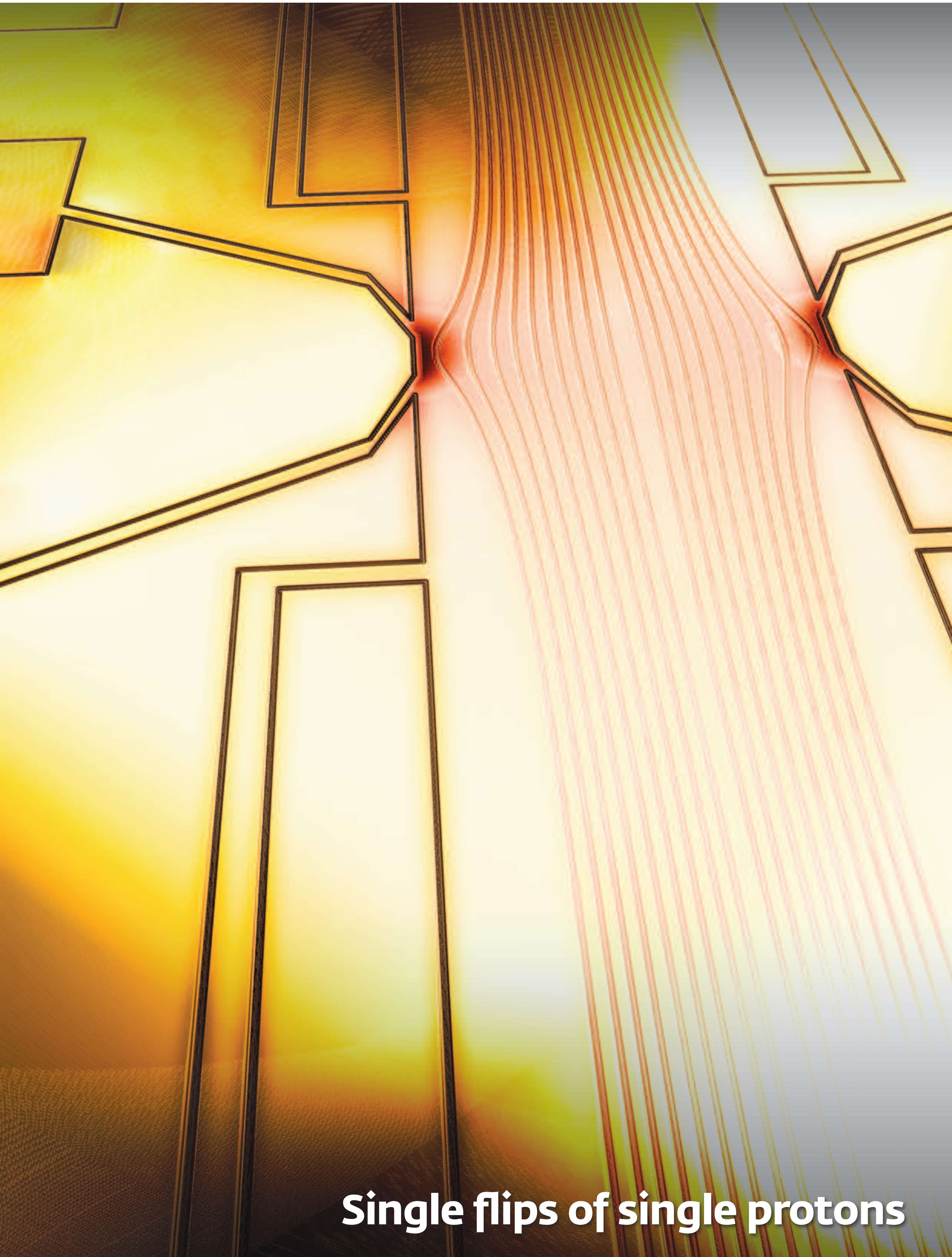
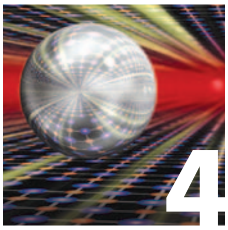
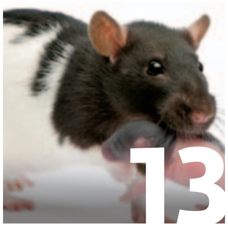
RIKEN RESEARCH
AUGUST 2013
VOLUME 8 NUMBER 8



RIKEN PLACES: The Advanced Institute for Computational Science in Kobe is the home of the K computer

Table of contents





RIKEN RESEARCH

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Materials

Putting the heat on semimetals

A layered semimetal laced with atomic impurities offers highly efficient conversion between heat and electrical current

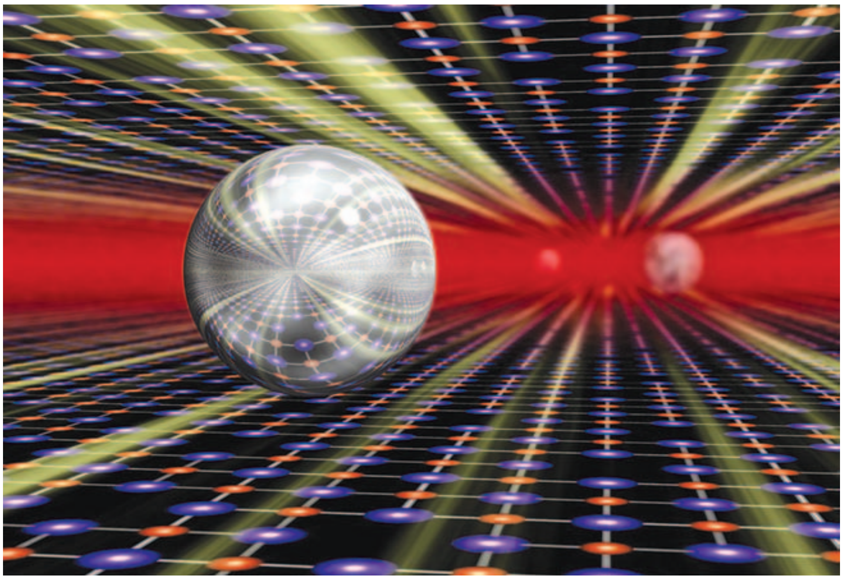


Figure 1: Electrons in the layered semimetal CuAgSe can move particularly fast through the material.

In the early twentieth century, the very notion of a semiconductor—a material that behaves somewhere between an electrical conductor and insulator—was something even the leading physicists of the time thought improbable and unappealing. Yet we now find that semiconductors have become the bedrock of modern electronics. Semimetals are similarly unclassifiable as either metal or non-metal, and like the early days of semiconductors, their utility in electronics has so far been limited. Shintaro Ishiwata and colleagues from the RIKEN Center for Emergent Matter Science (CEMS), in collaboration with researchers from the University of Tokyo, have now found a layered semimetal compound that provides unprecedented efficiency of heat to electric current conversion at room temperature[1], greatly expanding the possible applications of semimetals as thermoelectric materials.

From byproduct to main focus

Ishiwata, previously from the CEMS and now with the University of Tokyo, had led a collaborative team in research on novel 'spintronic' devices—systems in which the magnetic properties of electrons are used rather than their electrical charge. Through those studies, the team discovered that a byproduct produced during their research, silver selenide (Ag_2Se), displayed some interesting properties. The electrical resistance of the material was found to change remarkably depending on its interaction with magnetic fields. This effect, known as giant magnetoresistance (GMR), is used widely in modern electronic devices to read information from magnetic hard disk drives. Furthermore, the material also displayed high thermoelectric efficiency, generating a heat gradient when it passes an electrical current or generating an electrical current when cooled on one side and heated on the other. The combination of GMR and high thermoelectric efficiency is unusual, and the occurrence of GMR, in particular, shows that electrons can flow very easily through the material.

These behaviors had already been reported before for Ag_2Se, but Ishiwata and his colleagues were spurred to look deeper. "We started studying related materials and found that one of them, CuAgSe, shows stronger GMR effects and better thermoelectric efficiency," he says. CuAgSe is a multilayered semimetal consisting of alternating layers of silver (Ag) and copper selenide (CuSe) (Fig. 1).

Although Ishiwata notes that his research on CuAgSe began by "accident," it turned out the material presented some exciting possibilities. The team's work showed that the electrons in CuAgSe are particularly mobile, increasing its usefulness for device applications. More interesting, however, was the discovery that the electron mobility was increased when the material had been 'doped' with nickel atoms. Atomic impurities interrupt the regular atomic lattice of the host material and can be used to manipulate a material's bulk electronic properties. Impurity doping, for example, is a conventional method used to control the conductive properties of semiconductors, and also the thermal and electrical conductive behavior of thermoelectric materials. However, the introduction of impurities generally has the unwelcome side effect of

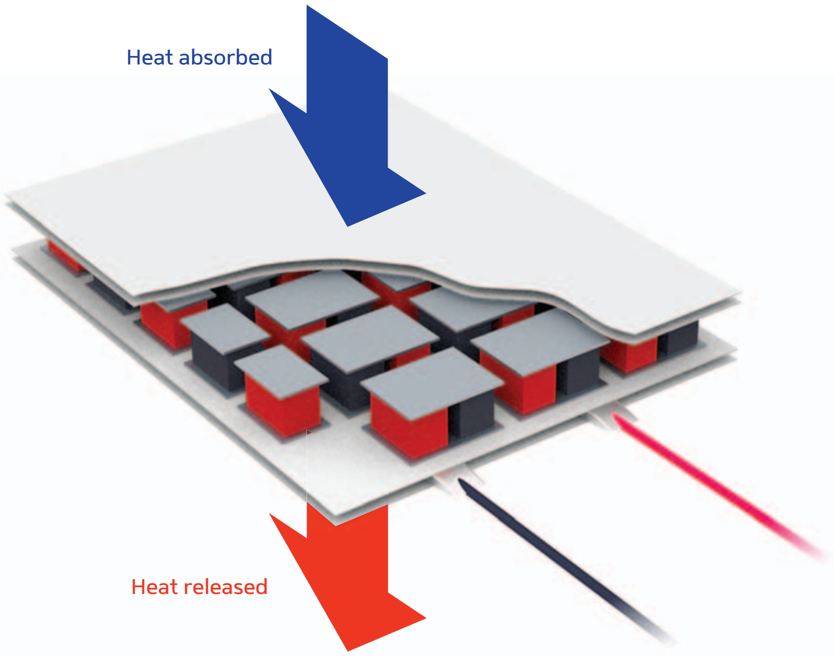


Figure 2: Peltier elements use an electric current to drive the transfer of heat from one side of the device to the other.

reducing the material's electrical conductivity, thereby impairing its overall performance. Contrary to this typical behavior, Ishiwata's team found that this is not the case in CuAgSe. "After the addition of nickel to CuAgSe, the electron mobility increased, even if we created a chemically 'dirty' system," says Ishiwata.

