RIKEN RESEARCH

SPRING 2023

SHOWCASING THE BEST OF JAPAN'S PREMIER RESEARCH ORGANIZATION • www.riken.jp/en/

PHOTO ESSAY

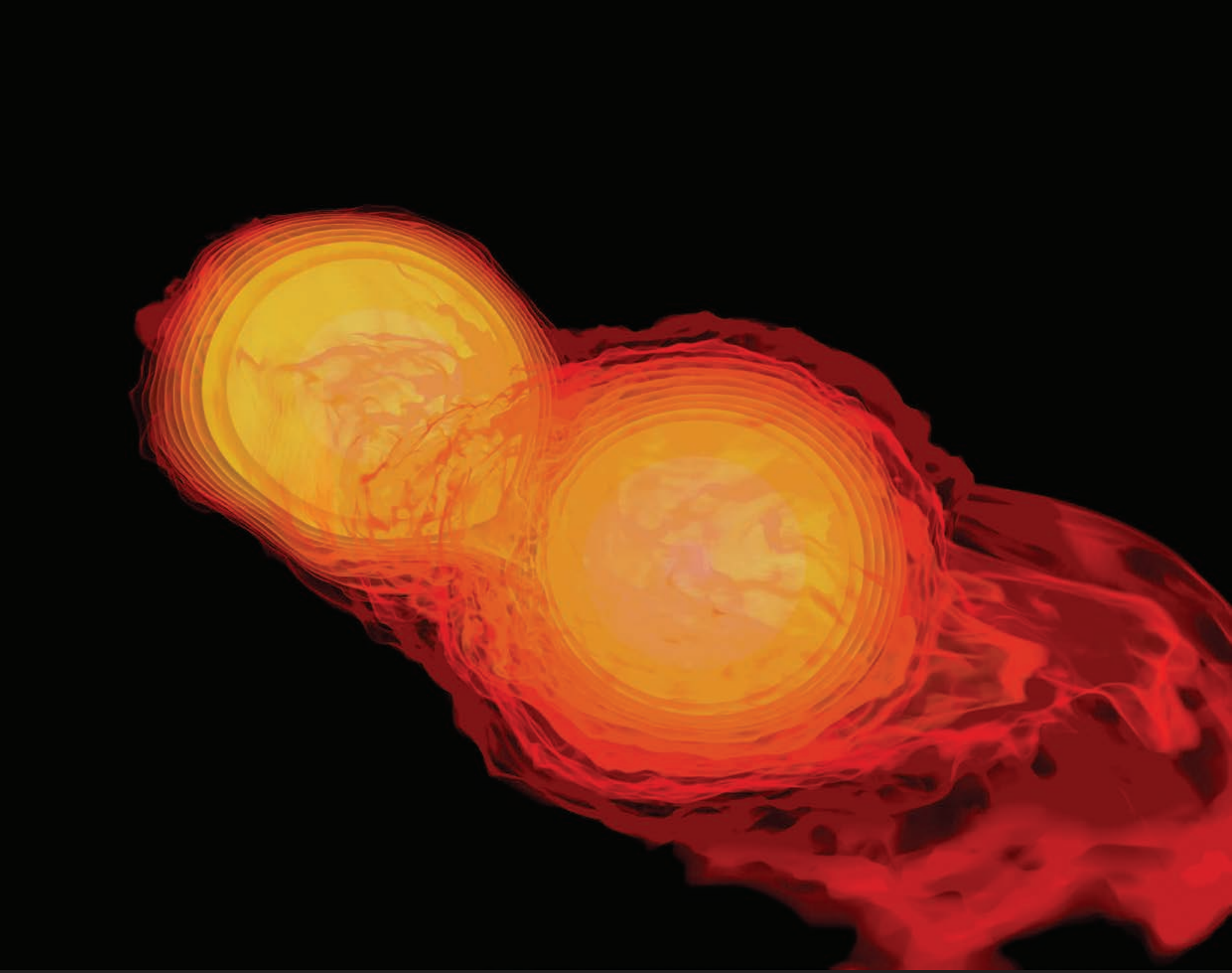
THE FACE OF THE FUTURE

Japan's next generation of robots

IMPROBABLE PHYSICS
The heavy form of sodium that shouldn't exist

AI TSUNAMI ALARM
Deep-learning model makes waves

SLOW AND STEADY
Hibernation for heart surgery



A PRODUCTIVE MERGER
The finding of an extremely neutron-rich form of the element sodium (see page 30) by a RIKEN team has implications for our understanding of the origins of Earth's heavier elements, some of which are thought to have been created during the merger of two neutron stars (pictured).

RIKEN RESEARCH

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

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

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

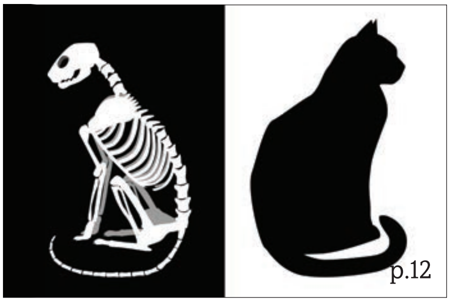
RIKEN Research is published by RIKEN in collaboration with Nature Research Custom Media, a part of Springer Nature.

For further information on the research in this publication or to arrange an interview with a researcher, please contact:
RIKEN International Affairs Division
2-1, Hirosawa, Wako, Saitama, 351-0198, Japan
Tel: +81 50 3500 5438
rikenresearch@riken.jp

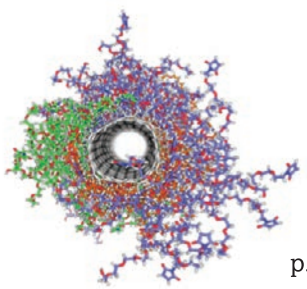
ISSN 1883-3519
www.riken.jp/en

RIKEN

p.9

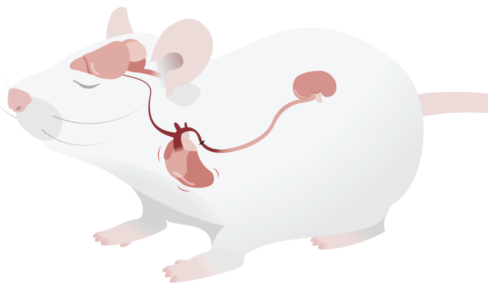


p.12



p.16

p.19



To our readers

Hiromichi Matsuo
Executive Director, RIKEN

I am delighted to be able to address our readers in this issue. I was appointed to serve as an Executive Director at RIKEN in April 2022. Previous to that, I was in charge of the project to develop the supercomputer Fugaku at the RIKEN Center for Computational Science, under the leadership of Center Director Satoshi Matsuoka.

I am very happy to report that we were able to develop Fugaku into a supercomputer that incorporated a number of innovations that put it ahead of its time and on a completely different level from its predecessor, the K computer. In addition, we were able to use it to launch an ambitious initiative to create solutions for the Japanese government's Society 5.0 vision by launching full-scale collaborations with different scientific areas and industry, taking advantage of the supercomputer's potential to create "digital twins"—an ability which was used for example to perform aerosol and droplet simulations as part of a special project to combat the COVID-19 pandemic.

We are currently pursuing a plan to establish a revolutionary digital transformation of research by leveraging our collective strengths to strategically link the cutting-edge platforms we have developed in various scientific fields. To do this, we will have to bring together the collective efforts of RIKEN researchers, drawing heavily on the various initiatives carried out with Fugaku as mentioned above. I believe that we will be able to provide future researchers at RIKEN with opportunities to conduct research in a way that is more interesting than ever before and that will naturally lead them to make contributions to solving the many problems facing humanity today.

I very much hope that RIKEN will attract the interest of researchers from all over the world.

COVER STORY: RIKEN's Guardian Robot Project has developed Nikola, a robot with a face that can express various emotions, including fear, happiness, surprise, disgust, anger and sadness. *Page 22*

Keep up to date

Online
www.riken.jp/en

Facebook
facebook.com/RIKENHQ

Twitter
twitter.com/RIKEN_en

LinkedIn
linkedin.com/company/riken

Modeling quantum environments

Neill Lambert
Senior Research Scientist, Theoretical Quantum Physics Laboratory, RIKEN Cluster for Pioneering Research

How and when did you join RIKEN?
I joined RIKEN in 2008 after spending several years at the University of Tokyo as a Japan Society for the Promotion of Science fellow. Initially, I came to give a seminar at RIKEN, and then applied for a postdoc position after enjoying the interactions I had with Dr. Franco Nori's group (the Theoretical Quantum Physics Laboratory within the RIKEN Cluster for Pioneering Research).

Please describe your role.
I study open quantum systems, or how a large environment affects the behavior of small quantum systems, particularly in situations where parts of the environment itself must be modeled quantum mechanically. This research could be important to understanding how to control noise within quantum computers, or how thermodynamics behaves in quantum regimes. Day to day, I mainly work on developing new methodologies and conduct numerical simulations. I also assist with developing and administering a popular open-source software package for simulating the dynamics of open quantum systems created by our group – QuTiP (the Quantum Toolbox in Python).

What tech do you use?
Recently, because of several demanding projects, I have been using the computing resources at RIKEN, in particular the Hokusai BigWaterFall supercomputer.

What excites you about your research?
The question of whether quantum effects can be observed with large objects is fascinating. Some of my recent work helps to unravel this issue, including research on how large collections of small quantum systems might start to appear to behave more like classical physical systems, which helps to make practical simulation methods and tools more efficient.

"It's exciting that I can access real [quantum] devices, through a cloud computing service, and conduct my own experiments.

What has been the most interesting recent discovery in your field?
The development of small-scale quantum computers by companies such as IBM and Google has truly changed the field I work in. As a theorist, it's exciting that I can access real devices, through a cloud computing service, and conduct my own experiments.

How did you become interested in your current research field?
As an undergraduate, I undertook an exciting quantum physics course taught by Professor Tobias Brandes at UMIST (now The University of Manchester) in the United Kingdom. He would eventually become my PhD supervisor.

What has been your most memorable experience at RIKEN?
I have very much enjoyed the opportunity to supervise and train international students. One student recently contacted me and told me he had found a tenured university position in his home country, which made me very happy. ■

A strong stomach for pathogens

Naoko Satoh-Takayama
Senior Research Scientist, Laboratory for Intestinal Ecosystem, RIKEN Center for Integrative Medical Sciences (IMS)

How did you join RIKEN?

My husband and I worked as researchers and lived in France with our baby until 2015. While there, I was on a team that discovered a new type of cell, the innate lymphoid cell, at the Pasteur Institute in Paris. Although I was an assistant professor at the time, my husband wanted to return to Japan. So I took a role as a permanent researcher at RIKEN.

The stomach is often thought of as just a storage organ, and therefore research on its immunological role has been lacking. ”

Please describe your current research.

I focus on interactions during infection between commensal microbiota—symbiotic bacteria mainly found in the digestive system—and innate lymphoid cells. The latter cells serve protective roles in innate immune responses to infectious microorganisms; in lymphoid tissue formation; in tissue remodeling after injury or infection damage; and, in the homeostasis of the supportive tissues around organs.

A plethora of evidence suggests that commensal microbiota regulate immune responses, and are involved in protection from pathogenic infections. So, clarifying the link between immune responses and bacterial interactions could lead to new methods to control diseases, and potentially even to non-chemical therapies.

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

Many researchers have become interested in mucosal immunology, which is regulated by mechanisms distinct to those of ‘basic’ immunology. The intestinal tract, one of the mucosal organs, is already being studied in relation to immune responses. But the stomach, which is also a mucosal organ, is often thought of as just a storage organ due to its strong, harsh acidity, and therefore research on its immunological role has been lacking. However, we have found that the stomach plays a critical role as an immune regulator controlled by both commensal and pathogenic bacteria.

How did you become interested in your current research?

I suffered from severe allergic dermatitis as a teenager. At that time, I thought a lot about why my skin was always itching and looked different from others, and I started to think about immunity. And then, later, when I was studying immunology at university, I came across a book with written by Dr. Hiroshi Kiyono, who is an eminent expert in mucosal immunology. That was the impetus for my current research.

How do you balance your family life with your work?

All RIKEN employees are protected by internal work–life balance regulations, such as those related to pregnancy, childbirth, childcare and long-term nursing care, and receive a week of general work–life balance holidays, as well as a certain amount of special paid leave for each specific situation. So I am usually able to take time off to spend holidays with family or friends, which is sometimes difficult to take at many universities. ■

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

Supercomputer Fugaku is at the top of two rankings, the HPCG, which measures efficiency at processing relevant to real-world applications, and the Graph 500, focused on the ability to deal with data-intensive loads.

Their Majesties the Emperor and Empress visit Fugaku

In November 2022, Their Majesties the Emperor and Empress of Japan visited the RIKEN Center for Computational Science (R-CCS) in Kobe. There, RIKEN President Mokoto Gonokami gave them an overview of RIKEN and the R-CCS, and R-CCS Director Satoshi Matsuoka talked about supercomputer Fugaku. As part of the visit, Their Majesties were given a laboratory tour by Makoto Tsubokura, team leader of the Complex Phenomena Unified Simulation Research Team, who explained how his group used Fugaku to simulate droplet dispersal of COVID-19, the results of which were incorporated into national guidelines for infectious disease control.

www.riken.jp/en/news_pubs/news/2022/20221128_2/

Fugaku maintains top rankings in 2022

In November 2022, Japan's supercomputer Fugaku took top place in the HPCG and Graph 500 rankings—as well as the second spot in the Top500 ranking and third place on the HPL-AI benchmark. Fugaku is being used in projects aimed at overcoming the COVID-19 pandemic, as well as at the development of innovative solutions to the world's challenges. In the near future, research aimed at the fusion of classical and quantum computing is expected.

www.riken.jp/en/news_pubs/2022/20221115_3

Fugaku research earns 2022 Gordon Bell Award

In November 2022, the prestigious Gordon Bell Award for outstanding achievement in high-performance computing was awarded for work on designing a new type of particle accelerator using plasma. It was carried out using four supercomputers around the world, including Fugaku in Japan, and Frontier, Summit, and Perlmutter, all in the United States. This research achievement, led by the French Alternative Energies and Atomic Energy Commission (CEA), could help the development of compact laser-based electron accelerators. These accelerators could be used for next-generation, high-energy physics experiments and ultrahigh-dose-rate FLASH radiotherapy, a promising new avenue for cancer therapy. Two of six finalists, one working on geostatistical modeling and prediction, and another on earthquake modeling, also used Fugaku. "We are very pleased that, for the second year in a row, the ACM Gordon Bell Prize, one of the most prestigious awards in supercomputing, has been awarded to a research achievement using Fugaku," commented RIKEN Center for Computational Science Director Satoshi Matsuoka. In particular it highlights "that Fugaku was designed with the spirit of being 'applications first' and is not merely excelling on synthetic benchmarks."

www.riken.jp/en/news_pubs/news/2022/20221118_3

The 26 Highly Cited Researchers at RIKEN in 2022

The following twenty-six RIKEN researchers, out of a total 90 representing Japanese universities or research institutes, have been listed as 2022 Clarivate Highly Cited Researchers, an annual list based on a researcher's citations from publications from the past decade or more.

