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A finer bone structure

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Caught in a trap

New understanding of hydrogen interactions with metal nanoparticles may pave the way for future hydrogen storage

The environmental impact of the use of hydrocarbon as fuels has led to a global search for cleaner energy sources. Hydrogen offers a greener alternative for transportation fuels, being easily generated from renewable energy sources and creating only environmentally benign water as a byproduct of electricity generation. However, a critical issue is the requirement of a safe and reliable hydrogen storage medium.

Current options for hydrogen storage include intensely pressurizing hydrogen or storing it as a liquid at cryogenic temperatures. These options are not practical for everyday use, so new approaches are being investigated. For example, hydrogen can be stored chemically in the form of hydrides. Another approach is to weakly adsorb hydrogen onto materials of large surface area. Nanoscale particles are a good example, they are advantageous over bulk materials as they have a larger solid/gas interface area and shorter hydrogen diffusion paths, yielding potentially faster kinetics for gas absorption and desorption.

In two studies recently published in the *Journal of the American Chemical Society,* Masaki Takata from the RIKEN SPring-8 Center, Harima, and his colleagues including Hiroshi Kitagawa from Kyushu University have revealed hydrogen trapping in nanoparticles made of metals that can form hydrides. Their findings were made by exploring the chemical and structural changes on exposure of the particles to high hydrogen pressures.

Hydrogen hide-and-seek

The hydrogen storage capability of bulk palladium has been shown previously to be higher than that of nanoparticulate palladium, but that nanoparticles of platinum stored more hydrogen than in the bulk form.

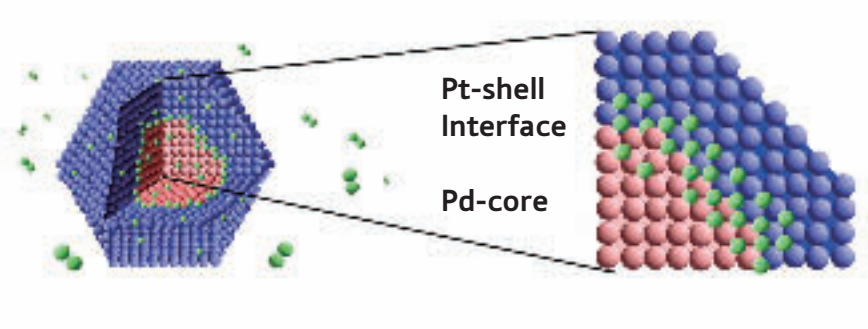

Figure 1: A schematic depiction of hydrogen storage of palladium (Pd) and platiunum (Pt) nanoparticles (green, hydrogen; red, Pd; blue Pt).

Takata, Kitagawa and colleagues felt that the strikingly different behavior of these materials could be exploited in core-shell type materials, which can be regarded as an alloy phase separated into a core of one metal surrounded by a shell of another. And so, for the first time, an investigation into the hydrogen storage properties of core-shell nanoparticles was undertaken[1]. They chose palladium as the core and platinum as the shell materials of the nanoparticles.

The team used a stepwise growth method to prepare structures with crystalline palladium cores of 6 nm diameter, using poly (*N*-vinyl-2-pyrrolidone), PVP, to prevent aggregation of the nanomaterials and control their shape and shape distribution. PVP does not show any hydrogen storage behavior of its own.

Crystalline platinum shells of thickness around 2 nm were then deposited around the palladium cores using hydrogen as a reducing agent, and the resulting core-shell structures were characterized using a variety of techniques. High-resolution transmission electron microscopy and energy dispersive spectroscopy revealed the core-shell structure, while x-ray diffraction revealed that both the core and the shell were crystalline. Pressure-composition isotherms showed that the core-shell nanoparticles absorbed the same amount of hydrogen as homogenous palladium nanoparticles.

Takata, Kitagawa and colleagues then performed solid state nuclear magnetic resonance (NMR) measurements with deuterium, a hydrogen isotope, to identify the absorption site of hydrogen. Surprisingly, they have found that while deuterium was dispersed in both palladium and platinum lattices, it was concentrated in the boundary region between core and shell (Fig. 1).

The atomic arrangements or chemical potential at the interfacial region are more favorable for the generation of hydrides than within the palladium core or the platinum shell of the nanoparticle, according to the researchers.

The 'big and small' of hydrogen storage with palladium

In their second study[2], Takata, Kitagawa and colleagues investigated the differences in storage behavior between the bulk palladium and palladium nanoparticles of 6 nm diameter coated with PVP (Fig. 2). Bulk palladium has been intensively studied because of its potential to store hydrogen as a hydride.

Composition isotherms of hydrogen pressure showed that the palladium nanoparticles require higher hydrogen pressures to reach the same hydrogen absorption levels as bulk palladium. On release of the high hydrogen pressure, the hydrogen pressure-composition isotherm for the bulk system was shown to be completely reversible; however, this was not the case for the nanoparticles. The atomic hydrogen somehow got trapped on, or inside, the palladium nanoparticles causing the hysteresis, the authors hypothesized.