By overcoming the traditional trade-off between 'polluting' the material in order to improve the thermoelectric performance and reduce electron mobility, the team has created a promising material that opens up the possibility of a range of interesting and new applications. One use of the technology the researchers have in mind involves applying the material as a Peltier cooling element (Fig. 2), in which electrical current is used to transfer heat from one side of the device to the other.

"So far, thermoelectric materials that work at low temperatures are limited to bismuth-based materials. Materials based on silver and copper are now promising candidates that offer better thermoelectric performance near or below room temperature," says Ishiwata. The increase in electron mobility achieved by doping also enhances the GMR performance, although GMR in this material only appears at very low temperatures, making it less promising for practical applications.

The benefits of collaboration

Further work will now be done to optimize the thermoelectric performance of the CuAgSe material. "For this, we are planning to collaborate with specialists in transmission electron microscopy," says Ishiwata. Electron microscopy observations will provide deeper insight into the structure of the material and especially how the impurities are organized. Collaboration, explains Ishiwata, has been a strong driving force throughout the project. Researchers with many different backgrounds come together at the CEMS and also within the collaboration between RIKEN and the University of Tokyo. "It is difficult to imagine that this project would have been successful elsewhere; the research groups cover such a broad range of condensed-matter science, and we have the opportunity to discuss ideas with each other frequently, which is essential for this kind of serendipitous work."

Semiconductors, the very existence of which was doubted in the past, can claim full responsibility for making modern electronics possible. Advanced thermoelectric materials like CuAgSe also have a lot to offer: they achieve their useful functionality without movable parts, they are compact, and they already have the potential for use in the cooling elements of various electronic devices and consumer products such as portable coolers (Fig. 2). The discovery of high-performance thermoelectric materials, and in particular the demonstration of doping-enhanced electron mobility, provides a promising new platform for exploring and harnessing thermoelectric effects.

1. Ishiwata, S., Shiomi, Y., Lee, J. S., Bahramy, M. S., Suzuki, T., Uchida, M., Arita, R., Taguchi, Y. & Tokura, Y. Extremely high electron mobility in a phonon-glass semimetal. *Nature Materials* **12**, 512–517 (2013).

ABOUT THE RESEARCHER

Shintaro Ishiwata was born in Tokyo, Japan, in 1975. He graduated from Kyoto University in 1998 and obtained his PhD in 2003 from the same university. Following a year of postdoctoral research, Ishiwata moved to Waseda University as a JSPS research fellow and later became a visiting researcher at Princeton University in the United States. Upon returning to Japan, he worked on the ERATO–JST multiferroics project and then joined the Cross-Correlated Materials Research Group at RIKEN. In 2010, he moved to the University of Tokyo where he has been an associate professor since 2012. Ishiwata is also a visiting research fellow at the RIKEN Center for Emergent Matter Science. His research explores new materials that exhibit useful properties such as thermoelectricity, spintronics and superconductivity.

Iridium's new lustre

The prediction of superconductivity in compounds based on iridium oxide opens a new chapter for superconductors

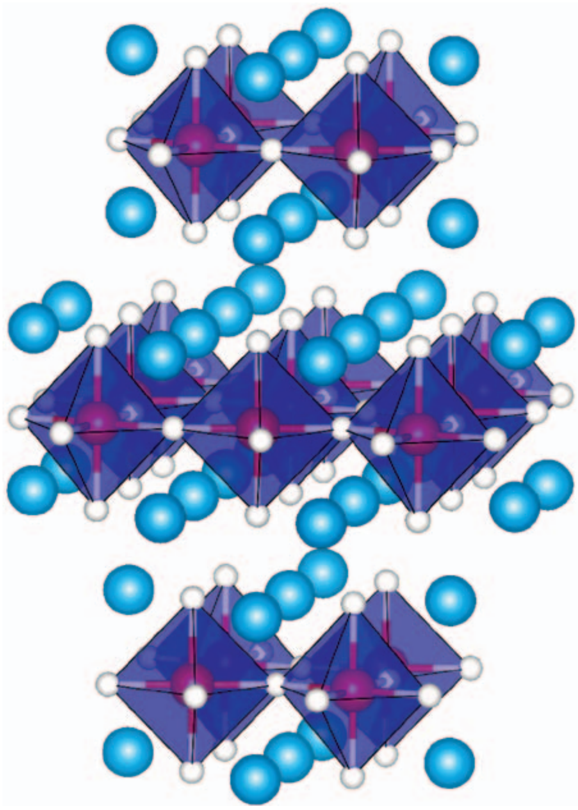


Figure 1: The layer-like crystal structure of the iridium oxide Sr_2IrO_4. Strontium, iridium and oxygen atoms are shown in blue, red and white, respectively.

High-temperature superconductors are some of the most widely studied materials in physics, where the discovery of new compounds often provides insight into the complex physics that underlies them, as well as revealing interesting new electronic phenomena. Seiji Yunoki and colleagues from the Computational Quantum Matter Research Team at the RIKEN Center for Emergent Matter Science may have made such a discovery through their prediction of an unconventional superconducting phase in compounds based on iridium oxide[1].

The high-temperature superconductors commonly investigated by scientists are often copper oxide structures consisting of different atomic layers stacked on top of each other. It is along these atomic planes that the superconducting electrical currents flow. Interestingly, the iridium oxide Sr_2IrO_4 studied by Yunoki and his colleagues has a very similar layered structure (Fig. 1). The magnetic arrangement of the atoms in these layers—important for the superconducting state in such materials—is also similar to that in copper oxides.

Not everything in the iridium oxide system is comparable to that in copper oxides, however. Iridium is a far heavier element than copper, and its outer electrons circle the atomic cores at a much greater distance. The different path of these electrons also influences their magnetic property, or spin. Indeed, 'spin-orbit coupling' leads to very different spin effects in the iridium oxides that influence not only superconductivity, but also other electronic properties—including those that make iridium oxides of possible interest for electronics applications.

"A number of groups have tried to make iridium oxide superconductors," says Yunoki. "So far, they have been able to make the compound metallic, but they have not yet succeeded in making it superconducting."

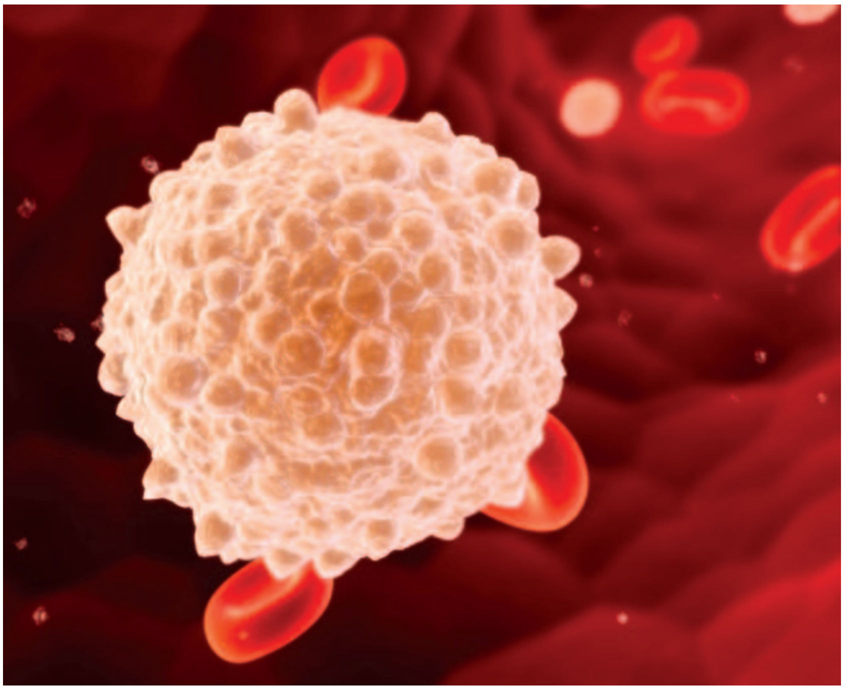
To probe the possible reasons for the elusiveness of superconductivity in iridium oxides, Yunoki's team developed a theoretical model to describe the compound's properties. They were able to calculate that superconductivity could be achieved by introducing atoms of other elements to provide a surplus of electrons—a process known as electron doping. "This is exactly where our theoretical work becomes valuable," says Yunoki. "We have provided a guideline by showing that, as opposed to copper oxides, the superconductivity in Sr_2IrO_4 appears most likely with an electron surplus, not with a deficit."

The researchers now plan to assist in the search for iridium oxide superconductors, and to investigate possible applications of their compound's spin properties in electronics. Already one of the rarest elements in the Earth's crust, iridium's true value may therefore be hiding in its useful electronic properties.

1. Watanabe, H., Shirakawa, T. & Yunoki, S. Monte Carlo study of an unconventional superconducting phase in iridium oxide J_{eff} = 1/2 Mott insulators induced by carrier doping. *Physical Review Letters* **110**, 027002 (2013).

Helping cells make a commitment

Multiple levels of gene inhibition help determine and maintain the developmental destiny of immune cells



Researchers at RIKEN have investigated the role of the *Thpok* gene in the development of the two classes of immune T cells.

Immune T cells can be broadly categorized into two classes: cytotoxic T lymphocytes (CTLs), which directly kill infected or cancerous cells, and helper T cells, which coordinate the overall immune response. Immature T cells commit to one or the other lineage via a process called positive selection, and generally remain locked into their developmental fate from that point onward. A research team led by Ichiro Taniuchi of the RIKEN Center for Integrative Medical Sciences have now gained insight into how these cells remain dedicated to their career path[1].

It is known that the *Thpok* gene is a critical activator of helper T cell development, and gets switched off in developing CTLs by a regulatory region called the silencer. However, Taniuchi's team determined that the silencer only provides the initial deactivation signal, and requires further support to make its orders 'official'.

Many genes undergo what is known as epigenetic regulation through the addition of various chemical modifications to the chromosome. For instance, different patterns of 'histone methylation' can either activate or repress nearby genes. The researchers determined that while the silencer facilitates the accumulation of repressive methylation patterns at the *Thpok* gene in CTL precursors, helper T cell precursors exhibit activating methylation patterns. When the researchers selectively deleted the silencer in cells that had already committed to CTL development, *Thpok* remained repressed, indicating that these marks are critical to long-term inhibition of this gene.

Taniuchi and his colleagues found that by engineering additional copies of the silencer region into the *Thpok* gene, they could induce repression in helper T cells where the gene would otherwise be active. If introduced into T cell precursors, these additional silencer copies caused the accumulation of repressive histone methylation marks normally observed in CTLs, and disrupted normal helper T cell development. This demonstrates the critical role of the silencer in establishing T cell fate.

"Our finding that the epigenetic processes that stably silence *Thpok* can occur independently of commitment to the cytotoxic-lineage is striking," says Hirokazu Tanaka, lead author of the study.