CROSS-FIELD

- **Takao Someya,** RIKEN Cluster for Pioneering Research (Thin-Film Device Lab), Chief Scientist
- **Wataru Suda,** RIKEN Center for Integrative Medical Sciences (Laboratory for Microbiome Sciences), Deputy Team Leader
- **Masahira Hattori,** RIKEN Center for Integrative Medical Sciences (Laboratory for Microbiome Sciences), Senior Visiting Scientist
- **Osamu Nureki,** RIKEN Center for Biosystems Dynamics Research (Laboratory for Protein Functional and Structural Biology), Senior Visiting Scientist
- **Takaomi Saido,** RIKEN Center for Brain Science (Laboratory for Proteolytic Neuroscience), Team Leader
- **Takashi Saito,** RIKEN Center for Brain Science (Laboratory for Proteolytic Neuroscience), Visiting Scientist
- **Ken Shirasu,** RIKEN Center for Sustainable Resource Science, Deputy Director
- **Ryotaro Arita,** RIKEN Center for Emergent Matter Science (First-Principles Materials Science Research Team), Team Leader
- **Yoshihiro Iwasa,** RIKEN Center for Emergent Matter Science (Emergent Device Research Team), Team Leader

IMMUNOLOGY

- **Shizuo Akira,** RIKEN Center for Integrative Medical Sciences, Senior Advisor
- **Kenya Honda,** RIKEN Center for Integrative Medical Sciences (Laboratory for Gut Homeostasis), Team Leader
- **Koji Atarashi,** RIKEN Center for Integrative Medical Sciences (Laboratory for Gut Homeostasis), Senior Visiting Scientist

PHYSICS

- **Franco Nori,** RIKEN Cluster for Pioneering Research (Theoretical Quantum Physics Laboratory), Chief Scientist
- **Chihaya Adachi,** RIKEN Cluster for Pioneering Research (Surface and Interface Science Laboratory), Senior Visiting Scientist
- **Yoshinori Tokura,** RIKEN Center for Emergent Matter Science, Director
- **Naoto Nagaosa,** RIKEN Center for Emergent Matter Science, Deputy Director
- **Motohiko Ezawa,** RIKEN Center for Emergent Matter Science (Strong Correlation Theory Research Group), Visiting Scientist

PLANT AND ANIMAL SCIENCE

- **Kazuki Saito,** RIKEN Center for Sustainable Resource Science, Director
- **Kazuo Shinozaki,** RIKEN Center for Sustainable Resource Science, Senior Advisor
- **Mitsunori Seo,** RIKEN Center for Sustainable Resource Science (Dormancy and Adaptation Research Unit), Unit Leader
- **Hitoshi Sakakibara,** RIKEN Center for Sustainable Resource Science (Technology Platform Division), Senior Visiting Scientist
- **Mikiko Kojima,** RIKEN Center for Sustainable Resource Science (Technology Platform Division), Expert Technician
- **Takayuki Tohge,** RIKEN Center for Sustainable Resource Science (Metabolomics Research Group), Visiting Scientist
- **Lam-Son Phan Tran,** RIKEN Center for Sustainable Resource Science (Bioproductivity Informatics Research Team), Senior Visiting Scientist

MOLECULAR BIOLOGY AND GENETICS

- **Toshiro Sato,** RIKEN Center for Biosystems Dynamics Research (Laboratory for Lung Development and Regeneration), Senior Visiting Scientist

GEOSCIENCE

- **Naoto Yokoya,** RIKEN Center for Advanced Intelligence Project (Goal-Oriented Technology Research Group), Unit Leader

Italian Ambassador to Japan visits RIKEN's Wako campus

In 2022, Italian Ambassador to Japan, Gianluigi Benedetti, visited RIKEN's Wako campus, accompanied by Enrico Traversa, the Science and Technology Counsellor of the Embassy of Italy in Tokyo. They briefly discussed cooperation between RIKEN and Italy with RIKEN President Mokoto Gonokami, then met a number of Italian researchers working at RIKEN, including Franco Nori, Andrea Benucci, and Marco Casolino.

www.riken.jp/en/news_pubs/news/2022/20221227_1

Yoshinori Tokura elected to The Japan Academy

Yoshinori Tokura, Director of the RIKEN Center for Emergent Matter Science (CEMS), has been elected a member of The Japan Academy, an organization that brings together leading Japanese scholars. Tokura helped develop guiding principles for the design of 'strongly correlated electron systems', a new class of materials that can give rise to ultrafast responses to external stimuli by efficiently controlling the electrons in solids. The academy noted that Tokura had led the field of solid-state physics, made many original contributions regarding the development of correlated electron materials and novel electronic functions, and helped develop quantum science around solid-state physics.

www.riken.jp/en/news_pubs/news/2022/20221214_1

DEVELOPMENTAL BIOLOGY

New recipes for recreating organs in the lab

Organ development has been modeled in the lab by selectively activating signaling pathways in the embryo

RIKEN researchers have imitated the formation of organs in the lab by 'hacking' certain signaling pathways that guide the development of connective tissues in the embryo, which support the formation of the liver, gut and other organs[1]. In addition to shedding light on organ development, this could eventually enable doctors to provide treatments tailored to individual patients.

The visceral organs are principally formed by embryonic epithelial cells—cells that line surfaces in the body. But recent research has revealed that this process involves close communication with the mesenchymal cells that ultimately give rise to the circulatory system, skeleton and various connective tissues (see image).

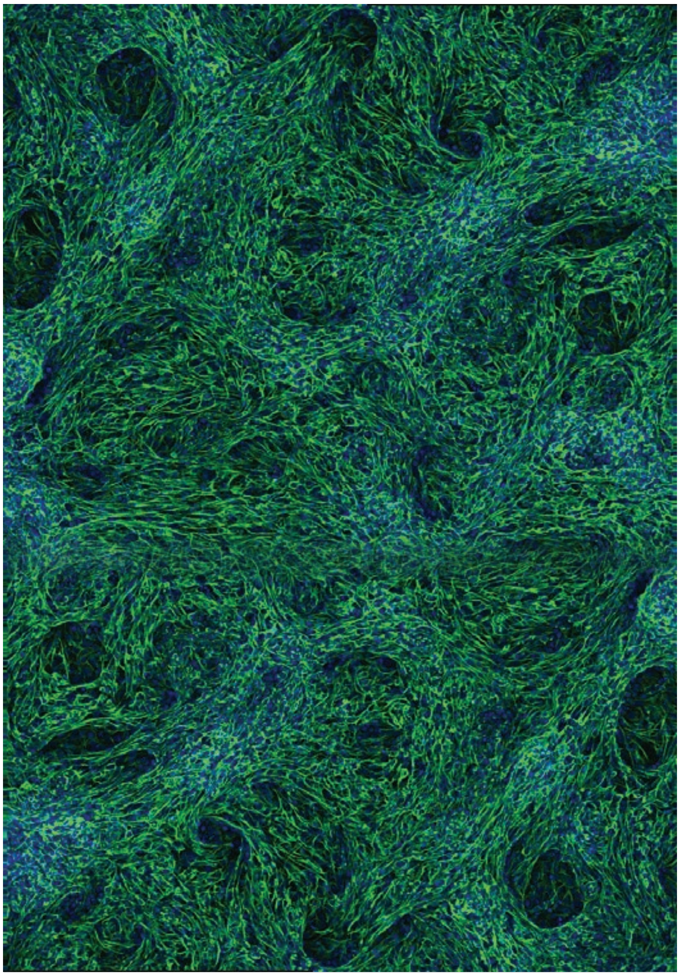
"We can generate models of human congenital diseases in the lab using this protocol."

"Mesenchymal niche cells maintain epithelial stem cells, and the mesenchymal tissue structure influences the fates of epithelial cells," explains Mitsuru Morimoto of the RIKEN Center for Biosystems Dynamics Research. This suggests that mesenchymal cells in various regions of the embryo provide distinct sets of instructions to the epithelial cells, which give rise to different organs.

In 2020, a team led by Aaron Zorn at Cincinnati Children's Hospital systematically analyzed gene expression in the developing gut with single-cell resolution. They found specific signaling pathways that are active during early embryonic development, and which in turn give rise to mesenchymal lineages associated with different organs in the body.

Now, by leveraging this knowledge, Morimoto and Zorn have developed a laboratory protocol that selectively activates these pathways to convert human stem cells into these various mesenchymal lineages. Using this approach, they were able to generate mesenchymal subtypes that help give rise to the liver, gastrointestinal tract or respiratory tissues after just one week of cell culture.

Keishi Kishimoto, a researcher from Morimoto's group who recently joined Zorn's lab, is enthusiastic about applying this approach in the context of regenerative medicine. "We can generate models of human congenital diseases in the lab using this protocol with patient-derived stem cells," he says.



Liver-specific mesenchymal tissue derived from human stem cells.

Cincinnati Children's Hospital is a major hub for research into organoids—3D cell-culture models that closely mirror key structural and functional features of complex organs—and Kishimoto envisions using such systems to understand how various genetic mutations derail developmental processes.

To begin with, he and Morimoto will look at tracheoesophageal fistula, a rare condition in which the esophagus and windpipe are fused together, creating potentially serious respiratory issues. "We will generate tracheoesophageal fistula organoids in the laboratory by creating a foregut organoid and simultaneously inducing the trachea on one side and the esophagus on the other," says Morimoto. ●

Reference

1. Kishimoto, K., Iwasawa, K., Sorel, A., Ferran-Heredia, C., Han, L., Morimoto, M., Wells, J. M., Takebe, T. & Zorn, A. M. Directed differentiation of human pluripotent stem cells into diverse organ-specific mesenchyme of the digestive and respiratory systems. *Nature Protocols* **17,** 2699–2719 (2022).

NITROGEN CYCLE

Restoring balance to the nitrogen cycle

A new approach to electrocatalysis allows researchers to selectively produce various nitrogen-containing compounds

Algal blooms, such as this one in a lake in Guatemala, are often caused by an excess of nitrogen-containing compounds due to run off from fertilizers. A new strategy for electrocatalysis could help restore balance to the nitrogen cycle thanks to its ability to selectively produce different nitrogen-containing compounds.

Electrochemists at RIKEN have found a way to selectively convert nitrites into one of four other nitrogen-containing compounds using the same catalyst[1]. This could help to replace fossil-fuel-intensive industrial processes with electrochemical ones powered by renewable energy.

Carbon dominates the news these days, and there is a high public consciousness of the problems ensuing from the disruption of the natural carbon cycle due to the combustion of fossil fuels. But nitrogen, carbon's neighbor on the periodic table, receives far less attention, despite the many environmental problems arising from the disturbance of its natural cycle.

"The nitrogen cycle has been seriously understudied," says Ryuhei Nakamura of the RIKEN Center for Sustainable Resource Science. "But it is critically important for agriculture, and its disruption can cause major ecological problems such as harmful algal blooms, and air and water pollution."

A major cause of these problems is that the industrial processes used to produce fertilizers and other important nitrogen-containing compounds drive the cycle in one direction only, disrupting its balance. "To restore balance, industrial processes are needed that can selectively produce nitrogen-containing compounds in different parts of the cycle," says Nakamura. "But so far this has proved difficult to realize in practice."

Now, Nakamura and his co-workers have demonstrated an electrocatalytic process using a single catalyst that can convert nitrites into nitrogen monoxide (NO), nitrous oxide (N_2O), molecular nitrogen (N_2) or ammonium (NH_4^+) depending on three easily varied experimental parameters.

Importantly, these target compounds were produced at high percentages (selectivities) that rival those obtained by specific catalysts optimized for a single target compound.

The secret to the team's success was the ability to transfer protons and electrons separately rather than simultaneously. Conventionally, electrons and protons are swapped at the same time in electrocatalytic reactions, but the team adopted a novel strategy that allowed electrons and protons to be exchanged one after the other. This enabled them to tailor the conditions for each transfer.

"This new approach provides much greater control over reactions, and there is a lot of potential to apply it to other chemical systems," says Nakamura. "Our work demonstrates that it's possible to achieve high control over product selectivity even when using a single catalyst for a complex reaction network."

Nakamura notes that the ability to produce fertilizers from renewable energy is particularly important for Japan in light of the country's high dependence on imported fertilizers and low self-sufficiency in food production.

The team now intends to apply the electrochemical regulation of the nitrogen cycle to fish farms, where the accumulation of nitrates and nitrites on the seafloor causes red tides.

Reference

1. He, D., Ooka, H., Li, Y., Kim, Y., Yamaguchi, A., Adachi, K., Hashizume, D., Yoshida, N., Toyoda, S., Kim, S. H. *et al.* Regulation of the electrocatalytic nitrogen cycle based on sequential proton–electron transfer. *Nature Catalysis* **5**, 798–806 (2022).

PROTOSTELLAR DISKS

Nascent planets may be lurking in dusty disk

Clumps of matter in a protostellar disk cast a cold shadow that could affect how some planets gestate

RIKEN astrophysicists may have identified the embryos of gas giant planets in a disk of gas and dust swirling around a newborn star[1]. These planetary precursors may grow up to be similar to Jupiter, a gas giant in our Solar System.

Nurseries for new planets, protostellar disks are oblate swathes of gas and dust that rotate about newly formed stars. The Earth and the other planets in the Solar System were birthed from such a disk.

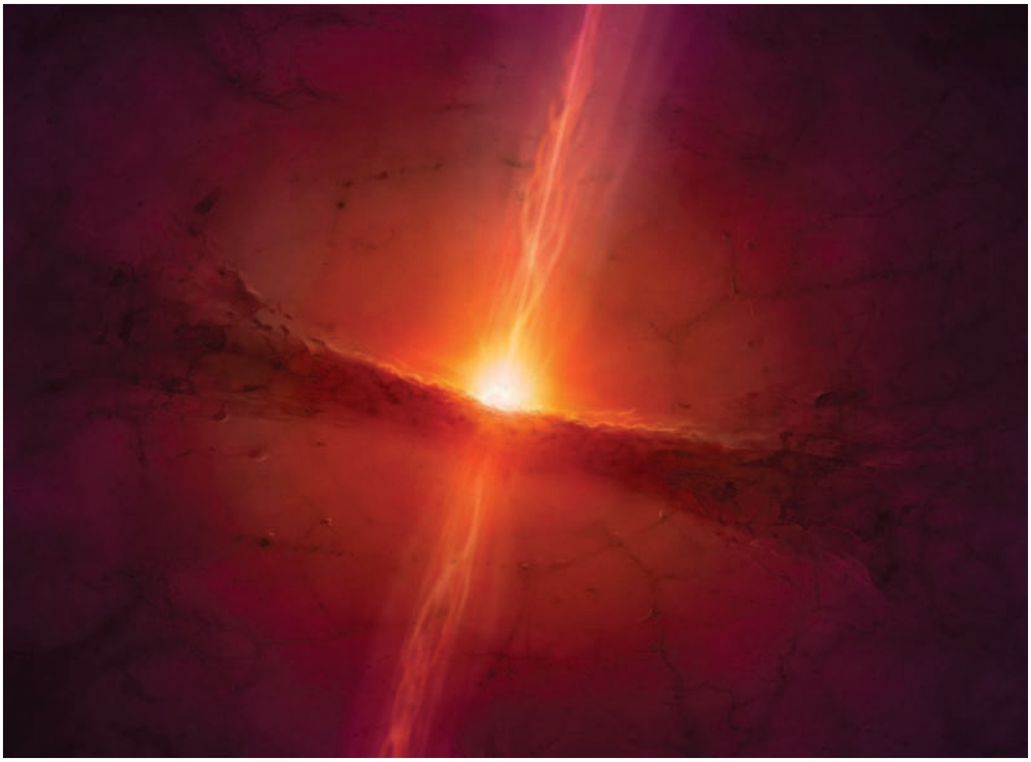
Now, Satoshi Ohashi of the RIKEN Star and Planet Formation Laboratory and his colleagues have studied a protostellar disk in one of the closest star-forming regions to Earth.

