuracy of quantum computers, the most problematic noise source for the accurate manipulation of data in quantum computers based on semiconductor quantum dots has been identified by a RIKEN-led team¹.

Quantum computers have the potential to solve problems that are intractable for conventional computers. Of the various technologies being investigated for realizing quantum computers, manipulating the spins of individual electrons trapped in tiny semiconductor blobs known as quantum dots is one of the most promising, particularly as it can use existing semiconductor fabrication technology.

Quantum computers operate by storing and manipulating qubits—the quantum equivalent of bits in conventional computers. In computers based on semiconductor quantum dots, a qubit is the spin of an electron trapped in a quantum dot.

Since electron spin is highly sensitive to its environment, it is critical to preserve its state for as long as possible—a parameter known as its coherence. It is also important to ensure that operations on the qubit are implemented accurately—a



Top: Physicists at RIKEN have investigated the effect of canceling low-frequency noise (present in the blue line on the right, but removed from the red line on the left) on the coherence and fidelity of qubits in gallium arsenide quantum dots, which are encoded as electron spin (red arrow). Bottom: The system undergoes coherent oscillations between the spin up and spin down states.

parameter called the fidelity. Engineers want to optimize both the coherence and fidelity of quantum computers.

“It’s generally believed that if you have a good coherence then you can expect a high fidelity,” says Takashi Nakajima of the RIKEN Center for Emergent Matter Science. “But the relationship between the two parameters wasn’t clear for spin qubits.”

Now, a team led by Seigo Tarucha has examined the effect of canceling the low-frequency component of the environmental noise, which can arise from control electronics, heat,

impurities and nuclear spins, on the coherence and fidelity of spin qubits.

They employed a similar technique to that used in noise-canceling headphones. “Noise-canceling headphones measure the environmental noise and generate a feedback signal to cancel it,” explains Nakajima. “We did a similar thing for qubits—we detected the noise in the semiconductor device and then applied a microwave signal to cancel this noise.” In this way, the team eliminated nearly all of the low-frequency noise (see image).

The team discovered that cutting out the low-frequency noise, which mostly comes from the nuclear spin in the material, improved both the coherence and the fidelity. But while the coherence was still affected by the residual low-frequency noise, the fidelity was more affected by the high-frequency noise. Thus, different approaches are needed to improve coherence and fidelity.

The researchers found that the high-frequency noise originates from charge fluctuations in their device. “It came as a surprise because most of the noise was thought to come from nuclear-spin noise in the system,” says Nakajima. To improve the fidelity, and hence the reliability of calculations, engineers will need to find ways to reduce this high-frequency noise, he adds. ●

Reference

1. Nakajima, T., Noiri, A., Kawasaki, K., Yoneda, J., Stano, P., Amaha, S., Otsuka, T., Takeda, K., Delbecq, M. R., Allison, G. *et al.* Coherence of a driven electron spin qubit actively decoupled from quasistatic noise. *Physical Review X* **10**, 011060 (2020).

NUCLEAR PHYSICS

The difference a single proton can make

An oxygen nucleus looks very different from the core of a fluorine nucleus despite containing the same numbers of protons and neutrons

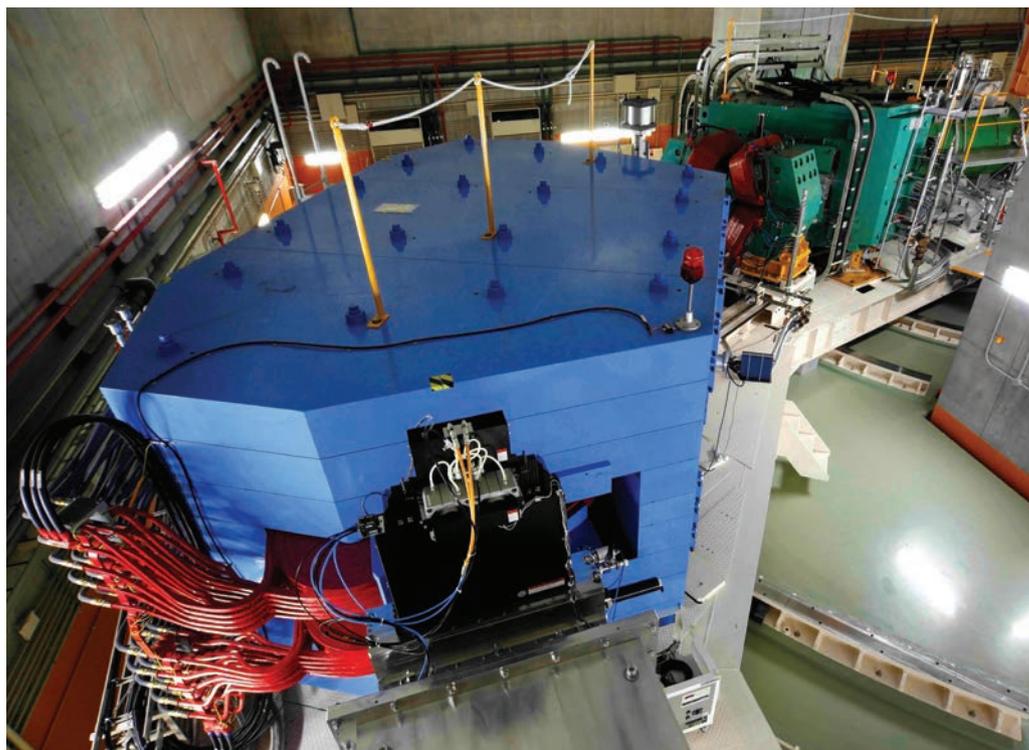
Converting a fluorine nucleus into an oxygen nucleus by knocking out a single proton can greatly affect the state of the nucleus, nuclear physicists at RIKEN have discovered¹. This could help to explain an anomaly with oxygen nuclei that has long puzzled physicists and advance their understanding of the physics of nuclei and neutron stars.

Nuclear physicists are interested in determining how many neutrons they can add to a nucleus of an element before it cannot hold any more and starts to drip neutrons—a point known as the neutron drip line. This is important for understanding both the physics of nuclei and that of neutron-rich environments, such as supernovae and neutron stars.

One mystery has been why the drip line jumps by six neutrons in going from oxygen to fluorine: an oxygen nucleus with eight protons can only accept up to 16 neutrons, whereas fluorine, with just one extra proton, can incorporate up to 22 neutrons.

This is important for understanding both the physics of nuclei and that of neutron-rich environments

To shed light on this conundrum, Tsz Leung Tang of the RIKEN Nishina Center for Accelerator-Based Science and his co-workers used the



Nuclear physicists at RIKEN used the Radioactive Isotope Beam Factory to convert fluorine-25 nuclei into oxygen-24 nuclei and found that the oxygen-24 nuclei were very different from the core of fluorine-25 nuclei.

Radioactive Isotope Beam Factory (see image) to create a beam of fluorine-25 nuclei, each one having nine protons and 16 neutrons. In each nucleus, eight protons and 16 neutrons form a core, while the ninth proton is a valence proton and lies outside the core. Because the core has two complete shells, it is ‘doubly magic’ and is especially stable.

The team knocked out the valence proton by colliding the fluorine-25 beam with a target. They then analyzed the resulting oxygen-24 nuclei using a spectrometer.

The expectation was that knocking out the valence

proton would leave the core—oxygen-24—in its lowest energy state. However, the team found that the oxygen-24 at the core of the fluorine isotope mostly existed in excited states, which were significantly different from a free oxygen-24 nucleus.

“This is quite an exciting result, and it tells us that the addition of a single valence proton to a nucleus core—a doubly magic one in this case—can have a significant effect on the state of the core,” says Tang. “Calculations showed that known interactions, including tensor force effects, were insufficient to explain this result.”

The team intends to probe deeper into what is producing the oxygen anomaly. “We plan to conduct further experiments to determine the mechanism responsible for the extension of the drip line in fluorine,” says Tang. ●

Reference

1. Tang, T. L., Uesaka, T., Kawase, S., Beaumel, D., Dozono, M., Fujii, T., Fukuda, N., Fukunaga, T., Galindo-Uribarri, A., Hwang, S. H. *et al.* How different is the core of ^{25}F from $^{24}\text{O}_{g.s.}$? *Physical Review Letters* **124**, 212502 (2020).