Importantly, their work also suggests how these instructions might be overridden. Previous studies have suggested that prolonged signaling via the T cell receptor (TCR) specifically promotes helper T cell development, and these prolonged signals may work by preventing inhibitory modifications that would otherwise accumulate through the influence of the *Thpok* silencer. "Our findings provide for the first time an epigenetic view as to why persistent TCR signals are necessary," says Tanaka.

1. Tanaka, H., Naito, T., Muroi, S., Seo, W., Chihara, R., Miyamoto, C., Kominami, R. & Taniuchi, I. Epigenetic *Thpok* silencing limits the time window to choose CD4+ helper-lineage fate in the thymus. *The EMBO Journal* **32**, 1183–1194 (2013).

A new tool for engineering crop tolerance

Tolerance of phosphorus limitation in plants is linked to a previously unidentified lipid family

Phosphorus (P) is one of three major nutrients required by plants but is lacking on approximately 40% of the world's arable land. Understanding the mechanisms that plants have evolved to cope with P limitation could therefore facilitate the engineering of P-limitation tolerant crops. Kazuki Saito, Yozo Okazaki and colleagues from the RIKEN Center for Sustainable Resource Science and other institutions in Japan have now identified a new class of plant lipid that is essential for P-limitation tolerance[1].

Phosphorus-rich phospholipids are the primary component of plant cellular membranes, and plants can mobilize P during times of scarcity by replacing phospholipids with non-P glycerolipids. However, little was known about these non-P glycerolipids due to difficulties in differentiating and characterizing plant lipids, which comprise hundreds of molecules yet are distinguishable only through slight differences in structure.

Saito's team used a novel mass spectrometry technique they developed previously for untargeted lipid profiling to produce distinctive molecular signatures that could be used for identification. Lipid profiles obtained for the model plant *Arabidopsis* grown under both P-limited and P-sufficient conditions revealed that the membranes of P-limited plants contained fewer phospholipids and more non-P glycerolipids. Most interestingly, the analysis revealed a previously unknown lipid, UK1.

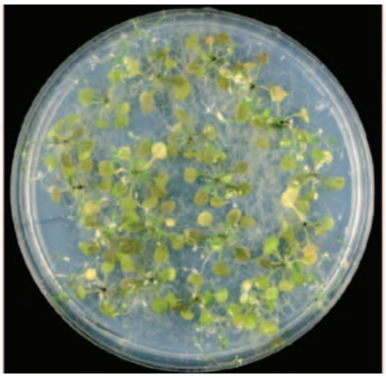
The mass spectrum data of UK1 matched the signature of GlcADG, a known fungal and bacterial lipid. The researchers could also show that the fatty acid portion of GlcADG is almost identical to that of SQDG, a non-P lipid, suggesting that both are partially produced by the same biochemical pathway.

To determine the function of GlcADG, Saito's team grew mutant and wild-type *Arabidopsis* plants in P-limited conditions. They found that mutants lacking both GlcADG and SQDG were severely damaged, displaying bleached leaves and reduced chlorophyll content (Fig. 1). However, plants that could produce at least one non-P glycerolipid—GlcADG—were healthy.

"Under P-limited conditions, membrane composition drastically changes to mobilize phosphorus, but membranes must still provide a suitable biochemical environment for essential enzymes," explains Okazaki. GlcADG thus appears to aid in tuning the low-P membrane environment for enzyme function.

Saito's team now plans to explore the pathways that produce GlcADG's basic components. "Understanding this mechanism would make it feasible to engineer the tolerance of plants against a low-phosphorus environment," says Saito. Given the finite global resources available for phosphorus fertilizers, P-limitation tolerant plants could be vitally important for future agriculture.

1. Okazaki, Y., Otsuki, H., Narisawa, T., Kobayashi, M., Sawai, S., Kamide, Y., Kusano, M., Aoki, T., Hirai, M. Y., & Saito, K. A new class of plant lipid is essential for protection against phosphorus depletion. *Nature Communications* **4**, 1510 (2013).



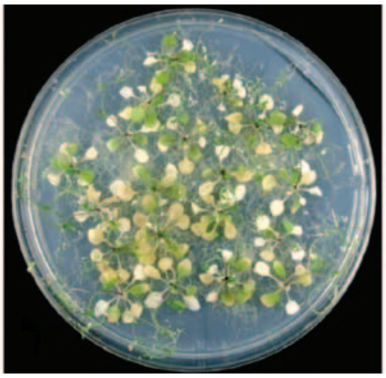


Figure 1: Wild-type (left) and mutant (right) *Arabidopsis* plants grown under phosphorus-limited (P-limited) conditions.

Searching for quantum physics in all the right places

An improved method for measuring quantum properties offers new insight into the unique characteristics of quantum systems

The properties of quantum physical systems are fundamentally different to those of classical systems in a way that makes them attractive for applications such as computing and communications. However, it is often difficult to determine whether a system is in a quantum or classical physical state. Franco Nori and colleagues from the RIKEN Center for Emergent Matter Science, together with collaborators in Taiwan, have now developed a mechanism that permits the reliable detection of quantum properties—even in complex systems[1].

The unique behavior of quantum states arises from the superposition of different states—a property known as quantum coherence. The physicist Erwin Schrödinger famously compared the concept of quantum coherence to a theoretical experiment in which a cat is sealed in a box with a vial of poison to be released by a random quantum mechanism. Without looking inside the box, it cannot be known whether the cat is dead or alive; the cat is therefore in a quantum coherent state. While some quantum states are used for computing, they also occur in nature—in certain biomolecules, for example.

Measuring the properties of quantum systems is important to further their technological utility. Unfortunately, existing measurement methods are impractical due to their complexity and the constraints they place on the quantum states that can be detected.

"Our main goal was to devise an unambiguous test that is easy and practical to implement, and which relies on as little 'foreknowledge' of the system as possible, to determine its quantum properties," explains Neill Lambert, a member of the research team.

The detection scheme developed by Nori, Lambert and colleagues involves the introduction of two 'quantum witnesses' that allow the comparison of two runs of an experiment: one in which the state of a system is observed twice, and one where it is only observed once. This procedure effectively sums the results of multiple random experiments to test whether there is any deviation from the expected classical values, which would provide evidence for a quantum state (Fig. 1). For Schrödinger's cat, such a deviation would suggest that the cat is neither dead nor alive but is instead in a quantum combination of both states.

Among the many possible quantum systems to which this method could be applied, experiments involving biological molecules are particularly interesting, says Nori. "The question of whether quantum coherence exists in biological organisms, for example in a photosynthetic complex, has triggered a surge of interest into the relationship between quantum coherence and biological function."

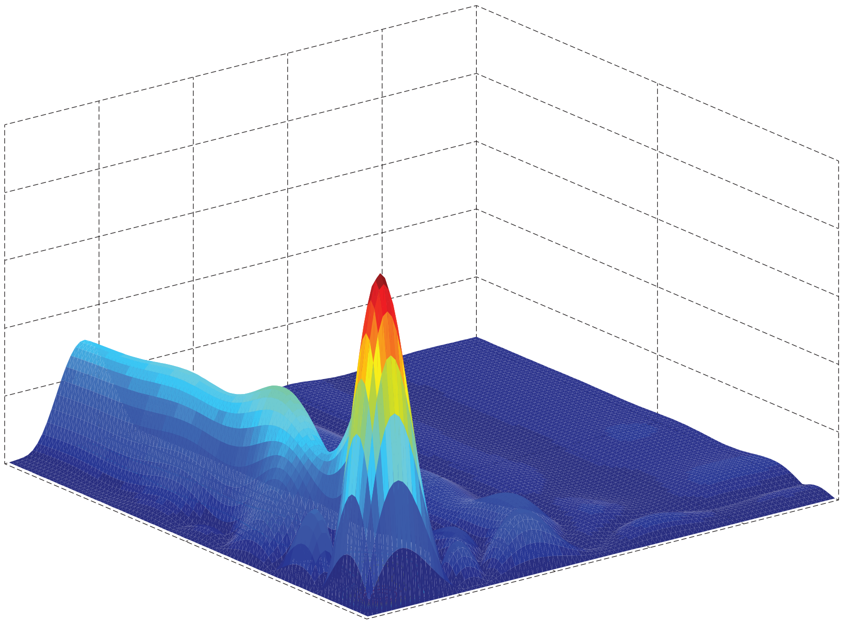


Figure 1: A 'quantum witness' plot of the quantum state of a biological pigment–protein complex—the FMO complex from green sulfur bacteria. Positive values (blue to red) reveal that the system's dynamics cannot be described classically, indicating that it is in a quantum state.

1. Li, C.-M., Lambert, N., Chen, Y.-N., Chen, G.-Y. & Nori, F. Witnessing quantum coherence: from solid-state to biological systems. *Scientific Reports* **2**, 885 (2012).

A genetic link to worsening lung disease

Symptoms of lung disease could be worsened by susceptibility to infection-triggered inflammation

Chronic obstructive pulmonary disease (COPD) is a form of lung disease characterized by narrowing of the airways and degeneration of lung tissue, and is a leading cause of death worldwide. The condition results from the inhalation of noxious chemicals, typically through smoking, and can worsen dramatically when the airways become infected. An international team of researchers led by Takashi Angata and colleagues of the Systems Glycobiology Research Group at the RIKEN–Max Planck Joint Research Center has now shown that this exacerbation of COPD occurs more frequently in patients with genes that actively generate the lectin or carbohydrate-binding protein Siglec-14[1].

Figure 1: Smoking is the main cause of COPD worldwide. The symptoms of the disease are more easily exacerbated by infection in patients with the active *Siglec-14* gene.

COPD can be stabilized and managed using a combination of drugs and rehabilitation. Worsening of COPD due to airway infection is the main cause of COPD-related hospitalization and death. A recent study by another group of researchers discovered a subgroup of patients that are particularly susceptible to exacerbation, suggesting that the process might have a genetic basis. Angata and his colleagues, noting that the nontypeable *Haemophilus influenzae* (NTHi) bacterium is a major cause of COPD exacerbation and a carrier of sialic acids, reasoned that the genes that encode siglecs—sialic acid-binding lectins that are found on immune system cells—may be involved.

The researchers developed tests for the genes encoding Siglec-14, which activates the immune system, Siglec-5, which inhibits it, and a fusion gene of the two—the product of which is identical to Siglec-5. They used these tests to investigate the genotypes of COPD patients and found that those with genes for Siglec-14 suffered exacerbation significantly more frequently. In the laboratory, they also demonstrated that Siglec-14 interacts with NTHi bacteria to stimulate an inflammatory response that could potentially worsen the COPD condition in patients. The researchers suggest that inflammation elicited by pathogens other than NTHi could also be enhanced by Siglec-14.

“The assay system we used in the laboratory study may, with appropriate modifications, be useful for screening drug candidates to treat or prevent COPD exacerbation,” says Angata. “At present, only limited drug options are available to treat COPD exacerbation. A drug that has a different mode of action from the ones currently on the market may be very beneficial.”