Using data from the Atacama Large Millimeter/submillimeter Array (ALMA) in Chile and the Jansky Very Large Array (VLA) in New Mexico, they found that the disk is 80–100 times wider than the distance from the Sun to the Earth, a span known as an astronomical unit.

The disk is unstable and collapsing in a region roughly 20 astronomical units from its young star. The VLA had previously identified several clumps of matter in the same area, and their formation may be driven by this gravitational instability.

"These clumps may be the precursors of gas giant planets, since they are massive and dense," says Ohashi. If this identification is correct, it would imply that planet formation can begin surprisingly early in protostellar disks.

The researchers also measured the temperature of the dust in different parts of the disk. The disk is heated by the star's radiation, so the temperature of the dust should decline gradually at greater distances from the star.



A computer-generated image depicting a dark protostellar disk seen edge-on at 90 degrees to jets (orange) emanating from the poles of a young star. Such disks are thought to be the precursors of planetary systems, with planets forming as the dust coalesces. RIKEN researchers may have spotted embryos of gas giant planets in one protostellar disk.

"Our Solar System is also suggested to have formed a shadowed region in the past."

Dust close to the star can reach a relatively warm –193 degrees Celsius. But on the far side of the clumps, the dust temperature drops sharply. This suggests that the clumps are blocking the star's radiation, chilling any dust in their shadow. In the outermost parts of the disk, the dust temperature falls to around –263 degrees Celsius—just 10 degrees above absolute zero.

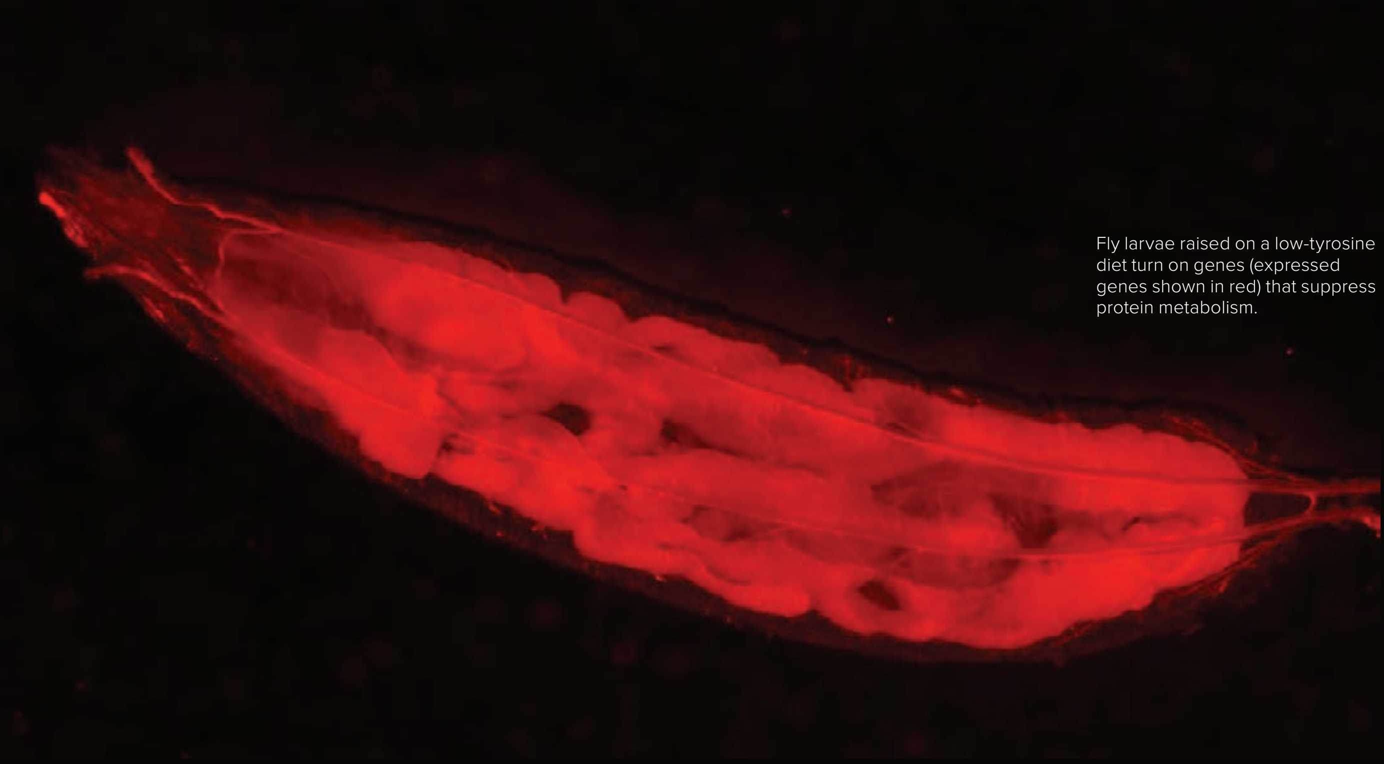
This shaded, cold environment may affect the chemical composition of planets that form in outer regions of the disk, Ohashi says.

This finding might help astrophysicists understand the origins of icy planets like Uranus and Neptune that orbit our own Sun. "Our Solar System is also suggested to have formed a shadowed region in the past," says Ohashi.

The team now hopes to observe other protostellar disks, with greater spatial resolution and sensitivity, to assess whether this shadowing effect is common.

Reference

1. Ohashi, S., Nakatani, R., Liu, H. B., Kobayashi, H., Zhang, Y., Hanawa, T. & Sakai, N. Formation of dust clumps with sub-Jupiter mass and cold shadowed region in gravitationally unstable disk around class 0/I protostar in L1527 IRS. *The Astrophysical Journal* **934,** 163 (2022).



Fly larvae raised on a low-tyrosine diet turn on genes (expressed genes shown in red) that suppress protein metabolism.

METABOLISM

The key to a healthy protein diet

Fruit fly study links nutrient-sensing pathway to an unexpected amino acid

A 'non-essential' amino acid—so-called because the body can make it from other nutrients—can act as a nutritional cue to guide the body's responses to a low-protein diet, a RIKEN-led team has found in a study on fruit fly larvae[1]. If a similar control mechanism operates in mammals, it may be possible to use it to control appetite.

To help us decide whether to chow down on another helping of beef or fish, our brains have evolved mechanisms for sensing changes in protein building blocks in the body and adjusting the intake of protein-rich foods accordingly. Researchers had long assumed this process relied only on those building blocks, known as amino acids, that the body cannot naturally produce on its own.

But now, a RIKEN-led study has found that is not always the case. "We've discovered a new mechanism of sensing and adaptation to dietary protein scarcity," says Fumiaki Obata of the RIKEN Center for Biosystems Dynamics Research (BDR).

"We've discovered a new mechanism of sensing and adaptation to dietary protein scarcity."

Known as tyrosine, the amino acid is found in dairy products, meats, nuts, beans and other protein-packed foods. But the body can also synthesize tyrosine from another amino acid called phenylalanine, which is similarly found in both plant and animal foods.

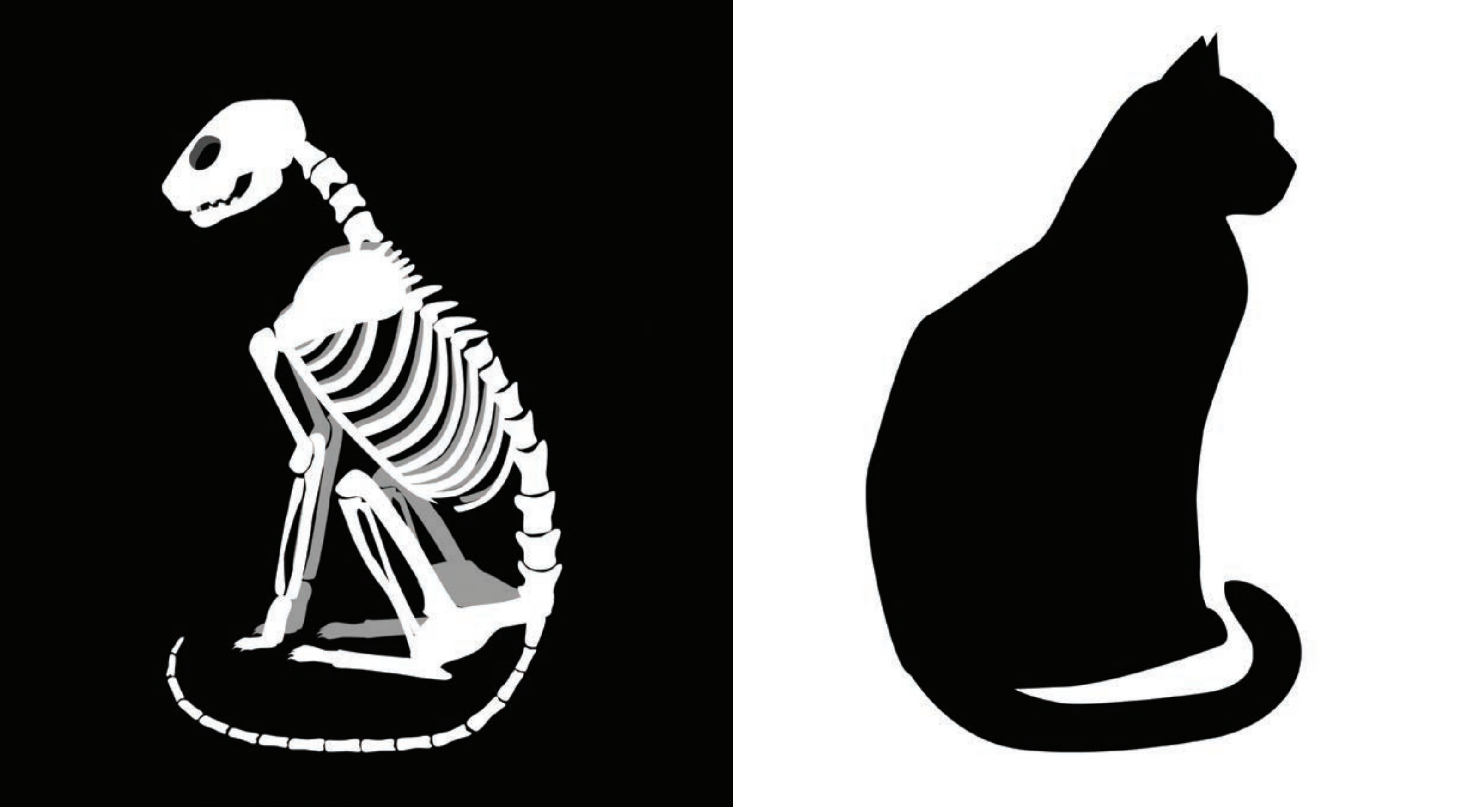
As Obata and BDR colleague Hina Kosakamoto have now shown, the flies slow down their rate of protein metabolism and ramp up food consumption when levels of tyrosine in the diet are low—a sign of adaptation to protein scarcity (see image). But, conversely, when tyrosine is ingested in greater amounts, the flies kick their protein metabolism into high gear. They also limit intake of extra protein, thus ensuring that levels of the macronutrient remain within a healthy range.

The team identified several of the molecular players and signaling pathways involved in regulating the body's response to tyrosine levels—although how exactly this happens remains unclear. They ruled out one common mechanism by which the brain senses nutrient imbalances. But as Kosakamoto points out: "We still don't know how tyrosine is sensed in cells."

Another research priority for the team is to corroborate the findings in mouse models. This will help determine how relevant the results are for human physiology and medicine, as well as for agriculture and animal husbandry. "If tyrosine plays a similar role in mammals, then we could use tyrosine restriction to control appetite, treat metabolic syndrome or even forestall aging," Obata says. "Potentially, our knowledge could also be applied in the livestock industry to improve animal health and production."

Reference

1. Kosakamoto, H., Okamoto, N., Aikawa, H., Sugiura, Y., Suematsu, M., Niwa, R., Miura, M. & Obata, F. Sensing of the non-essential amino acid tyrosine governs the response to protein restriction in *Drosophila*. *Nature Metabolism* **4,** 944–959 (2022).



Schrödinger's cat is a thought experiment describing a cat placed in a closed box with a bottle of poison that will break if a probabilistic event, such as the decay of a radioactive particle, occurs. Schrödinger conjectured that, until the box was opened—or 'observed', the cat was simultaneously alive and dead. Now, by using 'cat states', RIKEN researchers have proposed a scheme for realizing fault-tolerant gates to entangle multiple qubits.

QUANTUM COMPUTING

Realizing fault-tolerant quantum computers

A proposal to use cat states promises to make quantum computers less prone to errors

Error correction in quantum computers could be simplified by a new protocol proposed by an all-RIKEN team based on 'cat states'[1]. It could cut the computing resources needed to fix errors to the same level as conventional computers, making quantum computers cheaper and more compact.

Quantum computers are looming ever larger on the horizon of computing. They have already demonstrated the ability to outperform traditional computers for certain kinds of calculations. But they are more prone to errors than conventional computers.

Since traditional computers are based on bits that are either 0 or 1, the only error they are susceptible to is when a bit accidentally flips from 0 to 1 or vice versa.

But quantum computers use qubits, which can be in a superposition of two states. When the states are depicted on a sphere, the angle between the two states is known as the qubit's phase. This phase can also be flipped in quantum computers. They thus need more computing resources to correct for this additional source of error.

An attractive way to sidestep this problem is to use qubits based on so-called cat states. These states are named after Schrödinger's hypothetical cat, which is simultaneously dead and alive until observed. By analogy, cat states are superpositions of two states with opposite phase.

Unlike other qubits, cat-state qubits cannot undergo phase flips, so that engineers making quantum computers based on them need only worry about bit flips—just like in conventional computers. Researchers are now exploring how to use these cat-state qubits to perform computations.

Now, Ye-Hong Chen and four co-workers, all at the RIKEN Center for Quantum Computing, have theoretically demonstrated a way to use cat states to realize fault-tolerant gates for connecting multiple qubits in a process known as entanglement.

"Conventional computers can only process data one bit at a time, but entanglement allows quantum computers to process a lot of data simultaneously," explains Chen. "The gates can rapidly generate entangled cat states with high accuracy."

The team showed that such fault-tolerant quantum gates could be used to implement a quantum search algorithm with a high efficiency. The algorithm will allow databases to be searched faster than is currently possible using conventional computers.

"Let us assume that you are searching for one key that will open a box among 100 keys. On average, you would need to try 50 keys using a conventional search algorithm to identify the one key that opens that box," says Chen. "But with the quantum search algorithm the average is only 10 attempts," says Chen.

The team is now exploring how to develop other useful quantum algorithms based on fault-tolerant quantum codes. ●

Reference

1. Chen, Y.-H., Stassi, R., Qin, W., Miranowicz, A. & Nori, F. Fault-tolerant multiqubit geometric entangling gates using photonic cat-state qubits. *Physical Review Applied* **18,** 024076 (2022).