ATOMIC-LATTICE CLOCKS

Bringing space-based measurements down to earth

Two transportable clocks test relativity to an accuracy rivaling that of satellite-based measurements

RIKEN physicists have used Japan's tallest tower and two ultraprecise clocks to measure the time dilation effect predicted by Einstein's theory of general relativity¹. This measurement demonstrates the power of transportable ultraprecise clocks, which could find application in probing the structures of volcanoes.

Einstein hypothesized that the gravitational field of a massive object will warp space-time and cause time to run slower. Since the Earth's gravitational field gets weaker the further you are from the center of the Earth, a clock at the bottom of a tall building should run ever so slightly slower than one at the top.

But because this difference is minuscule, stringent testing of the theory of relativity requires either extremely precise clocks or a large difference in altitude. The best measurements in the laboratory have involved large, complex clocks such as the optical lattice clocks developed by the RIKEN group, which can measure height differences of around a centimeter. Measurements using satellites whose altitudes differ by thousands of kilometers have attained an even higher accuracy.

Now, a team led by Hidetoshi Katori of the RIKEN Center for Advanced Photonics has developed transportable optical lattice clocks that could precisely test general relativity, but by using Tokyo Skytree rather than satellites. They placed one clock at the base of the tower and one on the observation deck, which is 450 meters above street level. The measurements validated



The tallest tower in Japan, Tokyo Skytree looms over its surroundings. RIKEN physicists have used it and two transportable ultraprecise clocks to test the accuracy of Einstein's theory of general relativity to a precision comparable to that obtained using satellites orbiting the Earth.

Learn more about the experiment and atomic clocks on [page 32](#).

Einstein's theory to a precision comparable to the best space-based measurements.

The ultimate purpose, however, was not to prove or disprove Einstein. "We wanted to demonstrate that we could conduct these accurate measurements anywhere outside the laboratory, with transportable devices," says Katori.

"Ultraprecise clocks can distinguish small differences in altitude, allowing us to measure ground swelling in places such as active volcanoes or crustal deformation, or to define the reference for height. This is the first step toward making ultraprecise clocks into real-world devices."

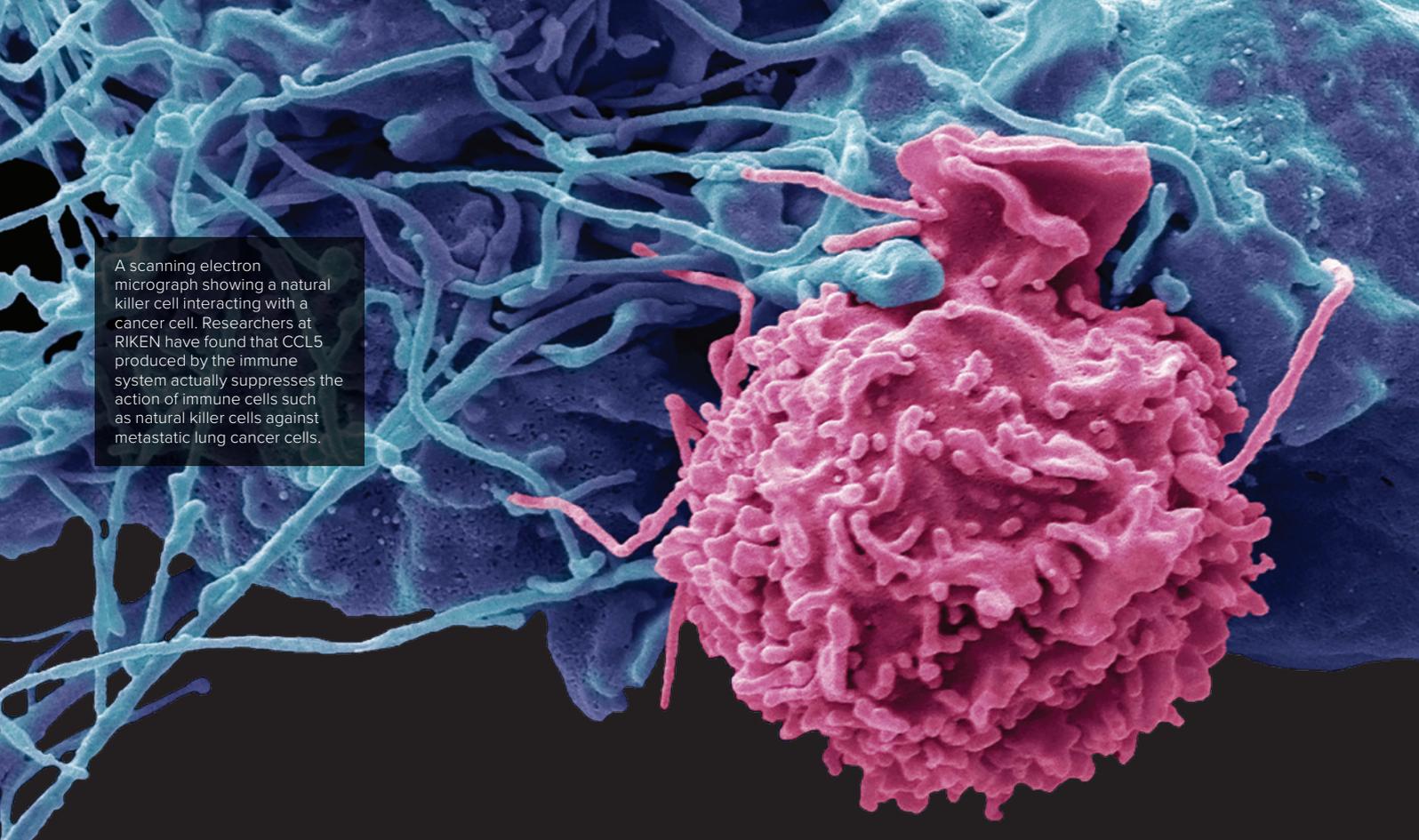
The key was to miniaturize the laboratory-sized clocks into transportable devices and to make them insensitive to environmental noise such as temperature changes, vibrations and electromagnetic fields. Each clock was enclosed in a magnetic-shield box, around 60 centimeters on each side, while the various lasers and electronic controllers

were housed in two rack-mountable boxes. The two clocks were connected by an optical fiber to measure the beat note.

The team plans to compare clocks hundreds of kilometers apart to monitor the long-term uplift and depression of the ground, a potential application of ultraprecise clocks. ●

Reference

1. Takamoto, M., Ushijima, I., Ohmae, N., Yahagi, T., Kokado, K., Shinkai, H. & Katori, H. Test of general relativity by a pair of transportable optical lattice clocks. *Nature Photonics* **14**, 411–415 (2020).



A scanning electron micrograph showing a natural killer cell interacting with a cancer cell. Researchers at RIKEN have found that CCL5 produced by the immune system actually suppresses the action of immune cells such as natural killer cells against metastatic lung cancer cells.

TUMOR IMMUNOLOGY

Chemokine produced by immune system aids cancer cells

A signaling molecule produced by the immune system hinders the immune cells from attacking cancer cells in mice

In a surprising discovery, RIKEN researchers have found that preventing the immune system of mice from producing a small signaling molecule known as CCL5 actually helps the immune system to fight metastatic lung cancer¹. This result highlights the pro-cancer role that CCL5 plays and could lead to new therapies.

CCL5 is a curious chemokine—a small protein secreted by cells that affects the immune system. For a start, it behaves differently from other chemokines. Most chemokines are quickly cranked out in response to a pathogen and

then their levels drop off rapidly. In contrast, CCL5 is produced in small amounts even under normal conditions and it exhibits a double peak in response to a pathogen, with the second peak occurring a few days after the first one.

Also, the role CCL5 plays in cancer has been unclear. It is produced both by the immune system and cancer cells. The evidence has been mixed, with some studies finding it helps cancer cells flourish while others have found that it appears to help the immune system fight them.

Now, Ichiro Taniuchi and Wooseok Seo of the RIKEN

Center for Integrative Medical Sciences and co-workers have shed light on both these aspects of CCL5.

The team has identified two enhancers—short sections of DNA that, when combined with proteins known as transcription factors, enhance the transcription of an associated gene—that increase the production of CCL5. One of the enhancers is close to *Ccl5*, the gene that codes for CCL5, and it regulates production of the chemokine under normal conditions. The second enhancer is a long way from *Ccl5* and it induces CCL5 expression in activated cells. Furthermore, the team found that the transcription factor RUNX suppresses the effect of these two enhancers.