Angata also notes that biomarker discovery is another potential application of the team’s findings. “A biomarker that could help doctors objectively diagnose COPD exacerbation would be useful,” he says.

1. Angata, T., Ishii, T., Motegi, T., Oka, R., Taylor, R. E., Soto, P. C., Chang, Y.-C., Secundino, I., Gao, C.-X., Ohtsubo, K. *et al.* (2013). Loss of Siglec-14 reduces the risk of chronic obstructive pulmonary disease exacerbation. *Cellular and Molecular Life Sciences* advance online publication, 22 March 2013 (doi: 10.1007/s00018-013-1311-7).

A lone proton's ups and downs

Observation of magnetic flipping in a single proton heralds high-precision studies into the nature of matter and antimatter

One of the greatest mysteries of modern physics is the imbalance of matter and antimatter in the Universe. As every particle is produced and destroyed in tandem with its antiparticle, which has an identical mass but opposite charge, scientists are baffled as to why our Universe is matter dominated. In a significant advance that could allow direct measurement of the most minute differences between a particle and its antiparticle—and therefore potentially explain this imbalance—an international collaboration co-led by Stefan Ulmer from the RIKEN Ulmer Initiative Research Unit has developed a method that now makes it possible to observe reorientation of the magnetic moment associated with a single proton[1].

The secret as to why matter and antimatter are not found in equal proportions may lie in tiny but so far imperceptible differences between the properties of particles and their corresponding antiparticles. One of the properties of fundamental particles like protons that could be targeted for such a study is the magnetic moment, which orientates the particle in a magnetic field. In the most elementary case, magnetic moments have two options: 'up' or 'down'. The transition between these two states can be induced by radio waves, producing an observable effect that can then be measured. The research team used a Penning trap and a special 'magnetic bottle' field (Fig. 1) to capture individual protons and measure their spin properties.

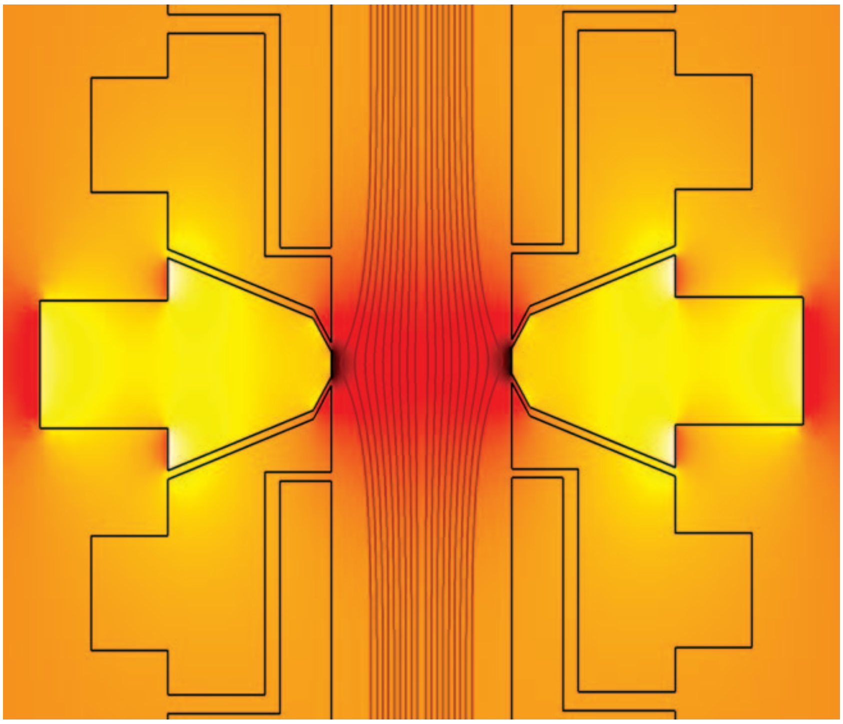


Figure 1: A Penning trap with a 'magnetic bottle' magnetic field in which single protons can be captured for several months. The magnetic field lines of the trap are shown.

"Similar effects can be caused, however, by other, much stronger mechanisms that have nothing to do with the transitions we are looking for," explains Ulmer. "We have now optimized our experimental setup and analysis methods to a point where we can unequivocally detect, for the first time, single flips of single protons."

The method allows the magnetic state of a proton to be determined reliably, and the researchers have already combined this with another technique that shuttles the proton to a second trap where its magnetic moment can be flipped with high accuracy—completing the requirements for a high-precision study.

This advance represents an essential move toward measuring the strength of the proton's magnetic moment with high precision. The next step is to develop the same measurement system for antiprotons produced by a particle accelerator, and the team is currently building a separate experimental system at CERN in Switzerland that will allow them to conduct such experiments.

1. Mooser, A., Kracke, H., Blaum, K., Bräuninger, S. A., Franke, K., Leiteritz, C., Quint, W., Rodegheri, C. C., Ulmer, S. & Walz, J. Resolution of single spin flips of a single proton. *Physical Review Letters* **110**, 140405 (2013).

Fluorescent probes shed light on brain development

Twin fluorescent probes help visualize the distribution of important developmental signaling molecules in living embryos

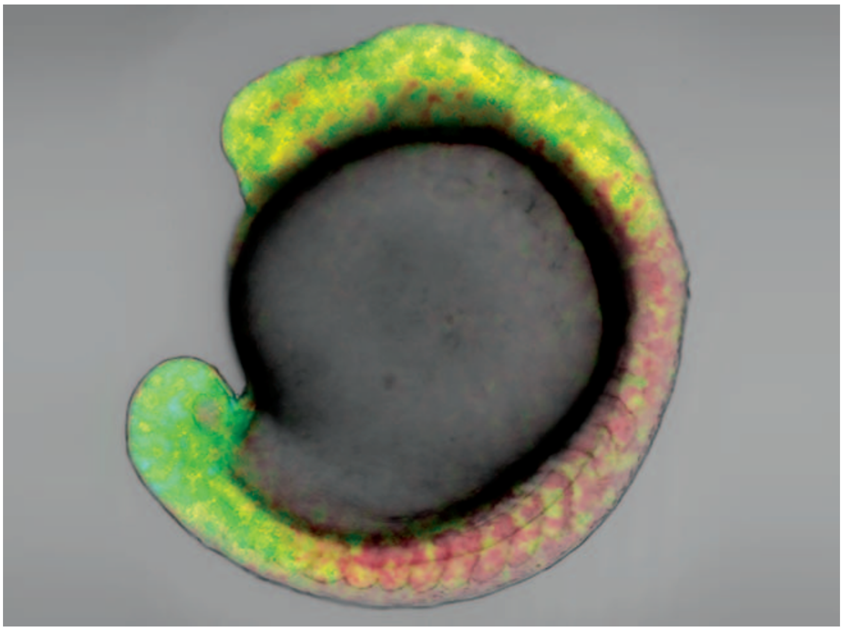


Figure 1: The retinoic acid concentration gradient in a zebrafish embryo expressing GEPRA-B, 16 hours after fertilization.

The formation of a 'body plan' during embryonic development is driven by the distribution of signaling molecules called morphogens in the embryo, determining front from back and left from right. Atsushi Miyawaki, Satoshi Shimozono and colleagues from the Laboratory for Cell Function Dynamics at the RIKEN Brain Science Institute, have now developed fluorescent probes that allow the distribution of the morphogen retinoic acid (RA) to be visualized in a living embryo for the first time, providing new insight into the important role that morphogens play in patterning the body during embryonic development[1].

Morphogens are produced in specific areas of the embryo and diffuse through the developing organism. The resulting concentration gradient guides the development of the embryo. Retinoic acid is thought to play a critical role in the formation of the front-to-back axis of the brain, but its concentration gradient has never been observed directly and its very existence remains controversial.

The research team genetically engineered probes consisting of a segment of the RA receptor fused to cyan and yellow fluorescent proteins, and then expressed these proteins in zebrafish embryos. These genetically encoded probes for RA—known as GEPRAs—change conformation when they bind to RA, resulting in a change in the fluorescence they produce.

Key to the technique was the use of two probes with different binding affinities for RA—one binding very strongly and the other relatively weakly such that they each fluoresce in response to different concentrations of RA. This enabled the researchers to visualize the changes in concentration of RA within a living zebrafish embryo by fluorescence imaging (Fig. 1).

The imaging studies confirmed that RA is distributed along a concentration gradient in the hindbrain region during the early stages of embryonic development. "RA is synthesized in the trunk and degraded in the head and tail," says Shimozono. "Therefore, two gradients should form, with the highest concentration at the trunk, and declining towards either end."

RA is known to interact with another morphogen called fibroblast growth factor 8 (FGF8), which was previously believed to be closely associated with the formation of the RA concentration gradient. However, Miyawaki's team found that the RA concentration was unaffected by the blocking of FGF8 during hindbrain development, suggesting that FGF8 is not needed for gradient formation.

"We will now use GEPRAs to investigate how RA diffuses in the body at the cellular and the molecular level," says Shimozono.

1. Shimozono, S., Iimura, T., Kitaguchi, T., Higashijima, S., & Miyawaki, A. Visualization of an endogenous retinoic acid gradient across embryonic development. *Nature* **496**, 363–366 (2013).

Carrying calms a restless baby

Carrying a baby elicits specific physiological and behavioral responses

Figure 1: Young mammal infants are calmed when carried—but not just held—by their mothers.

The bond between mother and child is the first and most important relationship for all mammals, including humans. Mammal infants are born with innate behaviors to seek closeness to their mothers and become distressed when separated from them, but the physiology underlying this response is largely unknown. Kumi Kuroda of the RIKEN Brain Science Institute and colleagues have now shown that being carried has a calming effect on infants, successfully identifying some of the brain mechanisms involved[1].

Kuroda and her colleagues recruited 12 healthy human infants aged between 1 and 6 months and recorded their heart rate, movement and crying while they were held or carried by their mothers. They cried and kicked more often when simply held by their mothers while seated and displayed an associated elevated heart rate. When carried by their mothers while walking, however, the infants became significantly calmer and adopted a characteristic posture in their mothers' arms.

The researchers found a similar calming response in mouse pups during maternal carrying. Like human infants, mouse pups also become still, cease their vocalizations and show a decreased heart rate when carried.

Kuroda's team then either blocked the pups' sense of touch using a local anesthetic, abolished their sense of balance by surgical damage to the vestibular organ of the inner ear, or abolished their proprioception, or 'muscle sense', with a toxic overdose of vitamin B6. Only pups without a sense of touch or proprioception failed to exhibit the calming response when carried, suggesting that the response depends upon these two senses rather than balance.

The researchers also found that mouse pups with genetic mutations that cause malformations of the cerebellum—a brain region involved in the control of movement—had abnormal postures during carrying, as did pups with surgical damage to the cerebellum. Finally, the team also showed that the calming response makes it easier for the pups to be carried.