DNA TRANSCRIPTION

Enzyme razes and rebuilds DNA beads

During DNA transcription, an enzyme takes apart nucleosomes and then puts them back together again

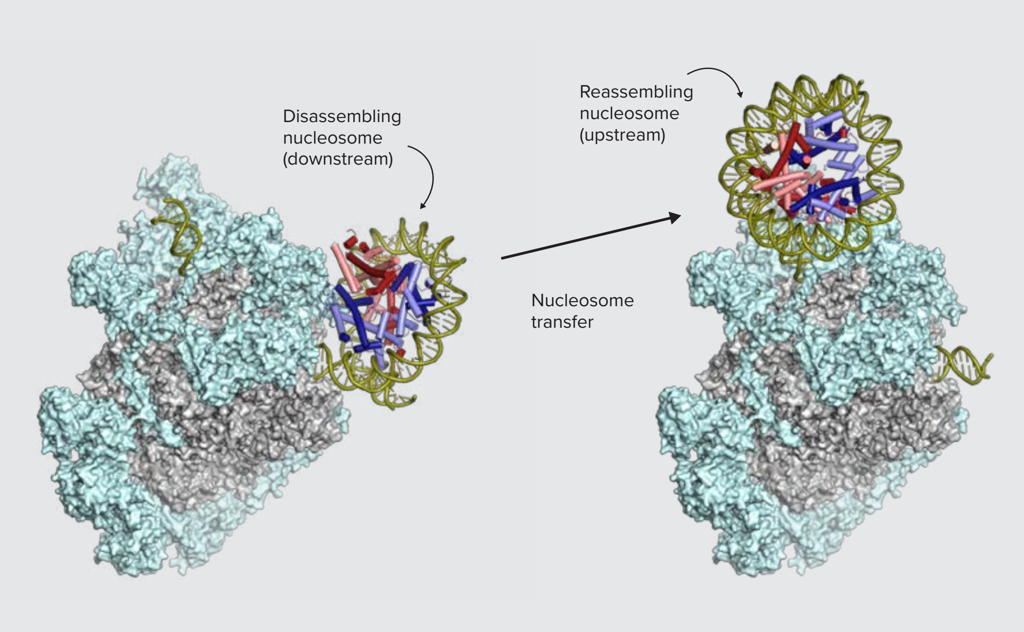
RIKEN researchers have shown how a gene-reading enzyme manages to dismantle bead-like structures of DNA and reassemble them at high speed, without disrupting the integrity of genomic organization[1]. Their findings could help inform the development of new therapies for diseases such as cancer.

Eukaryotic cells pack an awful lot of DNA into a tiny space. One way they achieve this is through the bead-on-string-like structure of chromatin—a mixture of DNA and proteins that make up chromosomes. The 'beads' are bundles of DNA known as nucleosomes.

While this structure is compact, nucleosomes pose a challenge to the DNA-transcribing enzyme called RNA polymerase II (see image), which is responsible for converting genetic information stored in DNA into messenger RNA transcripts. It has to pass through nucleosomes without altering their structure. But just how it achieves this had not been clear.

Now, a team led by Shun-ichi Sekine of the RIKEN Center for Biosystems Dynamics Research (BDR) has shown that RNA polymerase II first destroys and then rebuilds nucleosomes. This process allows RNA polymerase II to access genomic sequences while ensuring that epigenetic details in the structures are not lost.

To discover how RNA polymerase II sidesteps the nucleosome obstacles in its path, the team turned to cryo-electron microscopy—a powerful imaging technique that can reveal the shape of biomolecules with atomic resolution. They obtained snapshots of the polymerase's structure at six time points as it traversed the nucleosome.



Structure of RNA polymerase II (colored gray) in complex with elongation factors (colored cyan), before and after passage through the nucleosome. The black arrow indicates the direction of transcription.

> **"The knowledge we obtained in this study could help advance research on the mechanisms of disease."**

The before, during and after images revealed how the polymerase, with help from several proteins known as elongation factors, first broke down a nucleosome. This allowed it to read DNA sequences that are otherwise too tightly wound up inside the nucleosomes to be accessible to the enzyme. Following transcription, the polymerase and its partner factors then reconstructed the nucleosome, aided by an extra protein called FACT, which has a role in safeguarding chromatin architecture.

"Our study reveals for the first time that RNA polymerase II disassembles the nucleosome in front of it and re-assembles it behind it, with the help of multiple other factors," says Sekine. "As a result, the enzyme can pass through the nucleosome and continue transcription as if nothing had happened."

The findings will be helpful for gaining new insights into diseases such as cancer that involve the improper regulation of gene transcription due to defects in nucleosome remodeling.

"The knowledge we obtained in this study could help advance research on the mechanisms of disease and aging caused by disruption of transcriptional regulation and chromatin structure," says Haruhiko Ehara, also at BDR. ●

Reference

1. Ehara, H., Kujirai, T., Shirouzu, M., Kurumizaka, H. & Sekine, S. Structural basis of nucleosome disassembly and reassembly by RNAPII elongation complex with FACT. *Science* **377,** eabp9466 (2022).

SELF-HEALING POLYMERS

Easy-to-make self-healing polymers

A polymer that heals itself has been made from a readily available building block

Material scientists at RIKEN have created a self-healing polymer by using an off-the-shelf compound for the first time[1]. The strategy they used is promising for improving the durability and minimizing the environmental impact of various commercial polymers for a wide range of applications.

Polymers capable of healing themselves when damaged would last longer and thus reduce costs and the burden on the environment. Current strategies for producing self-healing polymers mainly employ reversible chemical reactions, but this usually entails complex synthesis processes. Furthermore, self-healing mechanisms based on chemical reactions may not work in certain environments such as in water and acidic and alkaline solutions.

“Making self-healable polyolefins would enhance...materials used in many applications.”

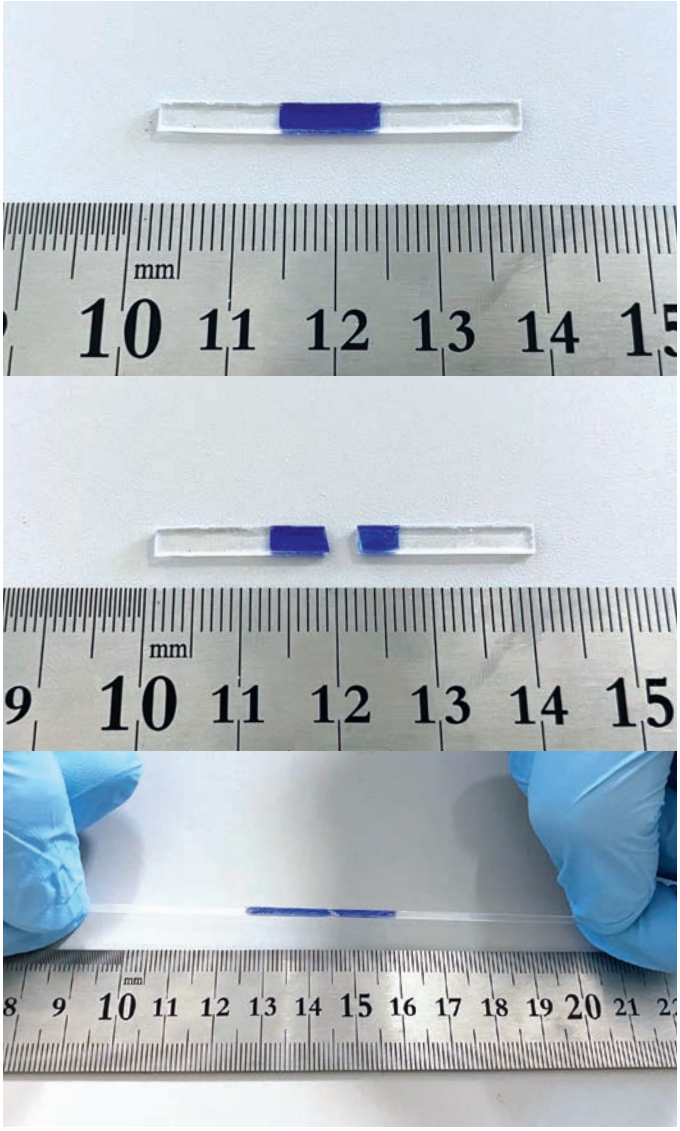
Ideally, material scientists would like to produce polymers that self-heal under a wide range of conditions, from readily available materials, using simple synthesis processes.

Polyolefins, which include polyethylene and polypropylene, are the most ubiquitous synthetic polymers in the world. “Polyolefins are all around us; they are used for food packaging, clothing, automobiles and electronic and medical devices,” says Zhaomin Hou of the RIKEN Center for Sustainable Resource Science. “Making self-healable polyolefins would enhance the lifetime, safety, and environmental impact of materials used in many applications.”

Now, Hou and co-workers have succeeded in making a form of the polyolefin polyisoprene—the synthetic equivalent of rubber latex, which is used in tires, rubber bands and shoe soles—that exhibits a robust, physical self-healing mechanism. Importantly, their self-healing polyisoprene is produced from the same building block as regular polyisoprene—isoprene.

To demonstrate the self-healing ability of their polymer, the team cut a block of it in half and then brought the two pieces together at room temperature for one minute (see image). The healed sample could bear weights up to 2.5 kilograms without tearing.

The secret to their success was using a rare-earth catalyst to produce a mixture of two different microstructures of polyisoprene. One microstructure was relatively hard, while the other one was soft. A ratio of the hard microstructure to the soft one of about 7:3 was optimal for the self-healing property. The team suspect that the hard microstructures link together to provide points that connect molecules and that this network gives rise to self-healing.



A sample of self-healing polyisoprene (top) was cut into two pieces (middle) and then pressed together for 15 seconds. After one minute, the sample could be stretched to more than double its original length without breaking (bottom).

“The ultimate goal is to use easily available commodity monomers to produce tough self-healing polymers that are capable of spontaneously repairing when they sustain mechanical damage in real-world environments without any external input,” says Hou. “We believe that this work offers unprecedented insights to help achieve this goal.”

Reference

1. Wang, H., Yang, Y., Nishiura, M., Hong, Y., Nishiyama, Y., Higaki, Y. & Hou, Z. Making polyisoprene self-healable through microstructure regulation by rare-earth catalysts. *Angewandte Chemie International Edition* e202210023 (2022).

MICROBIOME

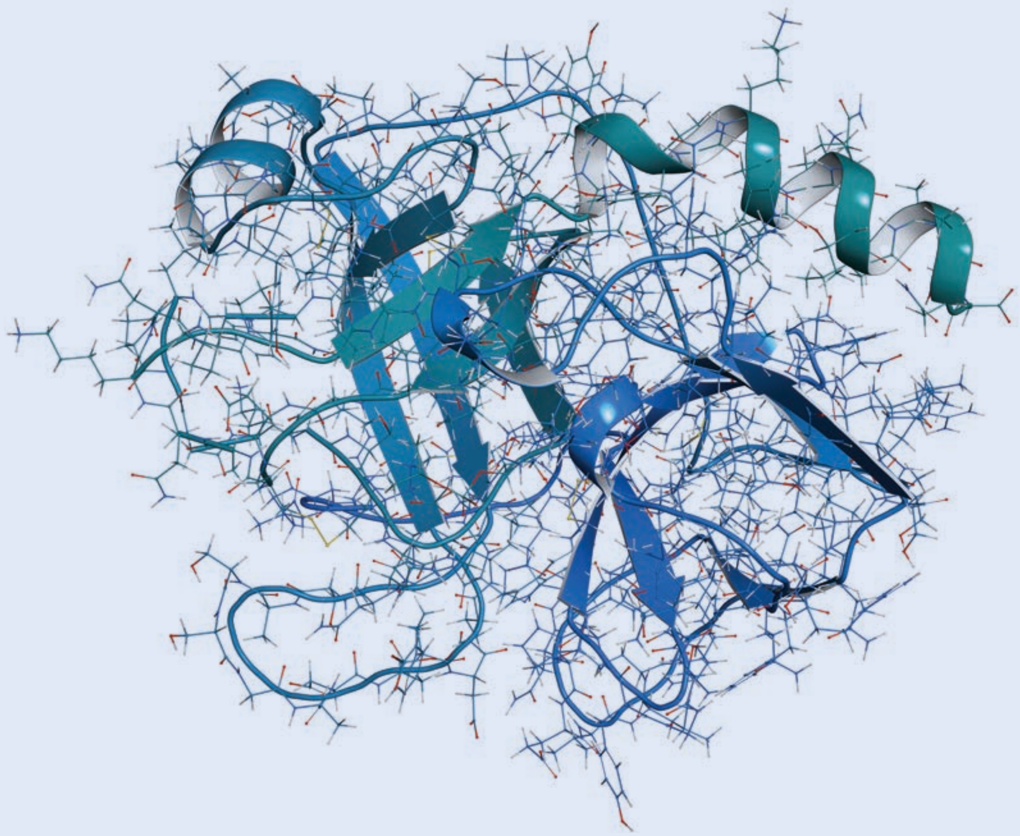
Gut microbe degrades a protein chopper

A gut bacterium in the large intestine may help keep a digestive enzyme in check and provide higher protection from viruses

A microbe that breaks down a key digestive enzyme in the large intestine of humans and mice has been identified by RIKEN biologists[1]. This finding could eventually lead to the development of probiotics that can help restore balance to people who have too much of the enzyme in their large intestines.

An enzyme known as trypsin (see image) helps us to digest food by chopping up proteins in the small intestine. But high levels of trypsin further down the digestive tract in the large intestine can be problematic, potentially leading to complications such as inflammatory bowel disease.

The interaction between digestive enzymes such as trypsin and the 10 trillion or so microbes that inhabit the human gut is highly complex. The average person has between 500 and 1,000 species if gut bacteria, and it is fiendishly difficult to untangle the roles that individual species play in the gut.



The molecular structure of trypsin, an important digestive enzyme for breaking down proteins. RIKEN researchers have discovered a gut microbe that can degrade trypsin, and which thus may help to keep trypsin levels in check in the large intestine, where the enzyme can cause problems.

"To isolate and culture the gut microbes outside the body is often challenging, especially since most of them are sensitive to oxygen," says Youxian Li of the RIKEN Center for Integrative Medical Sciences (IMS). "To establish a causal relationship between a microbe and a change in our body is even more difficult."

Now, a team led by Kenya Honda of IMS has succeeded in establishing that a species known as *Paraprevotella clara* degrades trypsin in the large intestine and thus could play a major role in keeping trypsin levels in check in this region of the gut.

The rod-shaped bacterium was first isolated from human feces in 2009 by researchers at the Japanese probiotic company Yakult, but there was nothing to indicate its role in breaking down trypsin. "There was no indication that this species was special," notes Li.