But the biggest discovery was the role CCL5 plays in cancer. The researchers produced mice that lacked the enhancer close to *Ccl5* and observed how they fared when injected with melanoma cells. They found that the mice lacking *Ccl5* enhancer had fewer and smaller tumorous flecks in their lungs than normal

mice. This shows that CCL5 produced by the first enhancer helps cancer cells to multiply. “This indicates that high levels of CCL5 are not good for the tumor immunity,” says Taniuchi.

The reason for this effect is because CCL5 suppresses the function of immune cells, which is why tumor cells produce the chemokine.

This finding could help realize new immunotherapies for cancer. “Our discovery suggests that if we can somehow remove CCL5 from our system, we may actually strengthen our immune system, which could help it better fight cancer,” adds Seo. ●

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CHROMOSOME
STRUCTUREFinding
more by
assuming
less

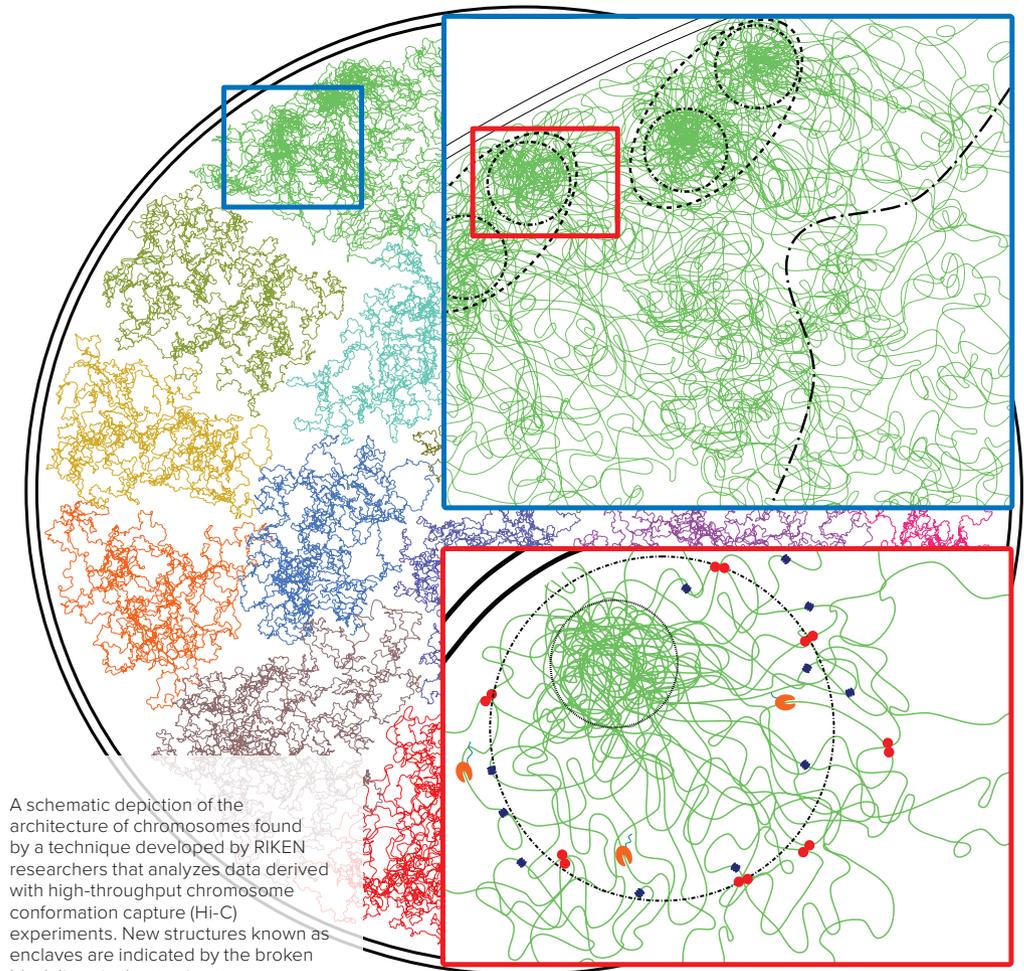
A more general analytic technique for looking for structures in chromosomes uncovers new interactions

A technique developed by three RIKEN researchers can identify interaction patterns within human chromosomes that conventional methods miss¹. It will help produce new maps of our chromosomes and uncover the complex interactions in them.

The cells in our bodies vary greatly in terms of shape and functions despite containing the same genetic information. One cause of this variety is the different ways genetic material is packaged in the nuclei of cells, which gives rise to the expression of different genes.

A powerful technique for analyzing the interactions between different regions of a chromosome is high-throughput chromosome conformation capture (Hi-C). The application of different clustering methods to Hi-C data has led to the identification of two levels of chromosomal structure: compartments on a large scale and topologically associating domains (TADs) on a much smaller scale.

“These two types of structures exist within the same chromosome and yet are detected using very different clustering techniques,” says Vipin Kumar, who was at the RIKEN Center for



A schematic depiction of the architecture of chromosomes found by a technique developed by RIKEN researchers that analyzes data derived with high-throughput chromosome conformation capture (Hi-C) experiments. New structures known as enclaves are indicated by the broken black lines in the two insets.

Biosystems Dynamics Research at the time of the study. “That was the motivation behind our study—to detect these different scales of organization with the same technique.”

Now, Kumar, Simon Leclerc and Yuichi Taniguchi have developed a more general version of the Hi-C data clustering technique, which they call BHi-Cect. It employs an iterative top-down approach. “Starting with the whole chromosome, BHi-Cect progressively separates it into its most likely clusters, beginning with the biggest ones and then looking for smaller ones,” explains Kumar.

“Unlike previous methods, BHi-Cect does not assume

specific criteria to identify different structural features,” says Taniguchi. “BHi-Cect allows us to identify many global and local structural features, including compartments, TADs and looping structures, and to associate them with a hierarchical tree—it’s a completely different approach.”

Kumar, who is now at the University of Oslo, agrees: “We don’t need to choose between looking for local or global structures; this technique gives you everything at once—that’s the big difference.”

Using BHi-Cect, the trio identified structures that they termed enclaves (see image). These include both compartments and TADs, but also other interactions that don’t fall into either category.

“We applied a very general definition: there is more interaction within an enclave than with the rest of the chromosome,” explains Kumar. “Consequently, our technique was able to detect much more-subtle interaction patterns in Hi-C data. I think this reflects the fact that chromosome structures are much more complex than previously thought.” ●

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SOIL SOLARIZATION

Why plants grow more under wraps

Organic nitrogen is largely responsible for the higher plant growth rates observed under plastic sheeting

A more sustainable approach to agriculture has been supported by research from RIKEN that shows natural sources of nitrogen are more important determinants of plant growth than synthetic sources¹.

Agriculture underwent a revolution in the early 20th century when it became possible to manufacture large amounts of nitrogen-based fertilizers. However, such fertilizers typically use inorganic nitrogen, which leaches through the soil into water, leading to contamination.

A method called soil solarization, which involves placing plastic sheets over a field to trap the heat of the sun, can promote plant growth without using environmentally damaging fertilizers. This raises the soil temperature, which is thought to inhibit weeds and parasites that hamper plant growth, but the mechanism has never been determined.

To explore how solarization works, Yasunori Ichihashi of the RIKEN BioResource Research Center and co-workers used a multiomics approach to examine a field containing Japanese mustard spinach. They assessed metabolites, the distribution of elements, the microbial profile and plant phenotypes. The field was split into sections where solarization was and was not used, and these sections were further split into areas given compost or chemical fertilizer.

In agreement with previous studies, the solarized area had fewer weeds and a greater mass of plant shoots. The plants had similar characteristics such as sugar content and leaf shape



Using a multiomics approach, RIKEN researchers have found that organic sources of nitrogen contribute greatly to the higher growth of plants grown using soil solarization.

regardless of whether they were grown in the solarized area or not. This suggested that the difference was related to soil nutrients.

Surprisingly, the researchers found no difference in the inorganic nitrogen concentrations between the solarized and non-solarized areas. The network analysis using digitalized information of the agricultural field by multiomics led them to suspect that organic nitrogen sources such as amino acids were fueling the growth in the solarized area. The researchers also found differences in the bacteria that grew on the roots of plants, which are important in making nitrogen available to plants.

This growth was still observed when the team planted seeds in a germ-free environment. This implied that the plants were directly taking up organic nitrogen. Certain forms of organic nitrogen, namely choline and alanine, encouraged growth even at very low concentrations, suggesting that they also act as biologically active compounds that promote growth.