"Infants with autism are reported to have difficulties adjusting their bodies to parental holding," says Kuroda. "Cerebellar abnormalities are among the most consistent neuropathological findings in autism, so we are now trying to test the hypothesis that children who develop autism may have atypical responses to maternal carrying."

"We would also like to identify the brain areas required for orchestrating the output components of the calming responses in the mouse model, and further investigate the human calming response to carrying," she adds.

1. Esposito, G., Yoshida, S., Ohnishi, R., Tsuneoka, Y., Rostagno, M. C., Yokota, S., Okabe, S., Kamiya, K., Hoshino, M., Shimizu, M. *et al.* Infant calming responses during maternal carrying in humans and mice. *Current Biology* **23**, 739–745 (2013).

A tighter fit with artificial DNA

An artificial base that enhances the protein-binding affinity and selectivity of DNA expands the DNA machinery

DNA aptamers are expected to play an important role in the diagnosis and treatment of various cancers and other gene-related diseases. These nucleic acids, which bind target substances such as proteins and cells, are typically generated through *in vitro* evolution methods. Ichiro Hirao and colleagues from the RIKEN Center for Life Science Technologies have now developed a new generation strategy based on an expanded genetic alphabet that improves the affinity and selectivity of DNA aptamers[1].

The generation of DNA aptamers by *in vitro* evolution involves several rounds of selection and amplification using a library of nucleic acid sequences until a target-specific strand is produced. Unfortunately, the isolated strand often exhibits inadequate affinity and selectivity, and modification of the natural bases or sugars of the nucleotides can result in the production of new nucleic acids without greatly enhancing the abilities of the DNA aptamers themselves.

Postulating that increasing the number of bases might improve the binding of DNA aptamers, Hirao and his colleagues incorporated an unnatural base, Ds, into a nucleic acid library in addition to the four natural DNA bases—adenine, guanine, thymine and cytosine.

To create their library, the researchers synthesized nucleic acids that contained Ds bases at only a few predetermined positions in randomized natural base sequences. After exposing the library to the target substance, they isolated the high-affinity strands and amplified them by polymerase chain reaction (PCR) for additional selection rounds (Fig. 1). They repeated the selection–amplification process while increasing the selection requirements until they obtained the desired aptamers.

Hirao's team found that the newly generated Ds-containing aptamers showed significantly higher affinity for two human target proteins than known aptamers that only contained natural bases. Moreover, by replacing all the Ds bases with adenine in these new aptamers, the researchers observed that the affinities were reduced by several hundred times, confirming the importance of the Ds bases in improving the binding of a target.

Hirao explains that inclusion of a fifth base might increase the structural diversity of DNA to better fit its target. Furthermore, unlike natural bases, Ds is highly hydrophobic, which might tighten interactions with hydrophobic parts of target proteins.

"Aptamer technology is only one example of the possible applications for our unnatural base pair system in synthetic biology," says Hirao. His team is currently using this system to label functional RNA molecules and generate new proteins with non-standard amino acids. The team is also trying to create artificial cells based on six different DNA bases.

1. Kimoto, M., Yamashige, R., Matsunaga, K., Yokoyama, S. & Hirao, I. Generation of high-affinity DNA aptamers using an expanded genetic alphabet. *Nature Biotechnology* **31**, 453–457 (2013).

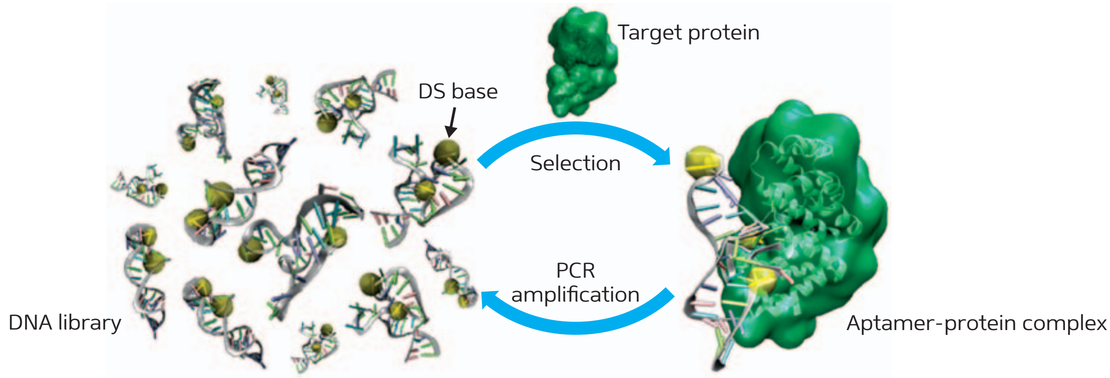


Figure 1: The generation strategy for artificial base-containing DNA aptamers.

A drug lead for leukemia

Scientists discover a compound that destroys stem cells responsible for relapse in patients with acute myeloid leukemia

Acute myeloid leukemia (AML) is a difficult cancer to overcome. Although most people with the disease achieve a period of remission following a standard dose of chemotherapy, the cancer will typically return. Now, in a breakthrough that could lead to the development of a drug that promises to prevent such relapses, a team of researchers led by Fumihiko Ishikawa of the Laboratory for Human Disease Models at the RIKEN Center for Integrative Medical Sciences has discovered a small-molecule drug that wipes out AML cells in a mouse model[1].

Ishikawa and his team previously found that the expression of hematopoietic cell kinase (HCK)—an enzyme involved in blood cell differentiation and proliferation—was greater in leukemia stem cells taken from individuals with AML than in blood stem cells obtained from people without cancer.

In their latest research, Ishikawa's team assessed the potential of targeting this enzyme as a possible therapeutic agent for human use. They found that by knocking down HCK expression in cell culture with counteracting RNA molecules, they could achieve a significant reduction in both the growth and survival of the AML cells.

The team then enlisted the help of Toshio Goto and colleagues at the RIKEN Program for Drug Discovery and Medical Technology Platforms to search for a chemical agent that possessed the same AML-defeating benefits. A high-throughput screen of 50,000 compounds for HCK inhibitors, in which the most likely compounds were compared with the results of a parallel computer model-based screen, identified one molecule as the most promising drug candidate. This chemical, a pyrrolo-pyrimidine derivative, was structurally analyzed by x-ray crystallography and subsequently optimized to yield the small molecule RK-20449.

Experiments with human AML cells, both in *in vitro* cultures and implanted into mice, showed that the drug reduced the number of leukemia stem cells and shrank the tumor burden of the disease (Fig. 1). If the results are translatable to the clinic, the drug could help prevent and overcome cancer relapse for the 28,000 people newly diagnosed with AML in the United States, Europe and Japan each year.

"If RK-20449 or its derivatives can eliminate AML cells, including leukemia stem cells, in patients, that will advance AML treatment significantly," Ishikawa says. "After thorough and careful examination of the toxicities of RK-20449, we hope that our findings can be translated into a safe and effective treatment for AML."

1. Saito, Y., Yuki, H., Kuratani, M., Hashizume, Y., Takagi, S., Honma, T., Tanaka, A., Shirouzu, M., Mikuni, J., Handa, N. *et al.* A pyrrolo-pyrimidine derivative targets human primary AML stem cells in vivo. *Science Translational Medicine* **5**, 181ra52 (2013).

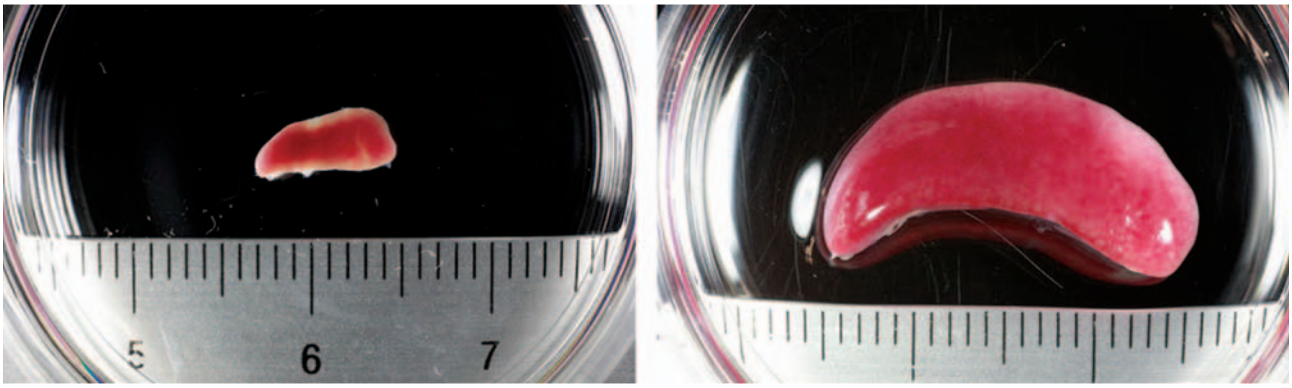


Figure 1: Spleens from mice engrafted with human AML cells after 52 days of treatment with the small-molecule drug RK-20449 (left) and prior to treatment (right).

The parenting switch

Activation of a nose-to-brain neural circuit controls whether male mice attack or care for pups

The transition from one life stage to another leads to behavioral changes in many species, including humans. In mice, virgin males display aggression towards pups but after mating show parental behaviors, even towards pups that are not their own offspring. Kashiko Tachikawa, Yoshihiro Yoshihara and Kumi Kuroda from the RIKEN Brain Science Institute have now identified a particular brain circuit that is activated in virgin males by the presence of pups to trigger aggressive behavior, and suppressed in fathers to induce parental behavior[1].

Aggression by virgin male mice towards pups is thought to be an adaptive reproductive response aimed at enhancing their chances to reproduce with the pups' mothers—without pups to care for, females cease lactating and restart ovulation. Adult mice sense pups by the pheromones they release, which activate vomeronasal sensory neurons (VSNs) within the vomeronasal organ (VNO) in the nose. The VSNs send information through a brain circuit that eventually leads to the hypothalamus to mediate behavioral responses to the pheromones. This vomeronasal neural pathway controls many social behaviors in mice, but until now its role in behavioral transitions has remained unclear.

The researchers found that sexually naive males displayed markedly stronger activation of neurons along the vomeronasal neural pathway after pup exposure compared with mouse fathers. Even the VSNs themselves within the VNO of fathers responded less to the presence of pups than those of virgin male mice. The role of the VNO in triggering aggressive behavior was confirmed when the research team lesioned the VNO in virgin males—such mice exhibited parental behaviors toward pups instead of their usual aggression.

The findings suggest that sexual interaction with a female reduces VSN sensitivity to pup pheromones, leading to a decrease in the level of activation of the downstream vomeronasal neural circuit. Future studies are needed to determine whether the changes in sensitivity in fathers are due to a reduction in the expression of chemical receptors on the surface of VSNs, or to neuronal death or changes in pheromone uptake into the VNO.