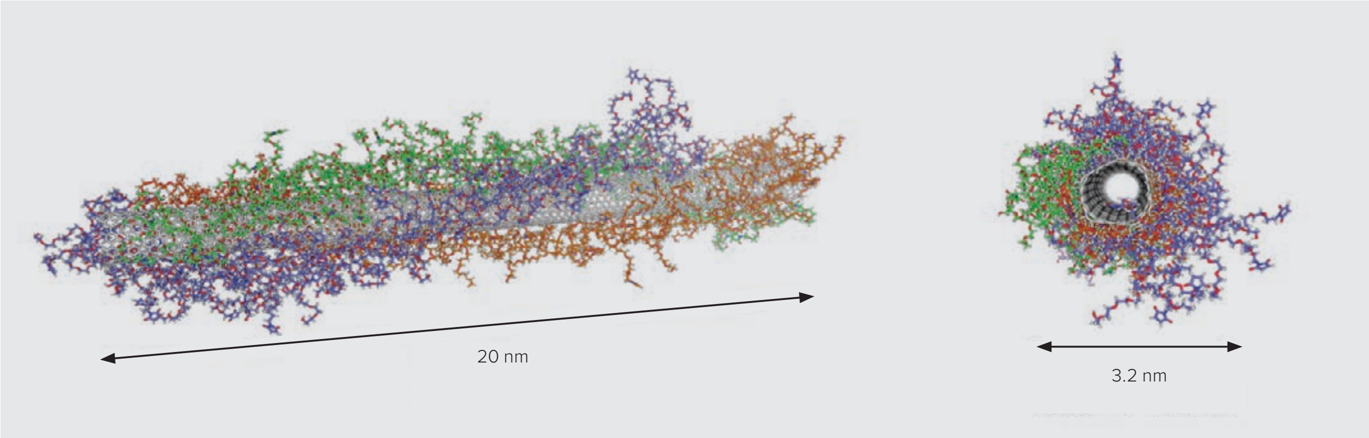
The team went further and showed that *P. clara*'s ability to degrade trypsin provided mice with added protection against intestinal infection by mouse hepatitis virus type 2 (MHV-2), a coronavirus that needs trypsin to gain entry into cells.

"We found that mice with low levels of trypsin in the large intestine were protected from infection when the virus was applied through the gastrointestinal route—more of them survived and they had less dissemination of viral particles in other organs," explains Li. "So this indicates that having trypsin-disintegrating species in the large intestine is probably protective when it comes to intestinal infections by viruses that depend on trypsin."

This opens up new avenues of research. "We now have a tool we can apply to different kinds of intestinal disease models to see if trypsin plays a role in various diseases," says Li.

Reference

1. Li, Y., Watanabe, E., Kawashima, Y., Plichta, D. R., Wang, Z., Ujike, M., Ang, Q. Y., Wu, R., Furuichi, M., Takeshita, K. *et al.* Identification of trypsin-degrading commensals in the large intestine. *Nature* **609,** 582–589 (2022).



A simulated image of a carbon nanotube (gray cylinder) coated with three peptide molecules (colored green, orange and blue). RIKEN researchers have used such peptide-coated carbon nanotubes to insert genetic material into plant mitochondria.

PLANT BIOTECHNOLOGY

Smuggling genes into plant mitochondria

DNA can be imported into the mitochondria of plants with a much higher efficiency than before, thanks to a new method for delivering genes

RIKEN biologists have found an effective way to smuggle genetic material into the energy generators of plant cells, opening up the possibility of coaxing plants to produce commercially useful compounds[1].

With the global population expected to reach nearly 10 billion people by 2050, the ability to tinker with the genetics of plants to boost the production of food will be vital to feed the world.

Plants are also anticipated to become biofactories for producing useful chemicals such as drugs and fuels. "They can be engineered to produce other stuff besides food, such as various chemicals, pharmaceuticals, and recombinant proteins," says Simon Law of the RIKEN Center for Sustainable Resource Science (CSRS). "The fact that you can use plants to make a lot of different things makes biotechnology such a promising field."

One way to 'reprogram' plants is to import genetic material into their cells, but this is challenging due to the thick cell wall that blocks many biomolecules.

> **"The first time I ran the experiment, I doubted the results as they seemed too high to be reasonable."**

Carbon nanotubes—rolled-up tubes of graphene that are a mere nanometer or so in diameter—are sufficiently slim to slip through the cell wall. But once inside plant cells, carbon nanotubes are not very effective at targeting mitochondria—a key organelle responsible for generating energy and making and breaking down various compounds.

"Getting stuff through the cell wall, the cell membrane and then past mitochondrial membranes is difficult and it hadn't been achieved with high efficiency previously," notes Law.

Now, Law, Keiji Numata, also of CSRS, and co-workers have used carbon nanotubes to ship snippets of DNA into plant mitochondria at high efficiency. They achieved this by first coating the carbon nanotubes with a polymer layer that allowed for conjugation of short strings of amino acids known as peptides (see image). The peptides enabled the carbon nanotubes to target mitochondria.

By conjugating the peptides on carbon nanotubes, the team enhanced the efficiency of DNA transfer to mitochondria by a remarkable 30 times compared with previous attempts that just used peptides.

"The first time I ran the experiment, I doubted the results as they seemed too high to be reasonable," recalls Law. "But I became more confident after repeating it a few times and obtaining similar results."

The researchers demonstrated the usefulness of their method by using it to import a gene that enhanced the growth rate of plants. Other potential uses include speeding up breeding programs and altering metabolic pathways so that they produce commercially useful chemicals. Furthermore, by varying the peptides coated on the nanotubes, it should be possible to target other organelles in plant cells. ●

Reference

1. Law, S. S. Y., Liou, G., Nagai, Y., Giménez-Dejoz, J., Tateishi, A., Tsuchiya, K., Kodama, Y., Fujigaya, T. & Numata, K. Polymer-coated carbon nanotube hybrids with functional peptides for gene delivery into plant mitochondria. *Nature Communications* **13,** 2417 (2022).

TSUNAMI PREDICTION

Predicting tsunami impact in a split second

Deep learning could save lives by slashing the time needed to predict the height and reach of tsunamis

Detailed predictions about how an approaching tsunami will impact the northeastern coastline in Japan can now be made in fractions of a second rather than half an hour or so—buying precious time for people to take appropriate action[1]. This potentially life-saving technology exploits the power of machine learning.

The catastrophic tsunami that struck northeast Japan on 11 March 2011 claimed the lives of about 18,500 people. Many lives might have been saved if early warning of the impending tsunami had included accurate predictions of how high the water would reach at different points along the coastline and further inland.

The coast now boasts the world's largest network of sensors for monitoring movement of the ocean floor. The 150 offshore stations making up this network provide early warning of tsunamis. But to be meaningful, the data generated by the sensors needs to be converted into tsunami heights and extents along the coastline.

A photograph taken from a helicopter showing the devastation wreaked by the 2011 tsunami in northeastern Japan. Knowing the height and reach of a tsunami in different places can mean the difference between life and death. A RIKEN team has used deep learning to predict such information in less than a second.

"Our model can make predictions within seconds."

This usually requires numerically solving difficult non-linear equations, which typically takes about 30 minutes on a standard computer. But the 2011 tsunami hit some parts of the coast a mere 45 minutes after the earthquake.

Now, Iyan Mulia of the RIKEN Prediction Science Laboratory and co-workers have used machine learning to cut the calculation time to less than one second.

"The main advantage of our method is the speed of predictions, which is crucial for early warning," explains Mulia. "Conventional tsunami modeling provides predictions after 30 minutes, which is too late. But our model can make predictions within seconds."

Since tsunamis are rare occurrences, the team trained their machine-learning system using more than 3,000 computer-generated tsunami events. They then tested it with 480 other tsunami scenarios and three actual tsunamis. Their machine-learning-based model could achieve comparable accuracy at only 1% the computational effort.

The same deep-learning approach could be used for other disaster scenarios where time is of the essence. "The sky's the limit—you can apply this method to any kind of disaster predictions where the time constraint is very limited," says Mulia, who first became interested in studying tsunamis after the 2004 Indian Ocean tsunami devastated coastal regions in his home country of Indonesia. "I'm now working on a storm surge prediction, also using machine learning."

Mulia notes that the method is only accurate for large tsunamis that are higher than about 1.5 meters, so he and his team are now seeking to improve its accuracy for smaller tsunamis. ●

Reference

1. Mulia, I. E., Ueda, N., Miyoshi, T., Gusman, A. R. & Satake, K. Machine learning-based tsunami inundation prediction derived from offshore observations. *Nature Communications* **13,** 5489 (2022).

SURGICAL INNOVATION

Hibernating during surgery could protect organs

A hibernation-like state that protects organs during heart surgery could one day be used in humans

Inducing a hibernation-like state in mice, by exciting specific neurons in the brain, can protect their kidneys from being damaged by a lack of oxygen, RIKEN researchers have shown[1]. This demonstration could lead to a new, safer way to protect the organs of human patients during certain heart surgeries.

For some kinds of heart and aortic surgery, doctors have to cut off blood circulation as they work to repair the aorta. For the past 50 years, such surgery has been performed after applying cold temperatures to induce deep hypothermia. This slows the metabolism, enabling organs to survive with very little oxygen. While this protects organs such as the kidneys, it reduces blood coagulation, leading to excessive bleeding, which sometimes necessitates blood transfusions.

Hidetoshi Masumoto's team at the RIKEN Center for Biosystems Dynamics Research (BDR) is exploring how to slow down metabolism without using hypothermia, and inducing a hibernation-like state seems a promising avenue. Many animals have extremely slow metabolisms during hibernation, yet remain healthy upon waking. One major problem remains—humans do not hibernate.

This limitation has not deterred researchers, however. A few years ago, a group led by BDR's Genshiro Sunagawa discovered a way to induce a hibernation-like state in mice—animals that do not normally hibernate.

"If we can induce them, there are many possibilities for using hibernation-like states in cardiovascular medicine," says Sunagawa.

A study that put mice into a hibernation-like state could lead to surgical innovations that allow heart surgery on people without inducing a risky state of hypothermia.

See infographic on hypometabolic states on **page 32**.

The researchers have now tested the technique's effectiveness using a mouse model of aortic surgery, which required pausing blood circulation.

The team induced hibernation-level hypometabolism by using an injection to activate Q neurons—special nerve cells in the hypothalamus. They then compared four groups of model mice: those that were and were not exposed to cold temperatures to induce hypometabolism, and those whose which were, or were not, subjected to activation of their Q neurons.

The team found that inducing hypometabolism by activating Q neurons at normal body temperatures protected the kidneys just as effectively as hypometabolism induced using hypothermia.

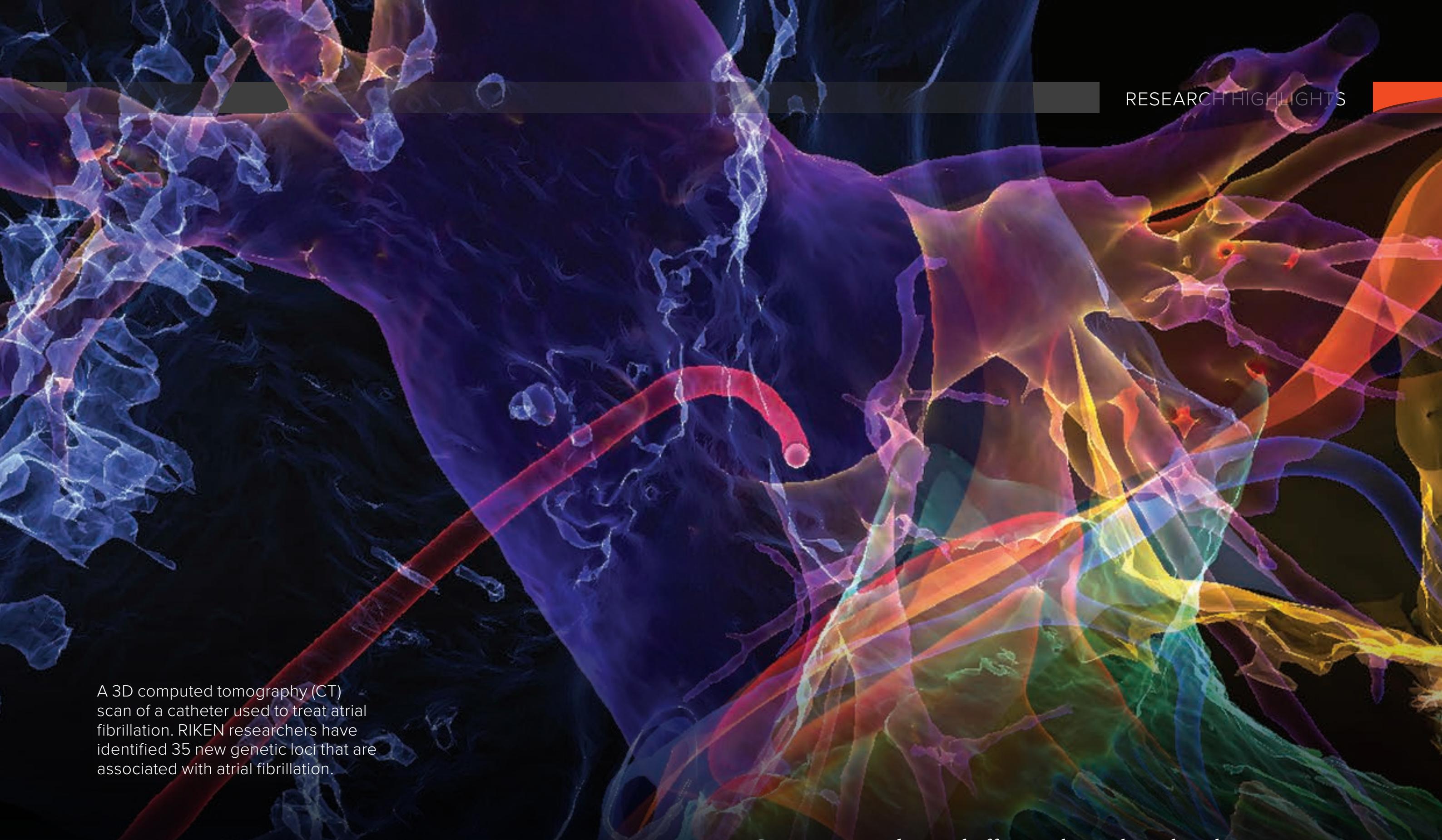
"With these results, we now know that Q neurons induced hibernation-like states that can be used to protect organs," says Masumoto.

Masumoto and Sunagawa ultimately hope to refine this technique to slow down people's metabolism during heart surgery. But because Q neurons cannot be selectively activated in people, the team is now exploring other ways to protect organs that involve intervening outside the brain.

"Activating Q neurons triggers some sequence of biological events that allows organs to exist in a hypometabolic state for days," explains Sunagawa. "Once we know precisely what these events are, we're confident we can induce them pharmacologically in the body, without the need to first activate the Q neurons."

Reference

1. Kyo, S., Murata, K., Kawatou, M., Minatoya, K., Sunagawa, G. A. & Masumoto, H. Quiescence-inducing neurons-induced hypometabolism ameliorates acute kidney injury in a mouse model mimicking cardiovascular surgery requiring circulatory arrest. *JTCVS Open* **12,** 201–210 (2022).



A 3D computed tomography (CT) scan of a catheter used to treat atrial fibrillation. RIKEN researchers have identified 35 new genetic loci that are associated with atrial fibrillation.

ATRIAL FIBRILLATION

Identifying genetic risk factors for heart arrhythmia

The links between atrial fibrillation and genetics have been determined in a massive study

In the largest genetic study of heart arrhythmia to date, RIKEN researchers have identified several genes and genetic variations associated with the heart condition atrial fibrillation[1]. Scores generated based on genetic data could predict atrial fibrillation, and even stroke and mortality.

Atrial fibrillation occurs when the heart beats rapidly and irregularly, causing blood to pool in the atria. This increases the risk of blood clots forming in the heart, which may then travel to the brain and cause a stroke by blocking blood flow.

Atrial fibrillation has been linked with some genetic factors, but the mechanisms behind this connection remain unclear.