“Digitalizing agroecosystems using multiomics is a very powerful tool for extracting key information in order to enhance crop production,” says Ichihashi. “Our findings imply that, contrary to the long-held belief that mineral nutrition was most important for plant growth,

organic nitrogen can also contribute to plant nutrition. This could pave the way to decreased use of chemical fertilizers in future crop production, helping to attain one of the important Sustainable Development Goals.” ●

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TERAHERTZ RADIATION

Radiation hinders protein filaments from forming

Terahertz radiation turns out to be more disruptive to living cells than previously thought

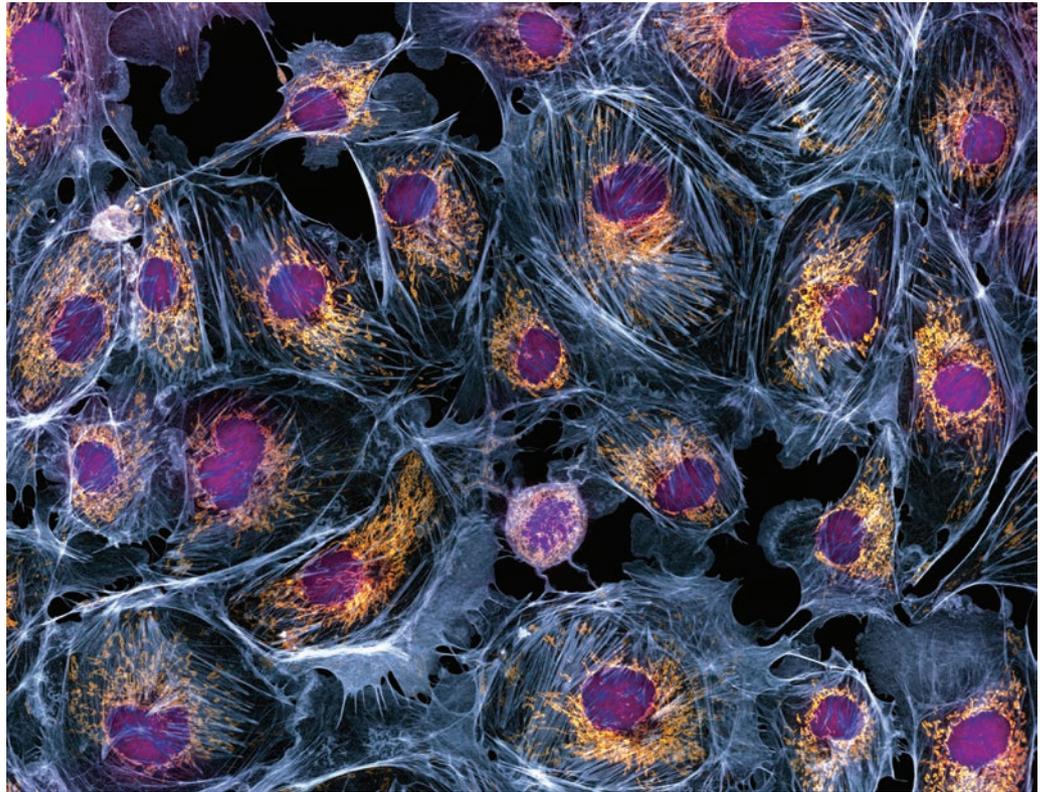
Contrary to conventional belief, terahertz radiation can disrupt proteins in living cells, physicists at RIKEN have discovered¹. This finding raises both the possibility of using terahertz radiation to treat cancer and safety concerns regarding its use in other applications.

Terahertz electromagnetic radiation is more energetic than microwaves but less energetic than infrared light. Because it does not damage DNA in the same way that x-rays do, it is being explored for use in various applications including baggage inspection at airports.

While terahertz radiation has generally been considered safe for tissue, recent studies have found that it may directly affect DNA. But because it does not penetrate tissue much, this would only affect cells on the surface skin. However, it is not known whether terahertz radiation affects biological tissues even after it has been stopped, through the propagation of energy waves into the tissue.

Shota Yamazaki of the RIKEN Center for Advanced Photonics and co-workers recently discovered that the energy from visible light can enter water as a shockwave. The team decided to investigate whether terahertz light has a similar effect on tissue.

They investigated the effect of terahertz radiation on a protein called actin—a key element that provides structure to living cells. It can exist in two forms, globular and filamentous actin, which have different structures and functions. As their names



Immunofluorescence light micrograph of pulmonary endothelial cells in the lungs. Actin filaments, which are major components of the cytoskeleton, are gray. RIKEN researchers have shown that terahertz radiation can prevent globular actin from forming chains and becoming filamentous actin in living cells.

suggest, globular actin is compact, whereas filamentous actin is made up of long protein chains.

Using fluorescence microscopy, the team found that terahertz radiation reduced the lengths of actin filaments growing in an aqueous solution of actin. This indicated that terahertz radiation was somehow preventing the globular actin from forming chains and becoming filamentous actin.

Since the temperature rise caused by the terahertz radiation was too small to induce this kind of change, the team concluded

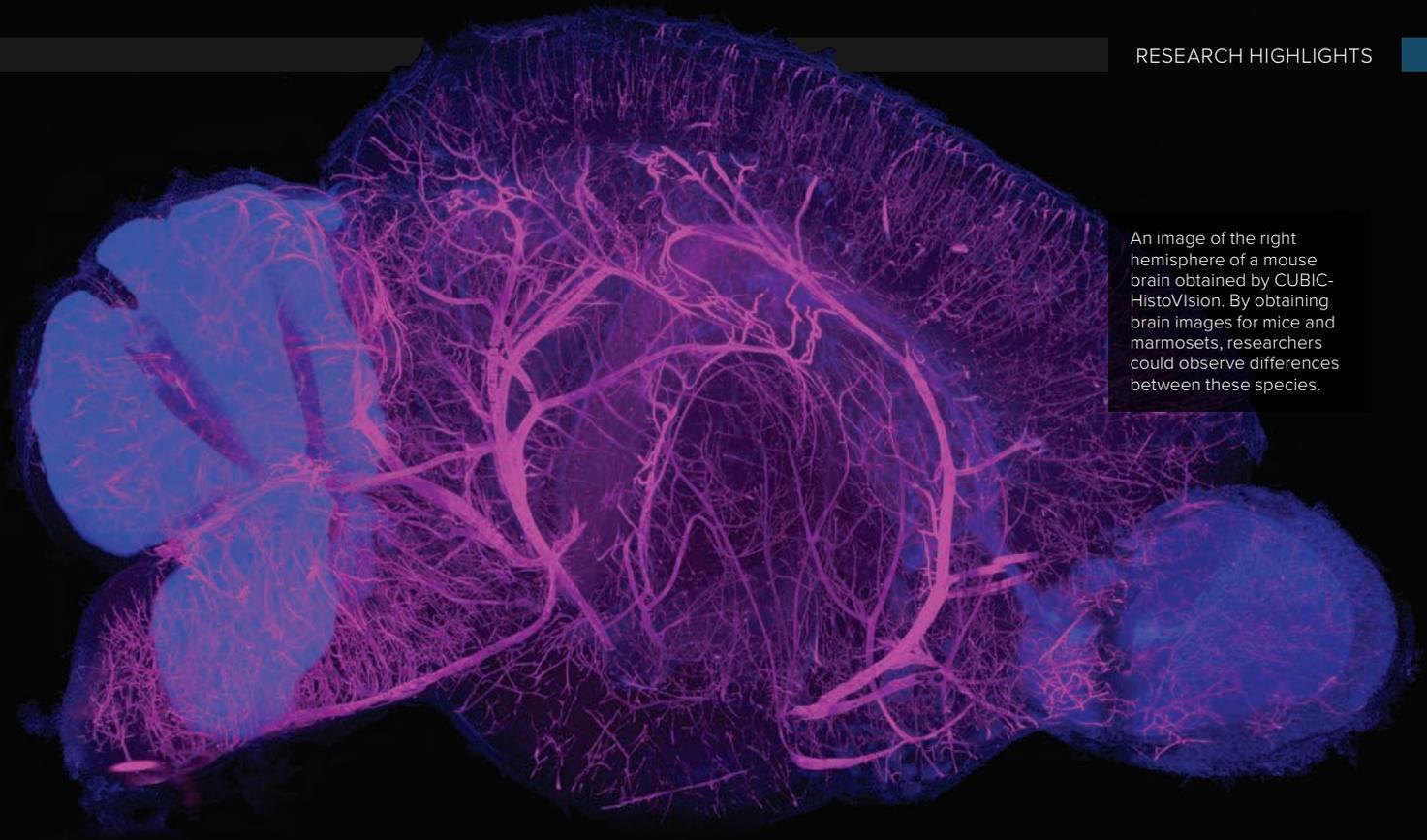
it was most likely caused by a shockwave. To test this, they performed experiments in living cells and found that the formation of actin filaments was also disrupted in the cells. However, there was no sign that the radiation caused cells to die.