The dependence of these changes in circuit activation on sexual history may be important for understanding how the brain causes transitions in behaviors that are driven by prior life experiences. In addition, the results may also inform research on sensory contributions to the transition to parental behavior in humans. "This study paves the way for understanding the brain mechanism of abnormal parental behavior in mammals," explains Tachikawa.

1. Tachikawa, K. S., Yoshihara, Y. & Kuroda, K. O. Behavioral transition from attack to parenting in male mice: A crucial role of the vomeronasal system. *The Journal of Neuroscience* **33**, 5120–5126 (2013).

Figure 1: Pup-derived pheromones activate the vomeronasal neural pathway in virgin males, leading to aggressive behavior toward pups. The same neural pathway is suppressed in fathers, resulting in parental behavior.

RIKEN Advanced Institute for Computational Science

Charting the future of supercomputing

Based at the RIKEN Kobe campus, the Advanced Institute for Computational Science is the home of the K computer, one of the fastest supercomputers in the world

Supercomputers have become essential for research and development in science and engineering due to their ability to simulate complex systems in areas as diverse as molecular dynamics, drug discovery and climate prediction.

In 2002, Japan first led the world in supercomputing technology with the Earth Simulator. Five times faster than its nearest competitor, the Earth Simulator held the top spot for five consecutive editions of the TOP500 list, a biannual list of the most powerful supercomputer systems in the world. Four years later under an initiative by the Japanese government designating supercomputing as a key technology of national importance, RIKEN was chosen to spearhead the construction of a new supercomputer and, in 2010, established the Advanced Institute for Computational Science (AICS) in Kobe to oversee its management.

The K computer—the AICS's core facility—became fully operational in September 2012 and is made up of 864 racks with a total of 88,128 interconnected central processing units. It is named after the Japanese word *kei*, which represents the term 10 quadrillion or 10 peta, a one followed by 16 zeros, in honor of its speed: the K computer is the first computer in the world to have achieved a speed of 10 peta floating point operations per second (FLOPS). Remarkably, it is approximately 293 times faster than the original Earth Simulator.

The K computer has already garnered many accolades. In 2011, the computer was twice recognized as the world's fastest by the TOP500 list, and the Gordon Bell Prize for outstanding achievement in high-performance computing was awarded to a group comprising researchers from RIKEN, the University of Tsukuba, the University of Tokyo and Fujitsu who used the K computer to perform simulations on the electronic states of 100,000 atoms within silicon nanowires.

A major objective of the AICS is to improve the science of forecasting by using large-scale simulations performed on the K computer to generate predictions of fundamental relationships in nature. This effort focuses on five crucial areas identified by the Japanese government—namely the life sciences, global climate and natural disasters, materials and energy, industrial innovation and the origin of matter and the Universe.

With a budget of 9.7 billion yen for the 2012 fiscal year, the AICS currently employs 182 members of staff including 43 women, 13 foreign researchers and 5 PhD students. To nurture the next generation of scientists and further extend its community outreach, the institute offers summer schools and seminars to postgraduate students and young researchers to assist them in taking advantage of supercomputing technologies.

Now that the K computer is fully operational, the AICS continues to create innovative projects that challenge its star machine. By utilizing the K computer's overwhelming capabilities, the AICS is looking forward to pushing Japan to the forefront of computational science, and enhancing the nation's position as a beacon upon which researchers from around the world can converge to expand their research horizons.

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Applying terahertz waves to future technologies

CHIKO OTANI

Team Leader
Terahertz Sensing and Imaging Laboratory
RIKEN Center for Advanced Photonics

Terahertz waves have been described as an 'unexplored' light. Following significant progress in the development of terahertz light-emitting sources and detectors, scientists are now focusing on the applications of terahertz waves, which include areas as diverse as communications, security, industry, medicine and agriculture. According to Chiko Otani, Japan is the world leader in applied research of terahertz waves, and his own research aims to fully explore their potential.

Terahertz waves: unexplored light

"I think you will increasingly hear about terahertz light and terahertz waves," says Otani. "In 2001, I formally started researching terahertz waves. At that time, terahertz waves were known as 'unexplored' light, meaning that the field was a new frontier of research. I remember being very excited by the possibilities of this research. Some 12 years later, the frontier has opened up considerably."

Electromagnetic radiation, a form of energy with a wave-like behavior, can be classified according to its frequency into radio waves, microwaves, infrared rays, visible light, ultraviolet light, x-rays and gamma rays, from lower to higher frequency, respectively. Terahertz waves are electromagnetic waves with a frequency of 0.1–100 terahertz (THz), where 1 THz = 10^{12} hertz (Hz), and they partly fall into the categories of microwaves and infrared rays.

"As radio waves, terahertz waves are too high in frequency, whereas for light and infrared rays, they are too low," Otani observes. "As a result, the development of technologies for emitting and detecting terahertz waves has lagged behind, as terahertz waves are located in the narrow space between electronic and laser technologies." However, since terahertz waves have the characteristics of both radio waves and light, they can efficiently penetrate substances and have a comparatively good spatial resolution. "We therefore expect terahertz waves to be useful across a very wide range of applications including industry, medicine, agriculture and astronomy. The most familiar applications would be security and communications" (Fig. 2).

Existing mobile phones typically use a frequency of either 1.5 or 2 gigahertz (GHz), and the higher the frequency employed, the more information that can be transmitted. Since 1 THz is equal to 1,000 GHz, a terahertz wave can transmit roughly a thousand times more data than the frequencies utilized by the mobile phone system. "Unfortunately, terahertz waves are not suitable for long-distance communication because they are easily absorbed by water vapor in the atmosphere, but they can deliver high performance for indoor wireless communications," notes Otani. "Advances in compact, power-saving terahertz light-emitting and light-detecting devices will enable data that is equivalent to a single movie to be transmitted in just a few minutes."

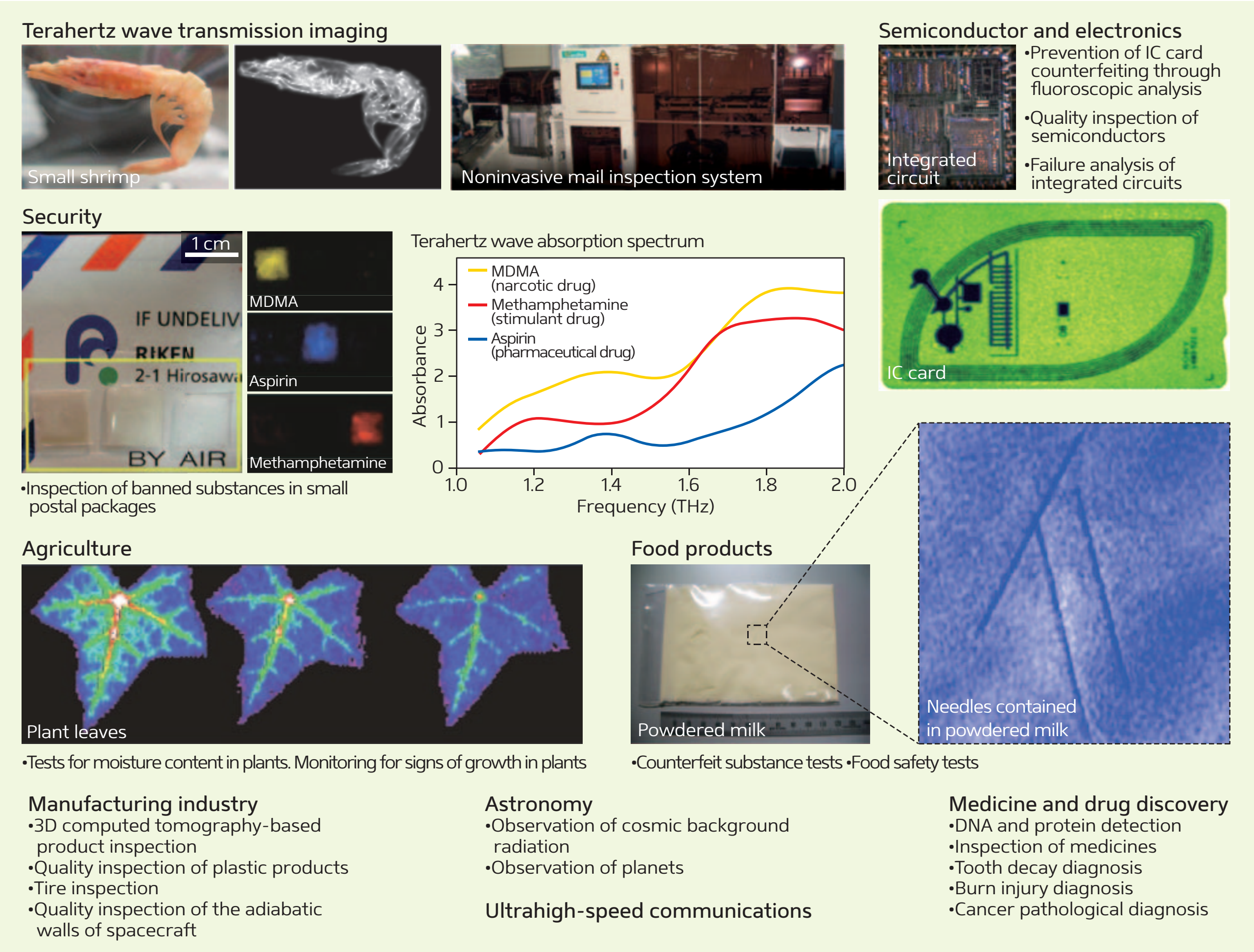


Figure 1: Various applications of terahertz waves

Using terahertz waves to inspect postal mail

Otani heads the Terahertz Sensing and Imaging Laboratory, based at the RIKEN Sendai Facility, where around 40 researchers conduct research into terahertz waves. "No other laboratory is so well equipped with staff and research equipment. It is the world's leading center for research on terahertz waves," says Otani.

At the facility, Otani's team is developing detectors with extreme sensitivity to terahertz or millimeter waves and examining ways to use terahertz waves for practical applications. A key research focus of the laboratory is the terahertz spectroscopic measurement of soft materials, which include soft substances such as gels, colloids and proteins, and polymers like plastic and nylon.

When a substance is irradiated with terahertz waves, only specific frequencies are absorbed. In terahertz spectroscopy, the amount of energy absorbed when terahertz waves of a specific frequency penetrate the substance is measured. An absorption spectrum, which charts the absorbance of the terahertz light by the substance against a range of frequencies, can then be plotted. "We can use the terahertz wave absorption spectrum to identify a substance because different substances exhibit different absorption spectra," explains Otani. "Our technique is almost ready to be used in practical applications, such as for security purposes."