The researchers examined the genomes of more than 150,000 Japanese individuals and found five locations within their chromosomes—called genetic loci—that had never before been associated with atrial fibrillation. Two of them included genetic variations unique to East Asian populations.

A subsequent cross-ancestry meta-analysis of more than 1.2 million people—the same Japanese population and those from two large European studies—yielded 150 critical genetic loci, including 35 that were new. Further analysis found more than 130 genes associated with these loci. Variations in these genes are thus highly likely to lead to atrial fibrillation.

Genes are turned on and off as needed by special regulatory proteins called transcription factors. To find transcription factors that turn on the genes at loci associated with atrial fibrillation, the researchers looked for proteins that bind to the newly discovered loci. They found transcription factor ERRg, which is associated with genes that regulate processes inside heart muscle cells.

To test whether overactive ERRg might be a direct cause of atrial fibrillation, the researchers grew human heart-muscle cells in the lab and facilitated ERRg activity. Several key genes related to heart function had reduced expression and the heart-muscle cells exhibited irregular beating and prolonged contraction.

"We discovered a key mechanism by integrating genomic data with epigenomic and transcriptomic data," says Kazuo Miyazawa of the RIKEN Center for Integrative Medical Sciences.

Polygenic risk scores can predict a person's genetic susceptibly to diseases, but they are not very reliable when applied to different populations from those whose data they were derived from. By combining the Japanese and European data, the team was able to improve predictions. The higher the score, the younger people were when they developed atrial fibrillation. Additionally, the score was significantly associated with stroke, including fatal ones.

"By applying our model to a person's genome, we can find clinically undetectable heart arrhythmias or other related conditions," explains Miyazawa.

The findings also suggest ideas for treatment. "ERRg represents a potential target for pharmaceutical intervention for those identified as at-risk," says Miyazawa.

Reference

1. Miyazawa, K., Ito, K., Ito, M., Zou, Z., Kubota, M., Nomura, S., Matsunaga, H., Koyama, S., Ieki, H., Akiyama, M. *et al.* Cross-ancestry genome-wide analysis of atrial fibrillation unveils disease biology and enables cardioembolic prediction. *Nature Genetics* **55**, 187–197 (2023).

QUANTUM COMMUNICATIONS

A cleaner, better way to produce single-photon emitters

A vapor-phase reaction makes carbon nanotubes even more attractive as single-photon emitters for quantum technologies

RIKEN scientists have created an effective source of single photons for emerging quantum technologies. They did this by adding molecules to carbon nanotubes using a reaction that occurs in the vapor phase[1].

Quantum technologies are on the verge of revolutionizing computing and communications, promising benefits such as secure communication, ultrasensitive sensing and parallel computing. Many of these applications require light sources that can generate single photons—the smallest packets of light possible—on demand.

> **“This method allowed us to introduce organic molecules without also incorporating undesirable defects.”**

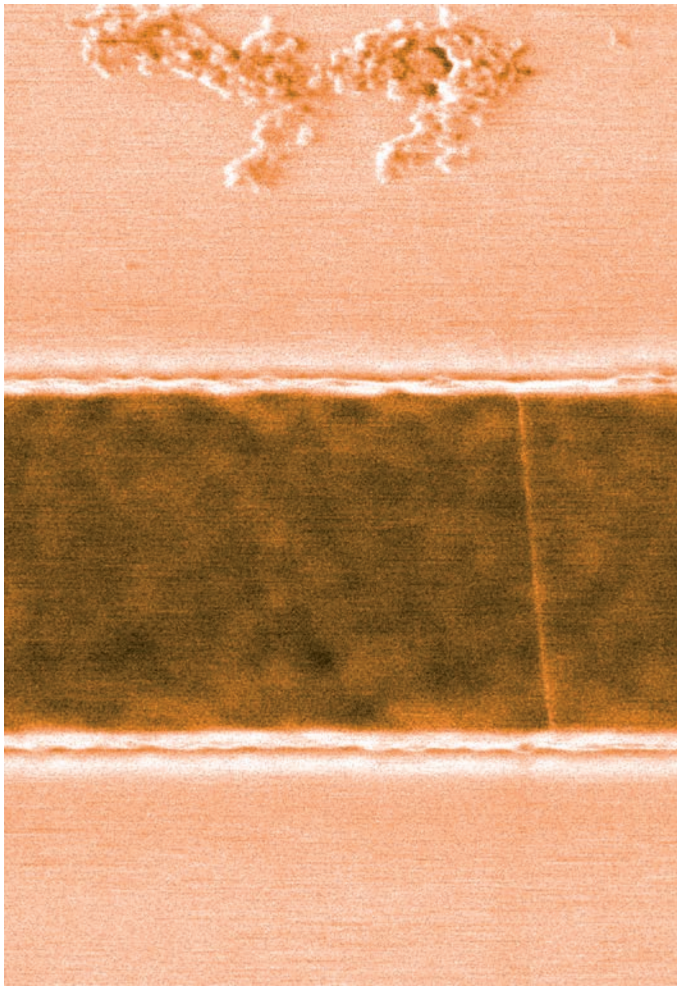
A promising source of single photons in the infrared wavelength range used in telecommunications is carbon nanotubes—cylinders of graphene sheets that are a mere nanometer or so in diameter—that have been imparted with new functions, or functionalized, by adding an organic molecule.

The cleanest way to do this would be to use carbon nanotubes suspended across an air gap, but unfortunately this isn’t compatible with the usual approach of functionalizing carbon nanotubes, which takes place in solutions. “Carbon nanotubes functionalized in solution tend to be really short and have defects all over them,” notes Yuichiro Kato of the RIKEN Center for Advanced Photonics (RAP).

Now, Kato and Daichi Kozawa, also of RAP, and their co-workers have developed a method for functionalizing carbon nanotubes that can be done in the vapor phase, and hence on nanotubes suspended across a trench in a silicon substrate (see image).

“We grew fairly long nanotubes and functionalized them in the vapor phase, so they had no contact with solutions, which contain a lot of impurities,” says Kato. ”This method allowed us to introduce organic molecules without also incorporating undesirable defects.”

The study was a collaboration born out of a pre-pandemic interaction at an international conference. Kato and Kozawa’s team at RAP produced the suspended nanotubes and then sent them to chemists in the University of Maryland in the United States for functionalization, who then sent them back for analysis. “YuHuang Wang at the University of Maryland is a great chemist, and he’s the one who got curious about the possibility of doing these reactions in the vapor phase,” says Kato. “It took us a few rounds, but we were able to see good emission from the organic molecules on the nanotubes.”



A carbon nanotube suspended across a trench in a silicon substrate. By developing a method that allows such suspended nanotubes to be functionalized with organic molecules, RIKEN researchers have enhanced their usefulness for sources of single photons.

The team verified the optical performance of their carbon nanotubes by performing spectroscopic measurements on more than 2,000 of them. They discovered that the number of organic molecules introduced per nanotube increased with smaller diameter nanotubes, and they were able to model this effect in terms of the greater reactivity of narrower nanotubes.

The team now intends to optimize the functionalization process so that just one organic molecule is introduced per nanotube. ●

Reference

1. Kozawa, D., Wu, X., Ishii, A., Fortner, J., Otsuka, K., Xiang, R., Inoue, T., Maruyama, S., Wang, Y. & Kato, Y. K. Formation of organic color centers in air-suspended carbon nanotubes using vapor-phase reaction. *Nature Communications* **13,** 2814 (2022).

QUANTUM DOT SYSTEMS

Nanoscale heat engines

A nanoscale device offers insights into how single electrons interact with vibrations in the presence of a temperature gradient

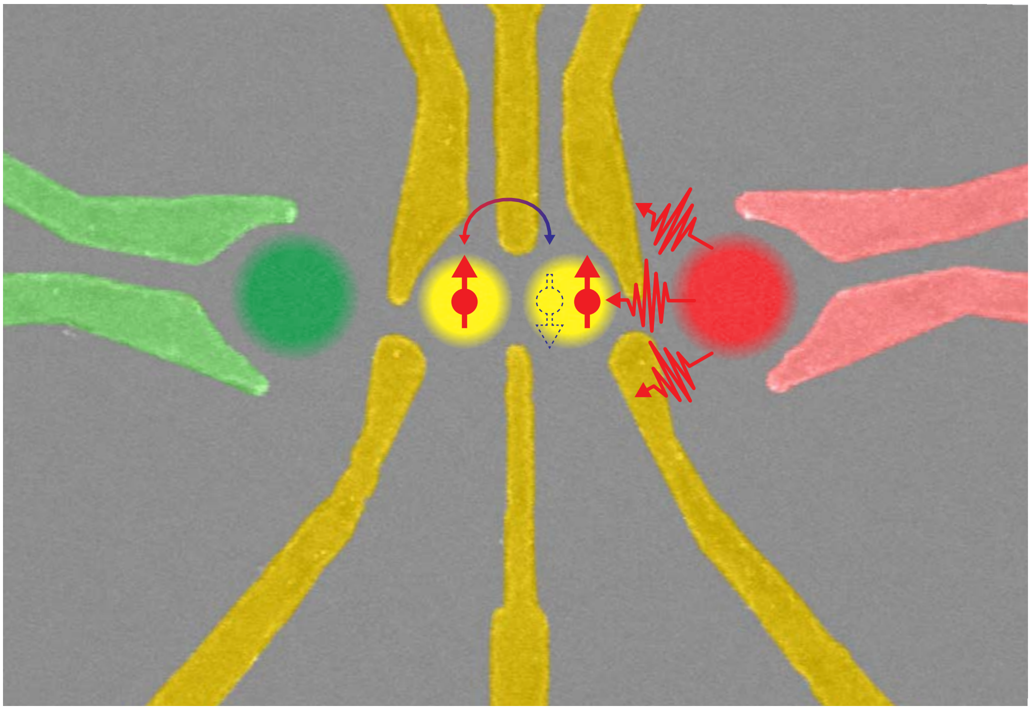
RIKEN physicists have fabricated a nanoscale 'heat engine' that uses a property of electrons known as spin as the effective working medium[1]. It is promising for exploring the development of spintronic heat engines capable of harvesting waste heat from devices.

Heat engines convert a heat difference into more useful forms of energy as heat flows from warmer to cooler regions of electronic devices. Reducing them to the nanoscale would enable waste heat generated to be converted back into electrical energy and thus improve efficiency.

One way to create nanoscale heat engines is to use tiny crystals of semiconductors known as quantum dots. Somewhere in the range of 10 to 100 nanometers in diameter, a quantum dot can trap one or a few electrons.

All heat engines are driven by a difference in temperature—one end of the heat engine needs to be hotter than the other for the heat engine to work. In quantum systems, there are two different temperatures: the temperature of the atoms (or lattice temperature) and that of the electrons.

Previous heat engines based on quantum dots have used reservoirs of electrons at different temperatures. However, to gain a better understanding of the underlying thermodynamics it is desirable to create a heat engine that operates on lattice temperature. But generating a lattice temperature gradient across a few hundred nanometers is technically challenging.



A double quantum dot device enables the study of how the spin and charge of an electron influences thermodynamic action in the presence of a lattice temperature gradient. Lattice vibrations known as phonons (three red squiggles) come from the quantum dot (colored red) on the right, which acts as a local heater. They can cause the spin on of the two electrons (yellow dots) to flip, which is detected by the quantum dot (colored green), which acts as a charge sensor.

Now, Seigo Tarucha at the RIKEN Center for Emergent Materials Science and his colleagues have succeeded in doing this in their quantum-dot heat engine.

In their device, electrons are confined using electric fields generated at surface metal electrodes on a gallium arsenide surface. The device had two interlinked quantum dots and a built-in charge sensor to passively monitor what was going on within the double quantum dot (see image). A third quantum dot was used to control the double quantum dot's thermal environment; effectively, it acted as a local heater.

The researchers anticipate the device will greatly contribute to our understanding of the fundamental physics of thermoelectric devices. "The results give valuable insights into developing spintronic heat engines," says Tarucha. "In particular, this setup will provide an experimental platform for studying the thermodynamics of cooperative spin–charge systems."

The next challenge will be to introduce on-demand control of heat flow in the spin–charge cooperative system. "We're now developing a technique to rapidly switch the heat flow," explains Tarucha. "This will provide a new platform to study the physics and apply for development of spintronic heat engines." ●

Reference

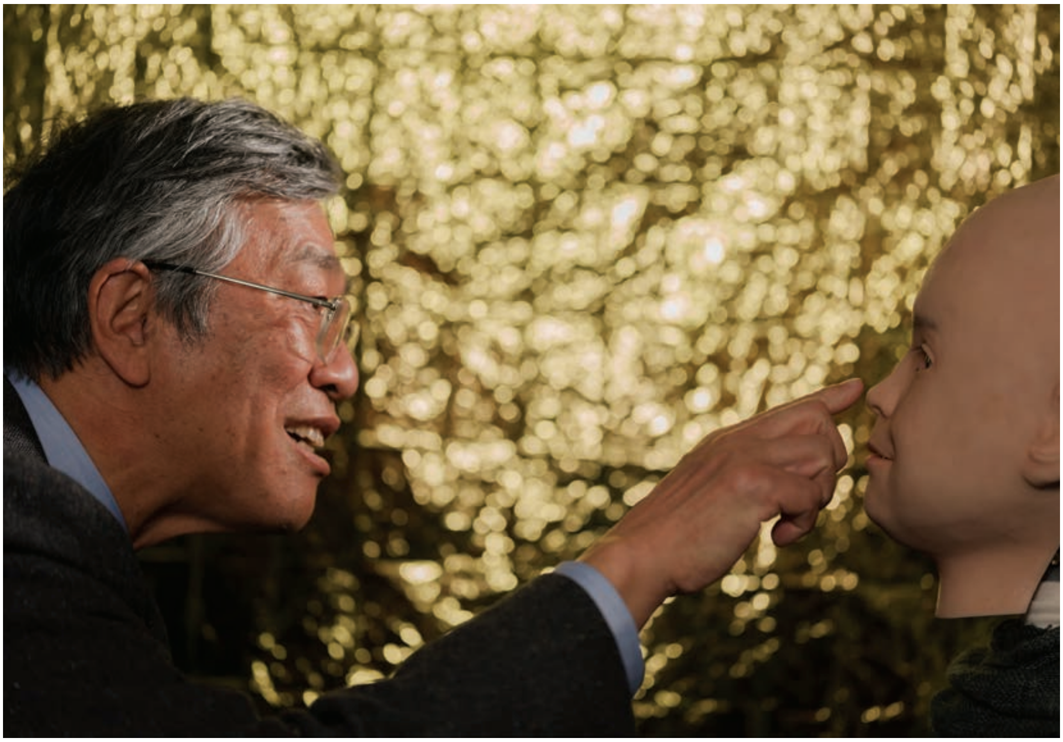
1. Kuroyama, K., Matsuo, S., Muramoto, J., Yabunaka, S., Valentin, S. R., Ludwig, A., Wieck, A. D., Tokura, Y. & Tarucha, S. Real-time observation of charge-spin cooperative dynamics driven by a nonequilibrium phonon environment. *Physical Review Letters* **129,** 095901 (2022).

This modular robotic exoskeleton was designed to help physically impaired users with movements that involve their knees, but only when they truly need support. Such a robot should proactively predict desired movements as a control strategy or risk becoming a burden, says Jun-ichiro Furukawa, an expert on man-machine interfaces.