“It was quite interesting for us to see that terahertz radiation can have an effect on proteins inside cells without killing the cells themselves,” says Shota Yamazaki. “We will be interested in looking for potential applications in cancer and other diseases. Terahertz radiation is coming into a

variety of applications today, and it is important to come to a full understanding of its effect on biological tissues, both to gauge any risks and to look for potential applications.” ●

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An image of the right hemisphere of a mouse brain obtained by CUBIC-HistoVIsion. By obtaining brain images for mice and marmosets, researchers could observe differences between these species.

BIOLOGICAL IMAGING

Imaging organs as never before

A new staining method allows whole organs and bodies to be compared between species

A versatile 3D tissue staining and imaging technique that can stain tissue and label cells in mouse and human brains and whole infant marmosets has been realized by RIKEN researchers¹. It allows detailed anatomical analysis and comparison of whole organs between species at the cellular level.

Tissue clearing renders tissues transparent and thus allows organs to be imaged in 3D by optical microscopy. In 2014, a team led by Etsuo Susaki and Hiroki Ueda at the RIKEN Center for Biosystems Dynamics Research developed CUBIC—a 3D tissue-clearing technology that can image the whole body at the single-cell level.

Tissue clearing can give fantastical images, but alone it does not provide much scientific insight. Scientists need to be able to stain and label specific tissues and cell types, which requires a system that works with a wide range of staining agents and antibodies. So far, no 3D staining and labeling method has been versatile enough.

Susaki's and Ueda's team performed detailed physical and chemical analyses of biological tissues and found that they can be defined as a type of electrolyte gel. They then constructed a screening system to examine a series of conditions using artificial gels that mimic biological tissues. By analyzing the

staining and antibody labeling of artificial gels with CUBIC, the researchers developed an optimized, versatile 3D-staining and imaging method, which they called CUBIC-HistoVIsion.

Combining this optimized system with high-speed 3D microscopy imaging, the team stained and imaged the whole brain of a mouse (see image), half a marmoset brain, and a square centimeter of human brain tissue. They also imaged the whole body of an infant marmoset in 3D. The system worked well with about 30 antibodies and nuclear staining agents, making it useful for different fields, from neuroscience to immunology.

“The 3D staining method developed in our study surpasses the performance of the typical staining methods published so far and is the best method in the world at present,” says Susaki.

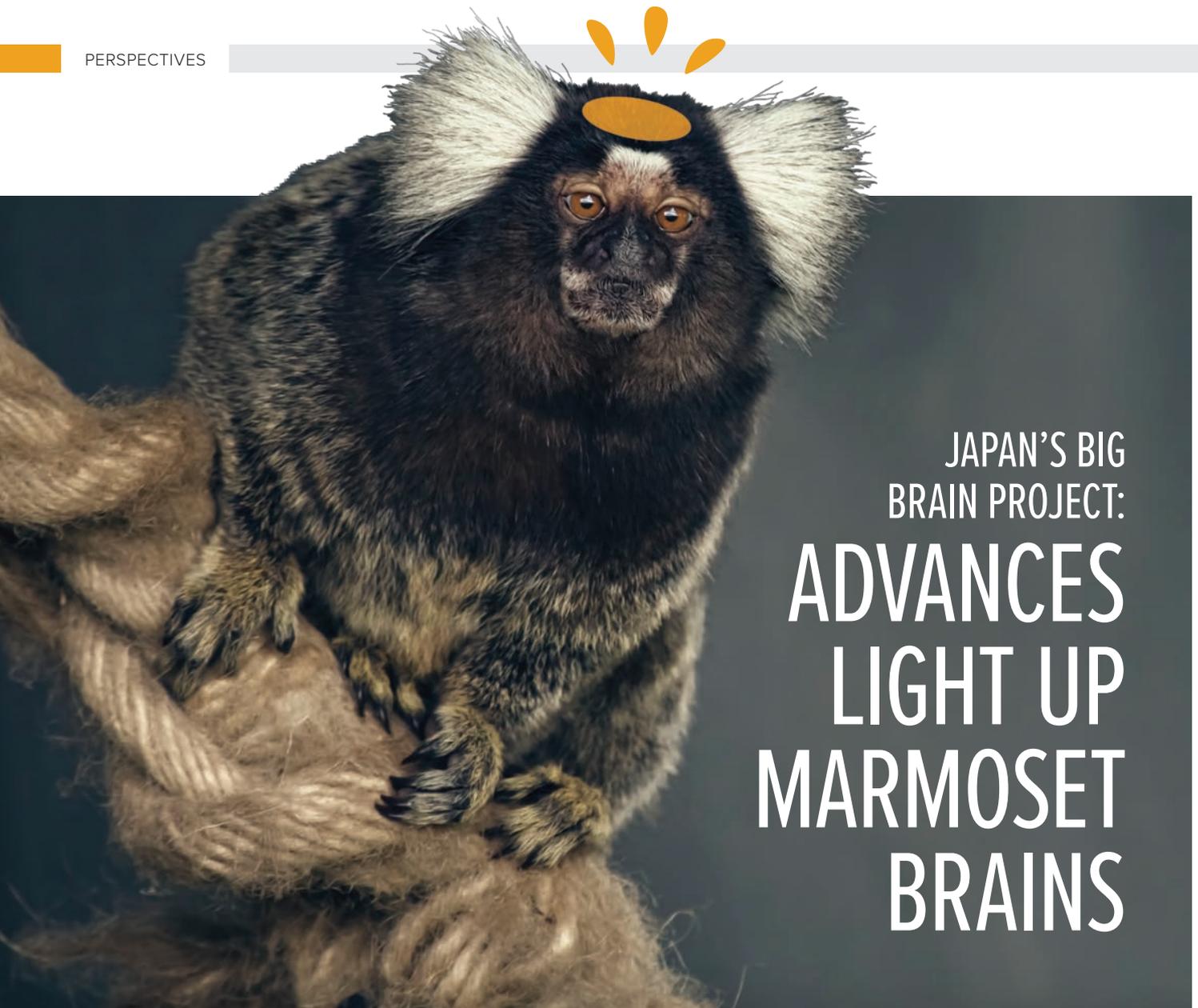
CUBIC-HistoVIsion can be used to compare whole-organ anatomical features between species. The method revealed that the overall distribution patterns of blood vessels in the

brains of mice and marmosets are very similar and thus likely evolutionarily preserved. CUBIC-HistoVIsion also showed that humans, mice and marmosets have different glia-cell distributions in the brain's cerebellum, which could lead to the well-known structural differences in the cerebellum among species.

“These results are expected to contribute to the understanding of biological systems at organ and organism scales, and to the improvement of the diagnostic accuracy and objectivity of 3D clinical pathology examination,” says Susaki. ●

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JAPAN'S BIG BRAIN PROJECT: ADVANCES LIGHT UP MARMOSET BRAINS

RIKEN researchers are coordinating Japan's **Brain/MINDS project** and illuminating marmoset neural networks—adding key primate brain data to other large-scale brain-mapping efforts.

Our knowledge of brain neural connections remains remarkably incomplete. To date, the nematode worm *Caenorhabditis elegans* is the only species that boasts a complete wiring diagram of its neurons.

While the last decade of studies have revealed insights into neurological and psychiatric diseases (such as Alzheimer's and Parkinson's diseases and schizophrenia), existing data is often scattered and incomplete. As a result, many neuroscience groups are now creating three-dimensional digital brain atlases that collate knowledge on mechanisms of brain activity to inform future experimental research.

In Japan, one of the largest projects of this kind is the Brain Mapping by Integrated Neurotechnologies for Disease Studies (Brain/MINDS) project, coordinated by the RIKEN Center for Brain Science (CBS). Launched in 2014, the 10 year, 40 billion yen (US\$350 million), multi-institutional project is developing mapping technologies and digitizing brain data, with a focus on primates.