Based on their technique, Otani's group has developed a noninvasive mail inspection system (Fig. 1). Commonly, x-rays are used to detect powders contained within envelopes but are unable to yield information about the type of powder. In contrast, terahertz waves allow the contents of the envelope to be definitively identified as lactose (a sugar), aspirin (a pharmaceutical), methamphetamine (a stimulant), MDMA (a narcotic), or dinitrotoluene (an explosive), for instance on the basis of the absorption spectrum of each substance. To screen large volumes of mail quickly, the system first uses the scattering of terahertz waves to screen for envelopes that contain powder and then measures the absorption spectra of the sorted envelopes, a process that has already been tested in the field by customs officials.

Observing property-determining structures

"The ability to use the terahertz-wave absorption spectrum to identify a substance has long attracted much attention," comments Otani. "However, we are going one step further by studying the relationship between the absorption spectrum and the properties of many different substances."

"The absorption spectrum of terahertz waves reflects large structures such as those within a molecule, or intermolecular structures across a number of molecules, as found in crystals," he continues. "In other words, the terahertz wave absorption spectrum of two materials with the same molecular formula will vary according to their structures."

Otani's group is studying the relationship between a material's structure and its absorption spectrum by measuring changes in the spectra when the temperature and crystalline states are altered. In particular, the team is focusing on the terahertz spectroscopic analysis of polymers, beginning with biodegradable plastic.

"Biodegradable plastic is a mixture of randomly entwined amorphous and lamellar crystalline materials in which molecular chains are helically structured. The helical structure is regularly arranged through hydrogen bonding," explains Otani. "The physical properties, such as durability, can vary depending on the ratio of these materials. We are using biodegradable plastic as a test case with which to probe the relationship between structure and the absorption spectrum."

By plotting the terahertz wave absorption spectra of biodegradable plastic as the direction of polarization is gradually altered from parallel to perpendicular in relation to the material's helical structure (Fig. 2), certain information can be gained. Strong absorption patterns occur at 2.4 and 2.9 THz when polarized waves are applied in parallel to the helical structure. However, no strong absorption patterns appear at these frequencies when polarized waves are applied perpendicular to the helical structure; instead, an absorption peak is found at 2.5 THz.

"Our calculations have verified that the absorption peaks at 2.4 and 2.9 THz are due to the expanding and contracting motion of the helically structured molecular chains, like the motion of a spring," he says. "The absorption peak at 2.5 THz is due to the expanding and contracting motion of the hydrogen bonding between two adjacent helical structures." By clarifying the relationship between the motion of the molecular chains or crystalline structures and the terahertz wave absorption spectrum, Otani intends to not only identify molecules, but also to discover the common spectrum patterns attributable to particular structures.

Non-destructive testing of conductive polymers

The Terahertz Sensing and Imaging Laboratory is also working on the non-destructive testing of conductive polymers. "This avenue of research was triggered by an industrial researcher that we met through a RIKEN–industry networking event, who wanted to know if terahertz waves could be used to evaluate the quality of conductive thin polymer films without destroying them," says Otani.

Conductive polymers—plastic materials capable of conducting electricity—were first discovered by Hideki Shirakawa, for which he was awarded the Nobel Prize in Chemistry in 2000, and are now widely used in various applications including electrodes for touch panels, and lithium ion cells. "Electrical conductivity is the key characteristic of conductive polymers," notes Otani. "However, there is no effective method for measuring the electrical conductivity of a conductive polymer without destroying it. The researcher had tried every method imaginable without success, including Hall-effect based approaches, and finally hit on the idea of using terahertz wave-based spectroscopic measurement."

The mechanism by which electricity flows through a conductive polymer is not yet fully understood. "We found that the terahertz wave absorption spectrum of a conductive polymer with high conductivity is significantly different to that with low conductivity," he says. "So we are continuing our research into terahertz waves in the hope that we can use them to shed light on the mechanism of electrical conduction."

Additionally, the electrical conductivity of such polymers is known to dramatically increase when ethylene glycol is added, but the reason is unknown. Otani believes that examining the way in which the terahertz absorption spectrum changes upon incorporation of ethylene glycol will reveal clues as to how the quality of such polymers can be improved. "We intend to clarify the relationship between the crystalline structure and physical properties of various materials such as nylon and gels, as well as conductive polymers, so that terahertz waves can be used to evaluate or make improvements to these materials in the future."

Modifying molecular structures with terahertz waves

Otani is working towards a clear but ambitious research goal. "The functions of substances are closely related to their molecular or crystalline structure,

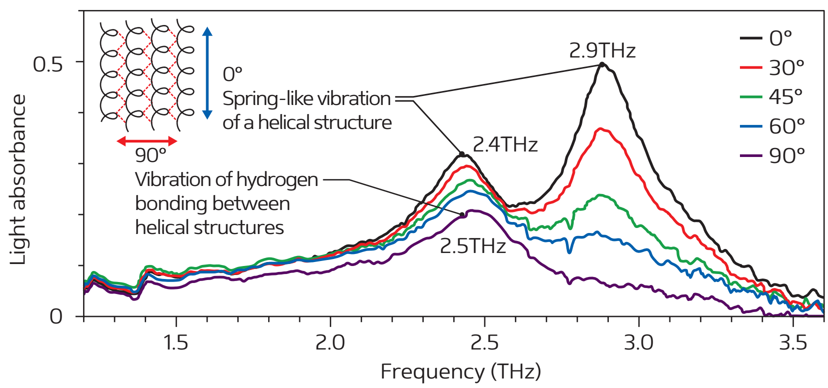


Figure 2: Terahertz wave polarized absorption spectra of a lamellar crystalline biodegradable plastic

The absorption peaks that appear at 2.4 and 2.9 THz when polarized waves are applied in a direction parallel to the helical structure (0°) are due to the spring-like vibration of the helical structure of the molecular chain, whereas the absorption peak that appears at 2.5 THz when polarized waves are applied in a direction perpendicular to the helical structure (90°) can be attributed to the vibration of the hydrogen bonding between the helical structures.

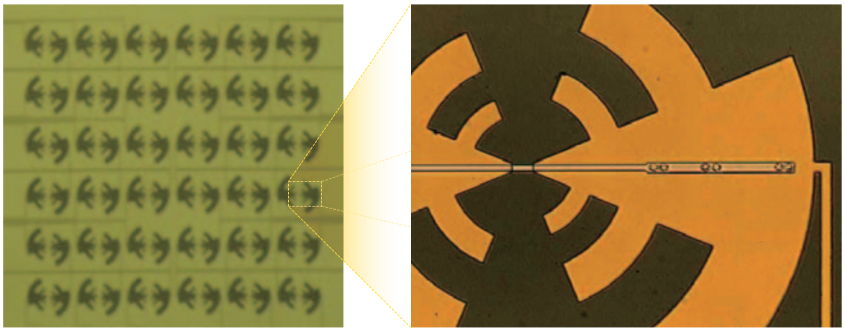


Figure 3: High-performance superconducting detector array
The high-performance superconducting detector array uses 1,000 tiny antenna devices that are fabricated and arranged by lithography. The detectors are cooled to an ultralow temperature of -273 °C for noise reduction, thus achieving an extremely high sensitivity.

and a change in structure leads to a change in the terahertz wave absorption spectrum," he observes. "Therefore, it may be possible to change the molecular or crystalline structure of a substance intentionally by irradiating it with terahertz waves of a specific frequency. If we can change the structure of a substance, we can change its function. Consequently, substances with new functions could be created by irradiating them with terahertz waves."

For instance, the functions of biomolecular proteins vary in accordance with their shape. Such proteins include prions, the infectious agents thought to cause bovine spongiform encephalopathy, a neurodegenerative disease of cattle. Normal prion molecules consist of four helical structures known as α-helices. In abnormal prions, however, two α-helices are unwound into β-sheets. Otani hopes to develop an innovative technique that can convert abnormal prions into normal molecules by irradiating them with terahertz waves.

Altering a molecular structure through terahertz-wave irradiation requires a powerful light source. Otani's laboratory has therefore launched a project to develop a new, air-plasma-based terahertz light source. When light from lasers converges in the air, molecules in the air become ionized, forming plasma that subsequently emits powerful terahertz waves. The group plan to use their light source to investigate the terahertz-wave irradiation of a variety of different substances.

Observing light from the beginning of the Universe

In addition to his other research interests, Otani is a member of The Physical Origin of the Universe Viewed through the Cosmic Background Radiation project, which is supported by the Ministry of Education, Culture, Sports, Science and Technology (MEXT). "The Universe began with the Big Bang. But what existed before this event? The project aims to answer this burning question," he says.

A widely accepted theory suggests that there was an extremely rapid expansion, known as 'inflation,' prior to the Big Bang. Immediately afterwards, the temperatures and pressures of the Universe were exceptionally high, with all matter existing in the plasma state. Thus, light was immediately scattered, and the Universe became opaque. Some 380,000 years after this event, as the temperature decreased, nuclei and electrons began to recombine, which allowed light to pass through the Universe. The trace of light still detectable from that time is known as cosmic background radiation. Inflation is thought to have produced primordial gravitational waves during the process of rapid expansion, and this fluctuation is likely to have been reflected in the cosmic background radiation.

"Cosmic background radiation can be observed as microwaves or millimeter waves. We are taking advantage of terahertz wave technology to develop a millimeter-wave superconducting detector with an extremely high level of sensitivity that will also let us study the polarization pattern of cosmic background radiation," explains Otani (Fig. 3). "I believe that by proving the existence of primordial gravitational waves we will not only provide conclusive evidence of inflation, but also move a step closer to clarifying the basic laws of physics that govern the Universe."