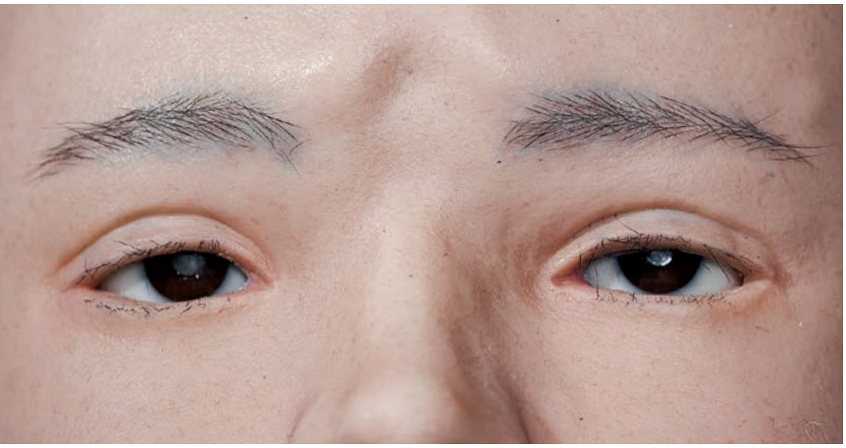
Irwin Wong

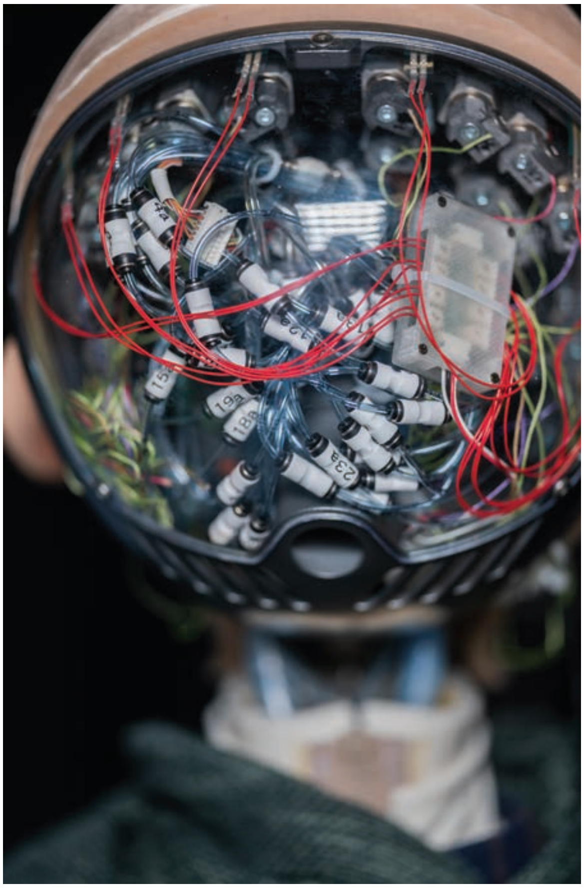
COULD YOU USE A ROBOT HELPER?

In a lab between the cities of Osaka and Kyoto, RIKEN's Guardian Robot Project (GRP) have been working on unobtrusive, autonomous robots designed to assist the public since 2019. Today, they focus on three—an exoskeleton that helps users move; an emotive, conversational robot named Nikola; and a mobile, task-oriented robot called Butsukusa. The initiative is helping these 'Guardian robots' recognize their environment and the state of the person they are supporting, so that they can help without limiting the autonomy of users. With Japan's population ageing more rapidly than anywhere else in the world, and the global market for nursing robots projected to reach US$2.2 billion by 2026, the technology behind the GRP's robots could soon be seeing much wider use. →



Michihiko Minoh (right) is a former executive director at RIKEN and he is currently director of the infrastructure research and development division. Here Minoh interacts with conversational robot Nikola. Minoh has led RIKEN's Guardian Robot Project since its launch in April 2019.





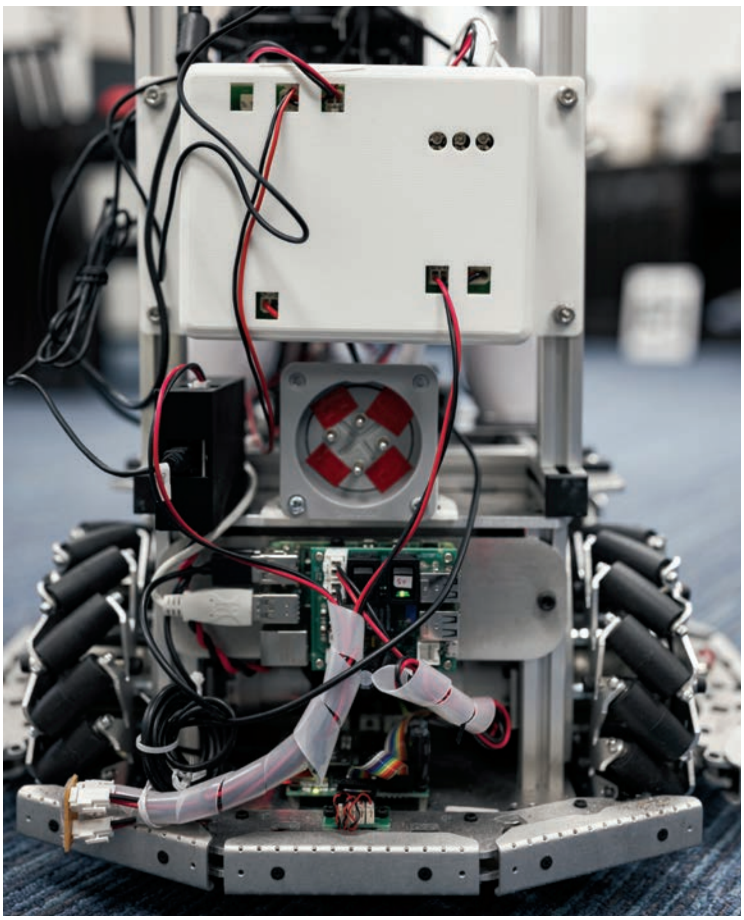
Testing involving 30 human subjects demonstrated that the robot 'child' Nikola (above and right) can recognizably show expressions that appear to evoke fear, happiness, surprise, disgust, anger and sadness. However, the fact that Nikola seems young is no mistake—its skin is still less elastic than natural human skin and does not perfectly mimic wrinkles. This makes disgust and a few other complex emotions harder to identify, although the absence of a nose wrinkling actuator contributes to this problem.

Nikola's face contains a total of 29 pneumatic actuators responsible for the control of artificial muscles. Six more actuators simulate realistic movements of the head and eyeballs. The actuators are controlled by air pressure to allow silent and smooth movements. Tests have revealed that emotions that are slower to settle on the face on humans, such as sadness, seem less realistic. Machine learning methods are aiding further improvements to Nikola's expressive range.

Irwin Wong

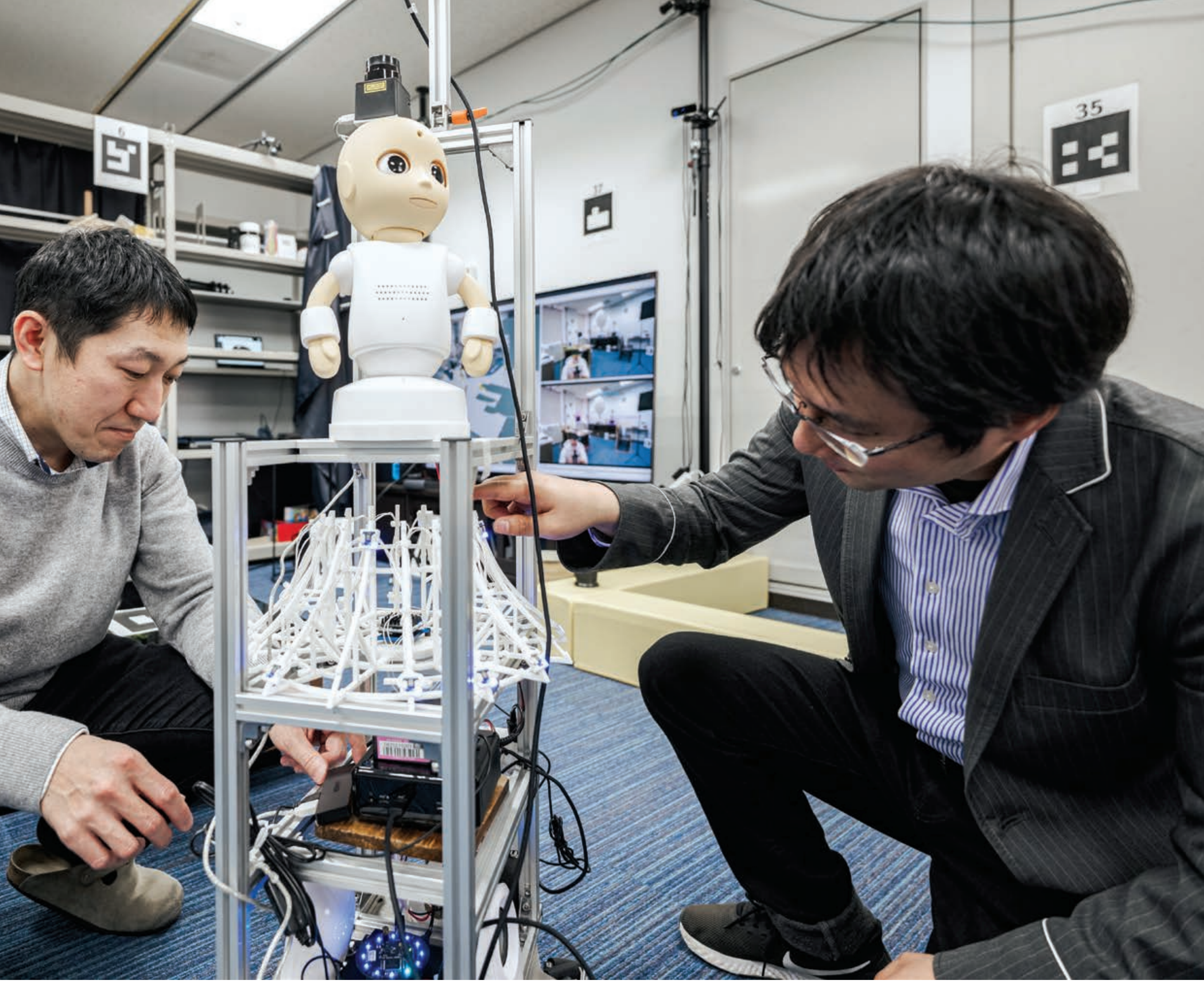
The GRP's exoskeleton, made of lightweight carbon fiber, uses artificial intelligence to predict and detect how a user wants to move, based on pattern recognition of the angle of the knee joint and electrical activity in the muscles picked up by sensors attached to the skin.

Wataru Sato (at right), leader of the Psychological Process Research Team, and Takashi Minato, leader of the Interactive Robot Research Team, stand with emotive android, Nikola, which will be used in social psychology experiments. The researchers may wish to examine, for instance, to what degree expressions of warmth from the robot reduce stress levels in aged care residents, allowing them to gather new information on how humans emotionally interact with robots.

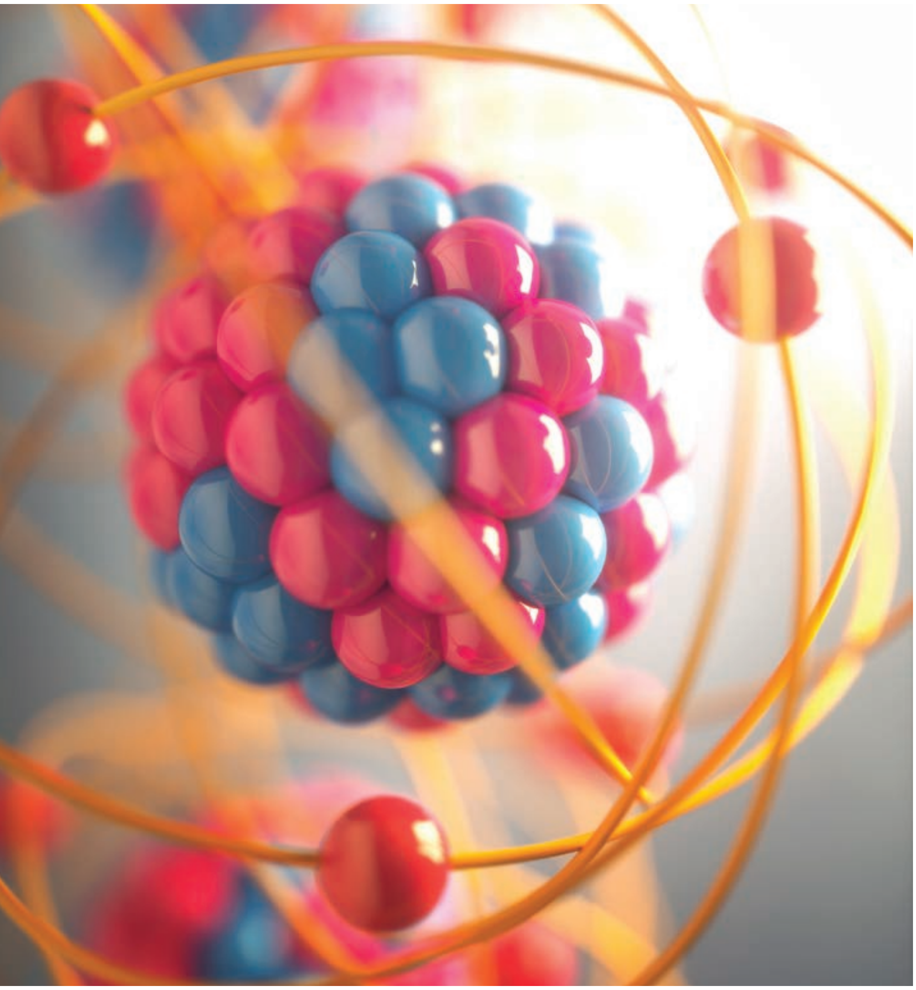


Irwin Wong

Task-oriented mobile robot, Butsukusa, autonomously patrols one of the GRP's rooms guided by a camera-and-laser system that helps it measure distance. It uses a deep-learning driven recognition module to identify objects, humans and the environment (above), as well as its location and speech. A combination of sensors that take in audio, visual and thermal information has been proposed to increase its ability to recognize people and their emotions.



A yet to be completed model of the GRP's patrol robot, Butsukusa (above), will be able to pick up objects using a robotic arm that is still in development (left). Yasutomo Kawanishi (above, at left), who leads the Multimodal Data Recognition Research Team, and Yutaka Nakamura, who leads the Behavior Learning Research Team, have developed a machine-learning based framework for Butsukusa, which roughly translates to muttering. Butsukusa's framework allows it to narrate what it has done in natural language. By describing the physical environment; its internal states during autonomous patrols; and what it tried to do and the result, Butsukusa helps the researchers understand its thinking and reasoning, and how it comes to its conclusions.



KTSDESIGN/SCIENCE PHOTO LIBRARY

STUFFING sodium nuclei with neutrons

Nuclear physicists have made the most neutron-rich form of sodium yet, which will help reveal more about the complex world of nuclei.

An extremely neutron-rich form of the element sodium—which many models of atomic nuclei predict shouldn't exist—has been created by nuclear physicists at RIKEN for the first time[1].