Japan's effort is a parallel to the large-scale brain mapping efforts launched in 2013 through the European Union's €1-billion (US\$1.3-billion) Human Brain Project (HPB) and the United States' US\$1-billion Brain Research through Advancing Innovative Neurotechnologies Initiative (BRAIN). Each of these efforts has

taken a slightly different approach: the HBP started as centralized enterprise with a computational focus, aimed at building detailed models of neural circuitry, whereas the BRAIN Initiative initially had more of an emphasis on the development of technologies to facilitate neuroscience research. An equivalent China Brain Project was launched in 2019.

While Japan's effort draws on a smaller funding pool than some of these huge initiative, Brain/MINDs has access to an in-demand and globally scarce resource—a population of teacup-sized, genetically modified marmosets (*Callithrix jacchus*, left) that have been developed over more than ten years by Erika Sasaki and her colleagues at the Central Institute for Experimental Animals in Kawasaki in collaboration with Hideyuki Okano at the Keio University School of Medicine.

The USA's research populations of these primates has tripled over the last ten years due to the fact that marmosets give birth more often and age faster than other common primate research models. This speeds up studies, particularly those on aging brains. In addition, the marmoset cortex structure is less folded than many other primate models, making it easier to image neuronal networks.

Marmosets also share many human developmental processes and anatomical structures. They boast similar social behaviors, including strong relationships between parents and offspring, a social vocal communication method, as well as parallel neurological diseases. As a result, data from marmosets fill a crucial research gap between disease models in common smaller experimental animals, such as mice, which often fail to mimic human brain disorders, and models of the human brain that need extensive and expensive data validation.

LIGHTING UP THE MARMOSET CONNECTOME

Currently, the Brain/MINDS project (which is co-led by RIKEN's Hideyuki Okano and Atsushi Miyawaki) is linking detailed data on brain physiology with macro-scale functional analysis. The hope is to improve the diagnosis and treatment of psychiatric and neurological disorders by drawing links between chemical and neural network activation and function. The project is also continuing to map brains, establish new mapping technologies and conduct clinical research.

At CBS, the Molecular Analysis of Higher Brain Function team is performing intermediate-scale mapping of the marmoset prefrontal cortex, a part of the neocortex, the outer layer of the brain unique to mammals (see page 30 for another RIKEN breakthrough on the neocortex). The neocortex is linked to high-level cognition, personality expression, decision making and the moderation of social behaviour.

Intermediate-scale brain mapping employs chemical tracers and light microscopy to show the structure of neurons and neural networks, revealing brain-wide connectivity and inter-area neuron activity.



TETSUO YAMAMORI | Team Leader, Molecular Analysis of Higher Brain Function, RIKEN Center for Brain Science

Tetsuo Yamamori joined RIKEN in 2014 as a team leader for the RIKEN Brain Science Institute. Prior to this he was Deputy Director-General of National Institute for Basic

Biology in Japan. He had previously worked as a research fellow in the RIKEN Frontier Research Program (1991 to 1994). He is an associate editor for *Frontiers in Neuroanatomy*.



HENRIK SKIBBE | Unit Leader, Brain Image Analysis Unit, RIKEN Center for Brain Science

Henrik Skibbe joined RIKEN in 2019. Previously he had been a Specially Appointed Assistant Professor at Kyoto University. Skibbe moved to Japan from Germany in 2013 to work as a

postdoctoral researcher at Kyoto University. In Germany, he worked in medical physics at the University Hospital Freiburg and in advanced computing at the University of Freiburg.



ALEXANDER WOODWARD | Unit Leader, Connectome Analysis Unit, RIKEN Center for Brain Science

Alexander Woodward joined RIKEN in 2015. Between 2010 and 2015 he was a Japan Society for the Promotion of Science (JSPS) Post Doctoral Fellow at the University of Tokyo.

He gained a PhD in computer vision, a field of AI that trains computers to interpret and understand the visual world, at the University of Auckland in New Zealand.

This type of mapping falls between macroscale mapping of brain region activation performed largely by MRIs and microscale mapping of tissue changes using electron-microscopic analysis.

The technique used by the team mirrors the tracer technology employed by the Allen Mouse Brain Connectivity Atlas, launched in 2014. However, the Molecular Analysis of Higher Brain Function team has developed a way to enhance tracer signals that is better able to map marmoset brains in live animals over the long-term compared to tracers developed for smaller model animals, such as mice, fish and flies.

A fluorescence protein gene is carried by an adeno-associated virus vector that is injected into brain tissue. These viruses also carry genes that enhance the detection of calcium in neurons by increasing a protein called "GCaMP", which activates the fluorescent proteins, lighting up neurons to their axial ends and across synapses. A TissueCyte machine can then perform a layered imaging technique known as serial

two-photon (STP) tomography to help build a 3D image of axonal spread from the injection site.

In 2015, the group published on the successful use of this tet-tre GCaMP fluorescence tracer system in the primate cortex for the first time. GCaMP highlights the calcium, a charge carrier and an intracellular messenger in neurons that's important for neuron growth, and synaptic and cognitive function. In the paper, the group detailed the use of the tet-tre GCaMP system to help achieve long-term two-photon neuronal imaging of marmoset brains, which was able to be detected for more than 100 days after injection, and showed responses to tactile stimulation imaged at subcellular resolution.

This method has since been widely used by other Brain/MINDS teams, including the Matsuzaki Lab, Ohki Lab and Okano Lab. In 2017, Keio University and CBS's Laboratory for Marmoset Neural Architecture (Okano Lab) used it to image neurons linked to marmosets moving levers with their arms and ladder climbing. In 2018, CBS's Brain Functional Dynamics Collaboration Laboratory (Matsuzaki Lab) used the technology to show the neurons activated by marmosets moving cursors on screens. It has also been used in a number of key experiments in laboratories beyond Brain/MINDS.

A separate imaging system has been developed by Brain/MINDS in CBS's Atsushi Miyawaki Lab. In 2018, the group reported a bioluminescent protein that strongly responds to long (red) wavelengths of light, genetically engineered from firefly luciferase (the light-emitting enzyme responsible for bioluminescence in

fireflies and click beetles). This protein is able to detect deep-tissue signals at a single-cell level in freely moving animals and create a brighter emission by up to a factor of 1,000 compared to conventional technology.

Using this technique, the Molecular Analysis of Higher Brain Function team and the Miyawaki Lab were able to detect and image small numbers of striatal neurons in the brains of naturally behaving marmosets.

DIGITAL BRAIN SIMULATIONS

A parallel challenge for Brain/MINDS is dealing with detailed 3D images of brain connections that can be hundreds of gigabytes in size. To tackle this, the Brain Image Analysis Unit is developing algorithms that process and automatically annotate marmoset brain images, which will allow efficient integration of a huge amount of imaging data from different Brain/MINDS research groups.

In addition, the Connectome Analysis Unit is making this data accessible through the Brain/MINDS online dataportal (www.brainminds.riken.jp/), and it is hoped that interactive web pages for the prefrontal cortex tracer studies mentioned previously will be made public within the coming year. These pages will allow the exploration of very high-resolution image data to easily see real connectivity patterns between brain regions. For example, researchers can map an atlas to new experimental data and carry out brain region to brain region analysis.

This will complement previous atlases developed by Brain/MINDS, including a 3D digital atlas of the marmoset brain based on macro-scale MRI data and micro-scale histology imaging (using staining of Nissl bodies, small granular bodies in neurons). Created in 2018, in collaboration with neuroanatomist Tsutomu Hashikawa, this atlas can be integrated with popular neuroscience tools. The new tracer map will help connect macro-scale functional insights and micro-scale tissue changes to neural networks.