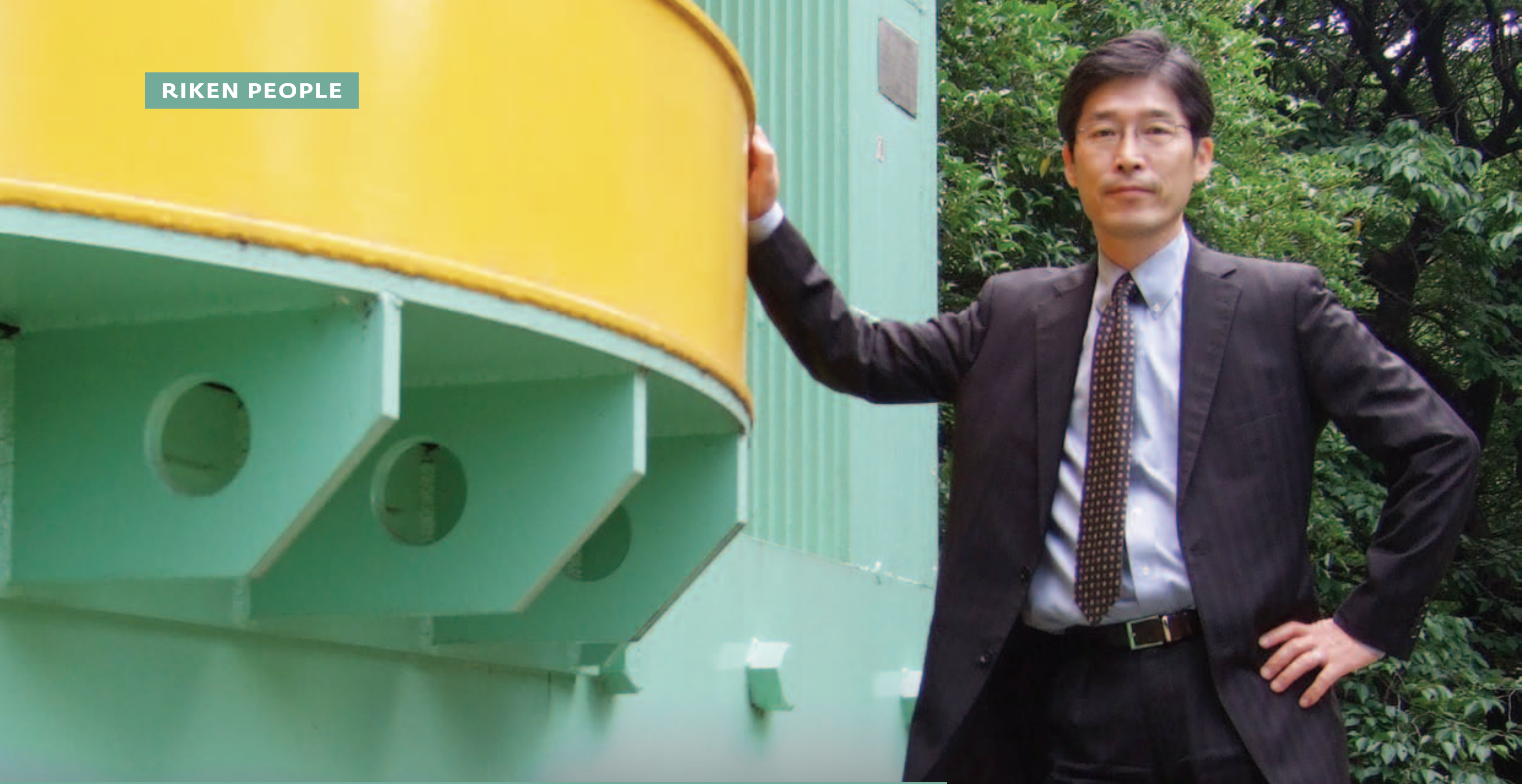
Prior to studying terahertz waves, Otani worked as an expert in x-ray astronomy, from which his deep interest in the origin of the Universe stems. "I would love to explain how the Universe began using terahertz wave research as this is a question to which everyone wants to know the answer."

In the future, Otani wishes to expand the application of terahertz waves to the life sciences, where a major challenge lies in developing techniques to facilitate the selection of proteins and molecules that combine with other protein targets. Existing approaches exploit fluorescent proteins that emit light when combined. "Other scientists believe that since the molecular structure of such moieties changes upon their combination, the terahertz wave absorption spectrum can be used to understand whether or not a molecule has combined with a target. We are also confident that we can use terahertz waves in such an innovative application."

ABOUT THE RESEARCHER

Chiko Otani was born in Ishikawa, Japan, in 1965. He graduated from the Faculty of Science at Kyoto University in 1990. In 1995, he obtained his PhD from the University of Tokyo and joined RIKEN, where he began his postdoctoral career in x-ray astronomy. Otani then began to work on the development of superconducting x-ray and terahertz detectors, and at present is focusing on terahertz science and technology. He was promoted to team leader in 2005 and group director in 2013. His research interests focus on terahertz sensing, imaging and industrial applications as well as quantum detection with superconductor devices for astronomy and cosmology.

RIKEN PEOPLE



Overseeing RIKEN's big picture

MINORU YONEKURA

Executive Director
RIKEN Board of Executive Directors

What is your role at RIKEN?

As a member of the Board of Executive Directors, I am involved in the entire management of RIKEN. The board is led by the president of RIKEN, Ryoji Noyori, and consists of five executive directors and two auditors. Our focus lies on strengthening the research and administrative systems of RIKEN so that we may achieve greater internationalization and competitiveness. We provide the leadership, direction and oversight required to maximize RIKEN's potential in the global research arena. Personally, I hold responsibilities in finance, audit and compliance, external funding and information infrastructure.

How did you join RIKEN?

I was seconded to RIKEN from the Ministry of Education, Culture, Sports, Science and Technology (MEXT) in April 2013. Previously at MEXT, I worked closely with RIKEN and in 2006, I became director of the Policy Planning Division—a position I held for just under two years.

Until March 2013, I served as a member of the board of trustees and vice president of the University of Tsukuba, during which I helped to launch a joint project with the RIKEN BioResource Center, as part of the larger Tsukuba Science City initiative. Despite having only been an executive director at RIKEN for three months, I feel that I have had a smooth start thanks to my previous experiences.

What has been the most memorable event for you during your time at RIKEN?

Most of my memorable events relate to the period of time when I worked closely with RIKEN while based at MEXT. I was involved in the launch of a number of exciting projects including the recently reorganized RIKEN International Frontier Research Program, the SACLA x-ray free electron laser and the K computer.

What is the best thing about working at RIKEN?

On a day-to-day basis at RIKEN, I am able to interact with scientists who are engaging in the world's most advanced research. I find it exciting to work here, knowing that RIKEN is leading not only in terms of the research performed, but also the research environment and systems that we provide. Political and business leaders often mention our research and achievements, something that makes me proud of me working at RIKEN.

What would you say to other people considering joining RIKEN?

In addition to pioneering new science and technology, RIKEN strives to adjust and improve as an organization over time. RIKEN is a highly invigorating environment in which to work, and we welcome those who wish to take on new challenges in both research and management positions.

What do you hope to achieve as part of your return to RIKEN?

I was extremely pleased to be granted an opportunity to work at RIKEN once again. The beginning of RIKEN's third five-year term coincided with my return, and major organizational changes have been introduced. Through my contributions, I hope to assist scientists to develop their research and RIKEN as a whole to mature into a world-leading science institution with the ability to flexibly adapt to changes both inside and outside of Japan.

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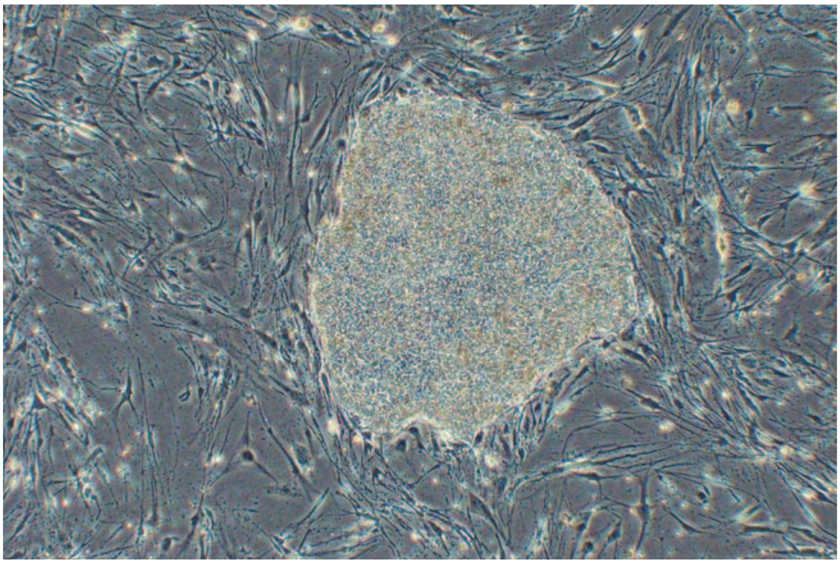
Key regulatory hurdle cleared in planned iPS cell clinical research



Research at RIKEN may lead to the first therapeutic application of human iPS cells.

A key panel of the Japanese Ministry of Health, Labor and Welfare has given a conditional green light to clinical research involving induced pluripotent stem (iPS) cells. The research, to be conducted by Masayo Takahashi of the RIKEN Center for Developmental Biology, Kobe, in close collaboration with the Institute of Biomedical Research and Innovation, also in Kobe, will investigate the use of iPS cells in patients suffering from age-related macular degeneration, a common disease in elderly people that can ultimately lead to loss of vision.

The group plans to create autologous iPS cells using skin cells taken from a small number of patients, and then induce retinal pigment epithelium cells, or RPE cells, from each patient's iPS cells. The RPE cells will be transplanted into the patients' retinas in the form of a cell sheet, initially to gauge the safety of the therapy. The plan will now go to two more panels and then to the Minister of Health, Labor and Welfare, who is expected to give his official endorsement.

The transplantations, which may begin next year at earliest, have promise to be the first clinical application of iPS cells. iPS cell therapy gained international fame in 2012, when Kyoto University Professor Shinya Yamanaka, who discovered the process for creating iPS cells, was awarded the Nobel Prize in Medicine and Physiology. The Japanese government has made research on iPS cells a key priority in its fiscal year 2013 science budget.

RIKEN and McGill University hold joint workshop on biomedical fields

RIKEN and McGill University held their third joint workshop in Montreal on 20–21 June 2013, focusing on collaborative research in biomedical fields. The event aimed to broaden collaboration between the two organizations, which first signed a cooperation agreement in 2010. The institutions signed another joint statement at this workshop reaffirming their partnership and pledging efforts from both sides for the establishment of a joint center.

Following two earlier workshops on green chemistry and nanotechnology, the third joint RIKEN–McGill workshop focused on biomedical research.

The workshop was divided into four sessions, focusing on quantitative biology and genomic medicine, pharmacology and structural-synthetic biology, stem cells, development, cancer and host resistance and immunology. Speakers from the two institutions, including RIKEN chief scientists and researchers from the Quantitative Biology Center, the Center for Integrated Medical Sciences, the Center for Developmental Biology and the Center for Life Science Technologies, presented their latest findings and research activities. Many young researchers and students from McGill jointed the sessions, exemplifying the high level of interest in research in this area.

Dr. Noyori receives honorary degree from Saint Petersburg State University

Ryoji Noyori, president of RIKEN, accepting an honorary doctorate from Saint Petersburg State University.

On 28–29 May 2013, Ryoji Noyori, president of RIKEN, visited Saint Petersburg State University, one of Russia's most prestigious universities and established in 1724. Noyori exchanged opinions with university officials during the two-day visit, exploring possibilities for future collaborations between RIKEN and the university. He also visited some of the university's nanotechnology and x-ray research laboratories and carried out lively discussions with the researchers.

At noon on 28 May, an honorary doctorate was awarded to Noyori in the presence of 50 people including the university's vice rector, Sergey Tunik, faculty members and students. Following the commencement, Noyori gave a lecture emphasizing that it is important for scientists with diverse cultural backgrounds to get to know and communicate with each other and reiterating that Russian scientists are welcome at RIKEN. In response to Noyori's lecture, Tunik encouraged the students and researchers in the audience to consider conducting research at RIKEN as a path to realizing their dreams as scientists.

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RIKEN 2013-020