If you made table salt from this super-heavy version of sodium—and the most neutron-rich isotope of chlorine, salt's other constituent—it would taste and behave like normal salt, except it would be roughly 1.6 times heavier, says nuclear physicist Toshiyuki Kubo.

But far more than being a scientific curiosity, this finding has important implications for theories on the structure of atomic nuclei. This knowledge in turn informs our understanding of the astrophysical processes that form Earth's heavier elements.

In terms of nuclear theory, the finding provides a vital reference point for tweaking models of neutron-rich nuclei and for assessing their accuracy, explains Kubo. Theoretical studies of neutron-rich nuclei involve extremely complicated calculations, and theoretical physicists have so far only been able to precisely model more stable nuclei with few neutrons. This finding could help refine calculations for nuclei with more neutrons.

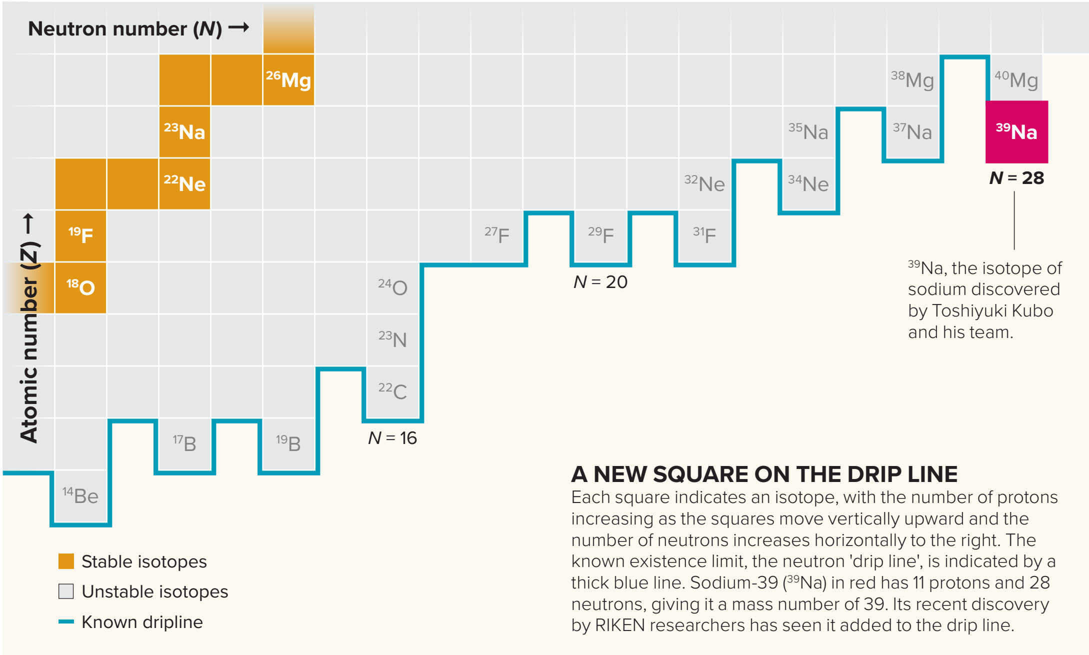
This in turn has implications for our understanding about the origins of heavier elements. For example, the nuclear astrophysical processes that create Earth's heavy metals are thought to be the result of the huge amounts of energy produced by the merger of two neutron stars or collisions of neutron stars and black holes. The gas and dust released eventually contribute to the rare materials of planets, such as Earth. However, the exact processes that produce heavy metals have long been debated.

PACKING NEUTRONS INTO SODIUM

Each of the 118 known elements has a fixed number of protons (11 in the case of sodium), but the number of neutrons in its nuclei has can vary, notes Kubo. The only stable form of sodium contains 12 neutrons, whereas the newly discovered one has more than double at 28, which is two more neutrons than the previous record holder for the most-neutron-rich isotope of sodium, ^{37}Na, which was discovered more than 20 years ago.

Since neutrons are electrically neutral, they don't influence an atom's electrons and hence have no effect on the element's chemistry. Thus, atoms of the same element that contain different numbers of neutrons—known as isotopes—are chemically indistinguishable.

The impetus to search for the new form of sodium (called ^{39}Na because its nucleus contains 39 neutrons and protons) came from a previous experiment, when a team led by Kubo at the RIKEN Nishina Center for Accelerator-Based Science stumbled upon what appeared to be one nucleus of ^{39}Na. "We were very surprised at this one event," recalls Kubo. "And so,



A NEW SQUARE ON THE DRIP LINE
Each square indicates an isotope, with the number of protons increasing as the squares move vertically upward and the number of neutrons increases horizontally to the right. The known existence limit, the neutron 'drip line', is indicated by a thick blue line. Sodium-39 (^{39}Na) in red has 11 protons and 28 neutrons, giving it a mass number of 39. Its recent discovery by RIKEN researchers has seen it added to the drip line.

This feature looks **at the work of** **TOSHIYUKI KUBO**

Toshiyuki Kubo is a RIKEN honorary scientist and a research consultant at RIKEN Nishina Center for Accelerator-Based Science (RNC). He earned his undergraduate in physics from the University of Tokyo in 1978, and his PhD in experimental nuclear physics from the Tokyo Institute of Technology in 1985. He joined RIKEN as an assistant research scientist in 1980, and was promoted to a research scientist in 1985 and to a senior research scientist in 1992. In 2001, he became the team leader of BigRIPS team, and was promoted to the group director of research instruments group at RNC in 2007. In 2016, he was appointed as a professor at Facility for Rare Isotope Beams, Michigan State University in USA, where he worked as a visiting scientist in 1992–1994. His current research interests include experimental studies on very neutron-rich nuclei, the search for new isotopes, the production of rare isotope beams, and in-flight separator issues.

we decided to revisit the search for ^{39}Na in our present experiment."

In the latest experiment, they put the existence of ^{39}Na beyond all doubt by creating nine nuclei of the isotope in a two-day run at RIKEN's Radioactive Isotope Beam Factory—one of only about three nuclear facilities in the world currently capable of producing such nuclei.

ISOTOPE HUNTER

It's far from the first time that Kubo has helped to create a new isotope during his four-decade-long career. "Actually, I've been involved in discoveries of about 200 new isotopes or so," he says. "I really enjoy creating and observing what nobody has ever seen before."

But the discovery of ^{39}Na, has special significance for him, not least because many nuclear models predict that it shouldn't exist. "The discovery makes a significant impact on nuclear mass models and nuclear theories that address the edge of the nuclear stability, because it provides a key benchmark for their validation," explains Kubo. For example, Kubo notes that a model developed by a Japanese team in 2020 correctly predicted the existence of ^{39}Na and its predictions for other isotopes have been on target[2], boosting its credibility.

TRACING THE DRIP LINE

One reason the discovery is important is because ^{39}Na could well be the most neutron-rich version of sodium that it is possible to produce. Nuclear physicists are particularly interested in determining the maximum number of neutrons an element can have before it starts leaking neutrons—a quantity known as the neutron drip line when plotted on a table of nuclei. The location of this limit provides a key benchmark to not only nuclear theories, but also nuclear mass models that play a key role in theories of nucleosynthesis.

But it is extremely difficult to ascertain the drip line for an element—nuclear physicists have so far only succeeded in determining it up to the tenth element in the periodic table, neon, which means they still have 108 more elements to go.

One reason why it is hard to measure the dripline is because of the tiny possibilities involved in creating nuclei that lie close to limits of stability. Another difficulty is that it is extremely challenging to rule out the existence of other nuclei that have even more neutrons. Kubo says that it may be possible to make ^{41}Na, in which case it would become the dripline for sodium, although he notes that the 2020 Japanese model predicts that ^{39}Na is the drip line.

Next Kubo and his team intend to attempt to experimentally determine the dripline for magnesium—one element up from sodium. They also want to probe the structure of ^{39}Na. "We would like to directly study the nuclear structure that allows ^{39}Na to exist," Kubo explains.

REFERENCES

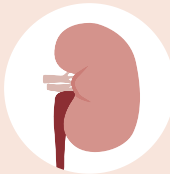
For a complete list of references, see the online version of this article: www.riken.jp/en/news_pubs/research_news/

HIBERNATING THROUGH SURGERY

During heart surgery, the kidneys can be damaged due to a lack of blood flow. The standard intervention for this involves cooling the body to a risky hypothermic state. Bringing about a different hibernation-like 'hypometabolic' state, which reduces the body's need for oxygen, could protect the kidneys with fewer side effects. RIKEN's Laboratory for Hibernation Biology has demonstrated how both hypometabolic and hypothermic states protect mouse kidneys when blood flow is stopped. Mice, however, can go into a daily torpor, an energy-saving, hibernation-like state. Humans do not, and so similar results in humans are likely some way off.

WHAT IS A HYPOMETABOLIC STATE?

During a hibernation-like hypometabolic state, normal physiological activities are suspended. It's often a response to environmental stress — such as cold temperatures or lack of food — providing animals with a greater chance to survive.



WHY INDUCE A HYPOMETABOLIC STATE?

Inducing hypothermia is standard to protect the kidneys when blood flow is stopped during heart surgery. But this can bring about dangerous complications, such as 'coagulopathy', which causes excessive bleeding. Inducing hypothermia also requires difficult blood transfusions. In theory, inducing a hypometabolic state could protect the kidneys from damage without some of these side effects.

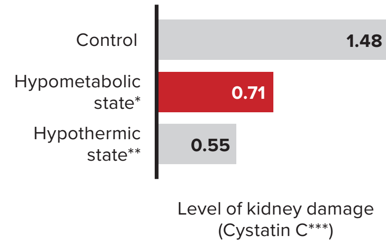
HOW WELL DID AN INDUCED HYPOMETABOLIC STATE PROTECT THE KIDNEYS?

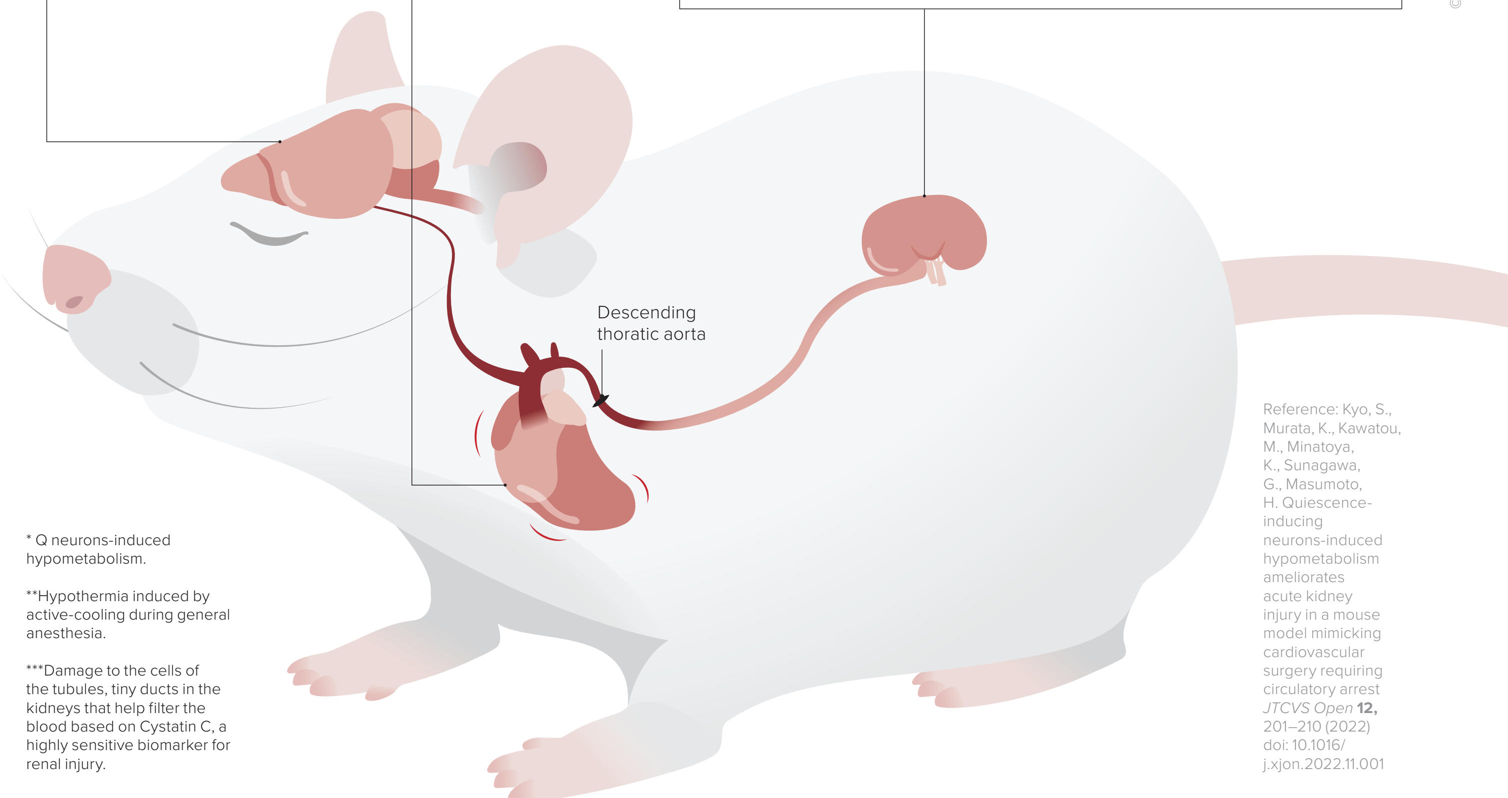
1 **Q neurons were stimulated.** In genetically modified mice, a hypometabolic state was induced by administering a chemical, clozapine-N-oxide. This excites a special group of neurons called quiescence-inducing neurons (Q neurons).

2 **Blood flow was stopped.** A clamp was placed across the descending thoracic aorta preventing blood from entering the kidneys.

3 **KIDNEY DAMAGE**

After blood flow from the heart is stopped, an induced hypometabolic state reduced kidney damage to a level similar to cooling the mouse body to a hypothermic state. In contrast, in a control mouse that didn't benefit from either intervention, the kidney damage was roughly two to three times as severe.





* Q neurons-induced hypometabolism.

**Hypothermia induced by active-cooling during general anesthesia.

***Damage to the cells of the tubules, tiny ducts in the kidneys that help filter the blood based on Cystatin C, a highly sensitive biomarker for renal injury.

Reference: Kyo, S., Murata, K., Kawatou, M., Minatoya, K., Sunagawa, G., Masumoto, H. Quiescence-inducing neurons-induced hypometabolism ameliorates acute kidney injury in a mouse model mimicking cardiovascular surgery requiring circulatory arrest *JTCVS Open* **12**, 201–210 (2022) doi: 10.1016/j.xjon.2022.11.001

RIKEN'S CENTERS AND FACILITIES
across Japan and around the world

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

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

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

NAGOYA

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

SENDAI
- ● Center for Advanced Photonics (RAP)

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

TOKYO
- ● Center for Advanced Intelligence Project (AIP)
- ▼ RIKEN Center for Computational Science (R-CCS)
- ▼ RIKEN Information R&D and Strategy Headquarters (R-IH)

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

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

OSAKA
- ● Center for Biosystems Dynamics Research (BDR)

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

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

RIKEN RESEARCH

www.riken.jp/en