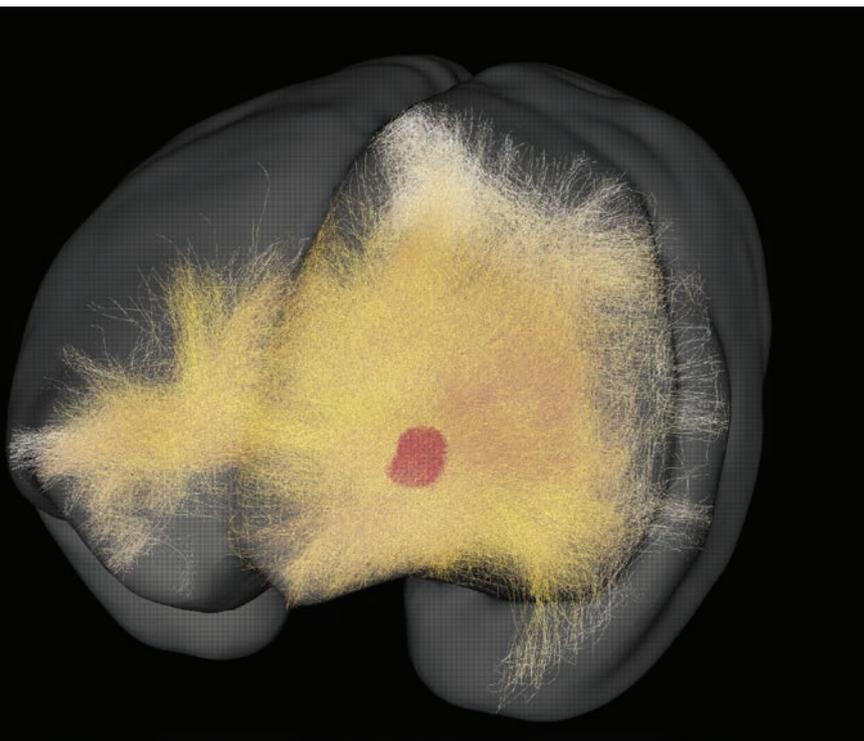
Digital advances will be key to addressing criticisms of existing brain mapping projects that note that brain simulations aren't being finalized as fast as predicted. Nonetheless, some projects are reporting important real-world results. For example, in 2019 the UK's HBP announced clinical trials for a brain simulator that can individualize therapeutic surgery for epilepsy patients.

The human brain has more than 15 billion neurons, so creating insights that have clinical applications is a mammoth task. However, this only underlines the case for marmoset brain maps, which should help narrow the search for relevant neural networks in humans. We anticipate that our digitized brain atlases will be important resources to the neuroscience community. ●

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For a full list of references, please visit the online version of this article: www.riken.jp/en/news_pubs/research_news/index.html

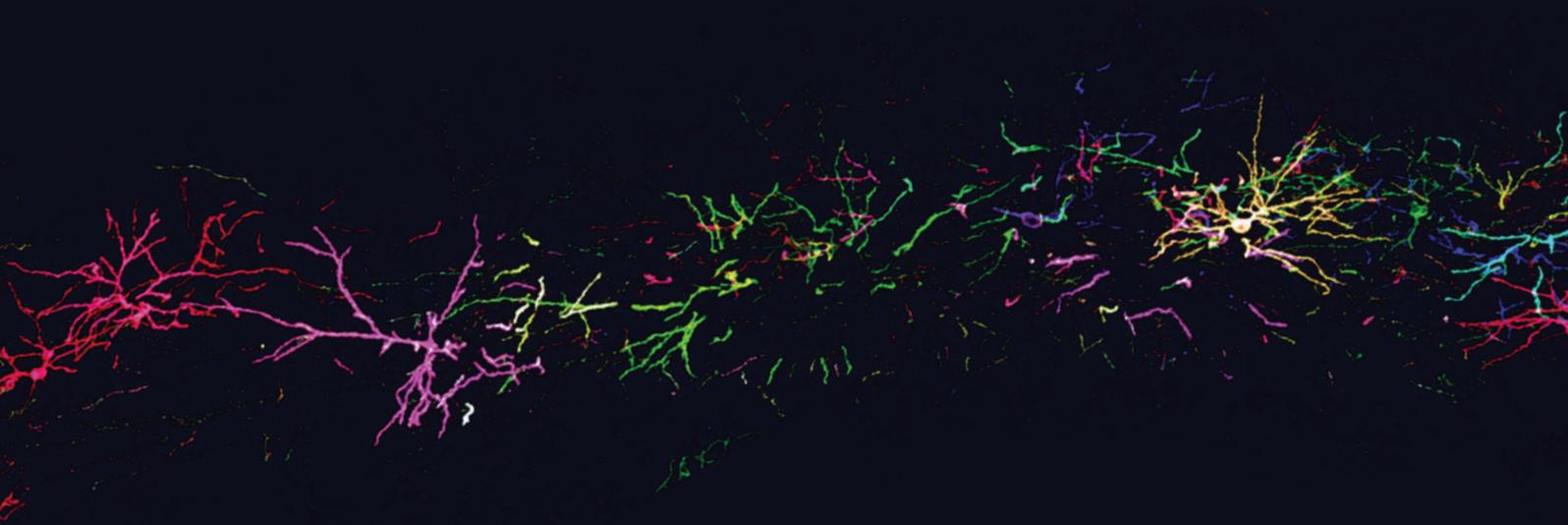
A 3D map of neural networks created by Tetsuo Yamamori's team can be explored on the Brain/MINDS website: www.brainminds.riken.jp/



MEET THE BRAIN REGION THAT MAY CONTROL YOUR CONSCIOUSNESS

The revelation that a small part of the brain, known as the **claustrum**, can silence cortical neurons and induce the slow-wave activity in mice could unlock new understandings of the brain's higher functions. →

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SLEEPING BEAUTY

Activation of neurons in a small region buried deep within the brain called the claustrum (pictured) induces a silence in cortical neurons characteristic of the slow waves of deep sleep. Claustrum neurons make connections with almost all areas of the neocortex. But rather than activating neurons, as some researchers theorized, the claustrum appears to deactivate neurons. The neurons pictured are expressing Cre recombinase and were genetically labeled with fluorescent proteins using a Brainbow technique.

For such a wispy, diminutive region of the brain, the claustrum has been the subject of some audacious speculation. The most remarkable came from Francis Crick, of DNA double-helix fame, and renowned neuroscientist Christof Koch: they speculated that the claustrum, which is located deep within the brain structure, might be the seat of consciousness, likening it to a conductor of an orchestra. This theory had never been proven. But now, a mouse study by an all-RIKEN team of neuroscientists has shown that the pair was partly right.

The study observed that optogenetic (light) activation of the claustrum silenced neurons in the brain's cortex, the outer 'grey matter' part of the brain linked to many higher functions. Moreover, this silencing is characteristic of the brain's slow waves that occur in deep sleep just before rapid-eye-movement (REM) sleep. These waves have been linked to brain-wide synaptic homeostasis and memory consolidation.

AN ENIGMATIC BRAIN REGION

The name claustrum derives from the Latin word for a locked or enclosed place. It's an appropriate name, because while neuroscientists have known about the claustrum for a long time (as a brain region hidden beneath the cerebral cortex) they have been unable to pin down its role. Its wispy, nebulous structure makes it difficult to access and manipulate.

Although the claustrum's function remained elusive, researchers had been able to determine its structure. They found that it has a characteristic 'crown of thorns' structure that makes connections with almost all areas in the neocortex, the area of the brain responsible for a diverse range of functions, including sensory perception and cognition.

"WAIT, DON'T DISCARD THAT LINE!"

Yoshihiro Yoshihara of the RIKEN Center for Brain Science never set out to investigate the claustrum; rather he stumbled upon it while he and his team were studying the neuroscience of smell. This research involved genetically manipulating mice so that certain neurons along the olfactory circuit that initially processes smell signals from the nose can be visualized and activated by light.

But in one line of transgenic mice the manipulation was not expressed in the target neurons. "The technician who screened the transgenic mice came to my office and told me that the transgene, Cre recombinase, wasn't expressed in smell-related neurons in these mice, but in an unknown region," Yoshihara recalls. "And she asked if we should discard these mice."

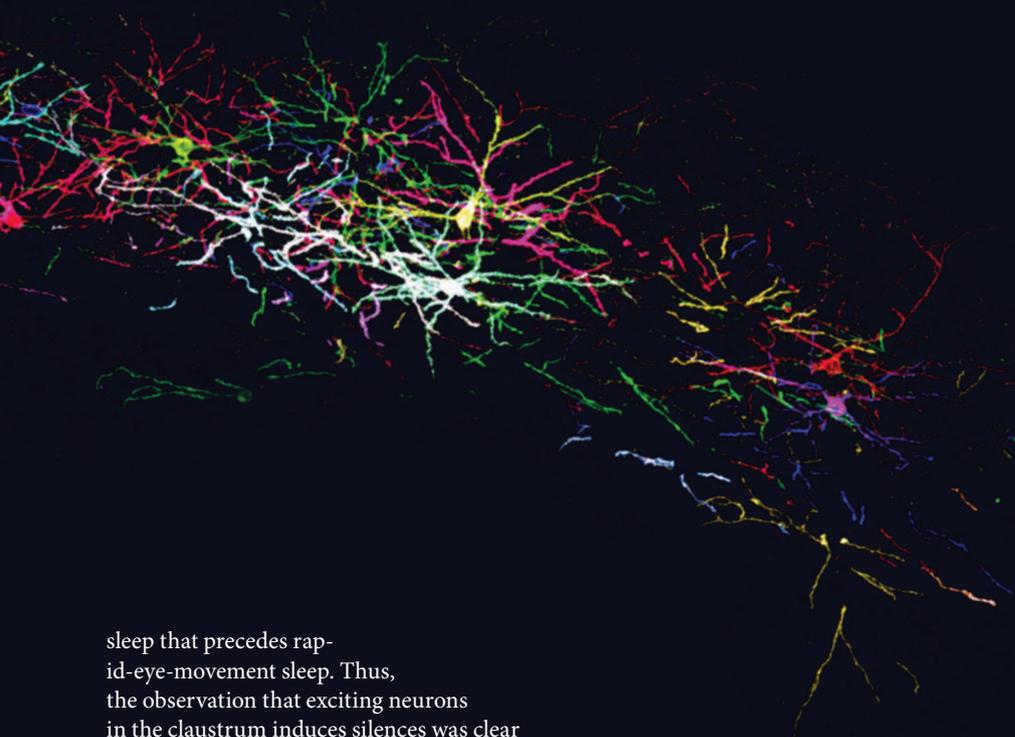
After poring over images of the mice's brains and consulting a brain atlas, Yoshihara came to a startling realization—the transgene was expressed only in the claustrum. "I told the technician, 'Whatever you do, don't discard that line! It could be a vitally important resource for neuroscience.'"

SILENCE IN THE CORTEX

This line of mice provided Yoshihara's team with the key for unlocking the claustrum, since for the first time they could genetically visualize, activate and ablate (remove) neurons in the claustrum alone.

They were surprised when they tried optogenetic activation. "When we activated claustrum neurons by light, we observed total silencing of cortical neurons for more than a tenth of a second—a very long period," says Yoshihara. "I was very excited when I saw the data and felt we had probably found a very important and interesting result for neuroscience."

The extended period of silence is a characteristic of slow waves in the brain, which occur during the deep



sleep that precedes rapid-eye-movement sleep. Thus, the observation that exciting neurons in the claustrum induces silences was clear evidence that the claustrum is responsible for coordinating slow-wave activity in the cortex.

“The critical finding is that the claustrum coordinates cortical activity very broadly in widespread areas—and that’s something that only claustrum neurons can do,” says Yoshihara. “This is highly significant not only for sleep research but also for research into higher brain functions.”

Yoshihara notes that the finding partially vindicates Crick and Koch, but that it also differs in at least one important respect. “They thought that the claustrum probably activates cortical neurons globally, but our result is the opposite—the claustrum inhibits or silences cortical neurons globally.”

FROM MICE TO HUMANS

While the finding was made in mice, there is at least some anecdotal evidence that the claustrum may play a similar role in humans. A doctor was treating an epilepsy patient by using an electrode between the left claustrum and the insular cortex to stimulate the claustrum. Prior to the stimulation, the patient was reading a book, but following it she stopped reading and did not respond to anything, only regaining consciousness when the stimulation stopped.

Yoshihara hopes that his team’s finding will stimulate fresh interest in the under-studied brain region. “I hope clinical researchers will pay attention to the claustrum,” he says. One reason for its neglect is

that until now functional magnetic resonance imaging (fMRI) systems have lacked the resolution to image it in much detail. But Yoshihara notes that this is changing and that RIKEN will be acquiring an fMRI system next year that will be able to image the claustrum in great detail.

Looking ahead, Yoshihara’s team intends to pursue two directions. One involves new mouse lines. In the first mouse line produced, only about one third of the neurons in the claustrum were made able to be genetically manipulated, but the team has since produced two more mouse lines that together cover most of the remaining populations of the claustrum. This will allow them to investigate both the role of the claustrum as a whole and the functions that the three different neuron populations perform. The team also plans to see what role the claustrum plays in memory acquisition and consolidation. ●

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This feature looks at the work of **YOSHIHIRO YOSHIHARA**

Yoshihiro Yoshihara is the Team Leader of the Laboratory for Systems Molecular Ethology at the RIKEN Center for Brain Science (CBS). He received his Ph.D. from the Faculty of Pharmaceutical Sciences at Kyoto University in 1989. He then moved to the Osaka Bioscience Institute and Osaka Medical College where he started looking at the olfactory system with Kensaku Mori. He launched his own laboratory at the RIKEN Brain Science Institute in 1998. His lab at RIKEN CBS now focuses on two main research topics: olfaction and consciousness. He has received a Young Investigator Award (2006) and Grand Prize (2019) from The Japanese Association for the Study of Taste and Smell, as well as an Ando Momofuku Award (2018).

THE TEST OF TIME

RIKEN researchers and their collaborators have developed two transportable hyper-accurate clocks. By placing one in the Tokyo Skytree tower roughly 450m above ground and the other at ground level, the researchers were able to demonstrate Einstein's theory of general relativity. This theory suggests that a warping of time-space caused by the gravity of a massive object, in this case Earth, causes time to run slightly more slowly close to the ground than high above it. While satellites have demonstrated this effect before, the new portable clocks may have other very practical uses (see *A stitch in time*).



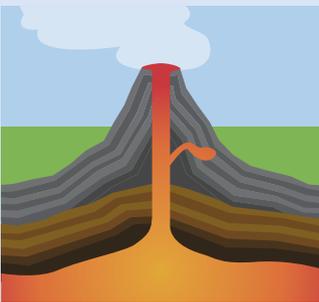
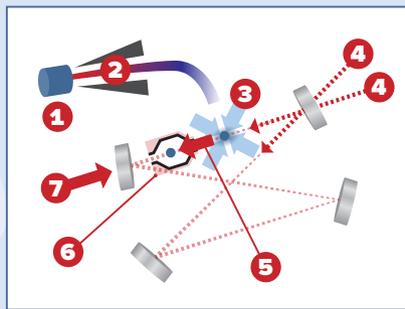
Atomic clock 1
Ground floor,
roughly 0m

Atomic clock 2
Tokyo Skytree
upper deck,
450m

Tokyo Skytree
lower deck,
350m

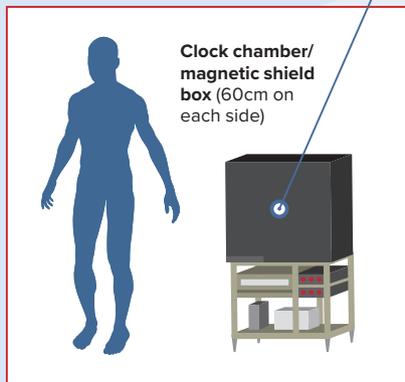
LASER PRECISION

These hyper-accurate clocks are called optical lattice clocks. It would take more than the age of the Universe for one to become out by half a second. To measure time, strontium atoms released by a beam oven (1) are decelerated by a laser (2). The atoms are then cooled by different lasers (blue arrows, 3) and trapped in an optical lattice formed by two further lasers (red arrows, 4). The atoms (blue dot) are transported (5) to a radiation shield (6), which protects the atoms from thermal radiation. Yet another laser excites transitions in the atoms (7). The frequency of these transitions is the 'tick' of the clock.



A STITCH IN TIME

The slope of a volcanic mountain is often slightly lifted when magma fills the chamber beneath it. This makes an optical lattice clock placed on the outside of a volcano tick measurably faster. Currently, volcanic activity is monitored using satellite systems and instruments that respond to ground motion, called seismometers. A network of local optical lattice clocks could provide additional information on the rate and level of volcanic activity.



IT TAKES TWO

The two miniaturized versions of laboratory-sized clocks (see above) were enclosed in a magnetic-shield box to protect lattice-trapped atoms from environmental magnetic fields. They were connected by an optical fiber to measure the difference in tick rate between them. Scientists also independently evaluated the height difference between the clocks.

THE FINER DETAILS OF FUNDAMENTAL PHYSICS

This work is part of a new collaboration, the Max Planck-RIKEN-Physikalisch-Technische Bundesanstalt Center for Time, Constants and Fundamental Symmetries. Launched in 2019, the center supports scientists working on leading questions in fundamental physics that require high-level precision, including work on the constancy over time of natural constants and subtle differences between matter and antimatter.

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across Japan and around the world



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

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

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