To test this theory, the authors carried out several additional experiments. They used x-ray diffraction and found that the lattice constant of the nanoparticles increases with exposure to 101.3 kPa of hydrogen pressure. However, on evacuation of the hydrogen, the lattice does not return to its original value, it remains slightly larger. Then, again using solid state NMR measurements with deuterium, the researchers found that some deuterium atoms remain within the palladium lattice after evacuation of 'free' deuterium from the system. The results suggest that hydrogen atoms are not deposited on the surface of the nanoparticles, or clustered, but are distributed throughout the nanoparticles.

Takata, Kitagawa and colleagues propose that some hydrogen atoms are stabilized and trapped firmly within the lattice strongly bound as hydrides, which expands the crystal lattice and hence the lattice constant of palladium. This, they say, explains why hydrogen absorption in these materials is not completely reversible on the removal of high pressure hydrogen from palladium materials.

A step in the right direction

The metal nanoparticles investigated in the study have potential for combining the hydrogen storage capabilities of hydrides with the kinetic benefits of large-surface-area nanomaterials. As such, the research team's detailed observations of strong hydrogen trapping in palladium nanoparticles, and of higher hydrogen accumulation at the interfaces between the core and shell of core-shell nanoparticles, could aid in the development of practical hydrogen storage materials. ■

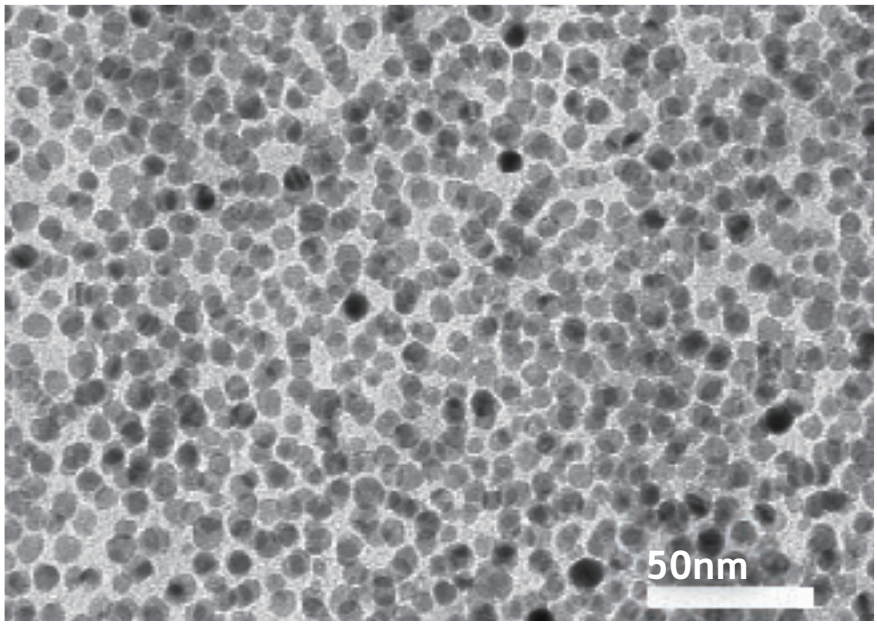

Figure 2: Transmission electron microscope image of palladium nanoparticles.

1. Kobayashi, H., Yamauchi, M., Kitagawa, H., Kubota, Y., Kato, K. & Takata, M. Hydrogen absorption in the core/shell interface of Pd/Pt nanoparticles. *Journal of the American Chemical Society* **130,** 1818–1819 (2008).

2. Kobayashi, H., Yamauchi, M., Kitagawa, H., Kubota, Y., Kato, K. & Takata, M. On the nature of strong hydrogen atom trapping inside Pd nanoparticles. *Journal of the American Chemical Society* **130,** 1828–1829 (2008).

About the researcher

Masaki Takata was born in Kure, Japan, in 1959. He graduated from the Faculty of Sciences, Hiroshima University, in 1982, and obtained his PhD in 1988 from the same university. After that, he was promoted to associate professor of Nagoya University, before becoming a professor of Shimane University in 1997, an associate professor of Nagoya University in 1999, a chief scientist of Japan Synchrotron Radiation Research Institute/SPring-8 in 2003, and a chief scientist of RIKEN SPring-8 Center in 2006. His research focuses on novel structural materials science using high brilliance synchrotron radiation x-rays at SPring-8.

Hiroshi Kitagawa graduated from the Faculty of Sciences, Kyoto University, in 1986, and obtained his PhD in 1992 from the same university. In 1991, he was promoted to research associate at the Institute for Molecular Science. He moved to the Japan Advanced Institute of Science and Technology in 1994, and became an associate professor at the University of Tsukuba in 2000, before becoming a professor at Kyushu University in 2003. His recent research focuses on the development of novel solid-state protonics in coordination nanospace.

Herring-bone print

X-rays reveal the fine structure of minerals and collagen in the bones of fish

Scientists at the RIKEN SPring-8 Center in Harima, Osaka University, Japan, and the University of California, US, are taking a close look at the structure of bone. Using an x-ray technique that provides nanometer-scale resolution, the group studied intramuscular bone in the alewife—a small herring found mostly along the North American coast (Fig. 1). Reporting their work in *Physical Review Letters*, the group proposes a dynamic model to explain the bone mineralization process[1].

Source: New York State Department of Environmental Conservation

Figure 1: The alewife, *Alosa pseudoharengus*, is a member of the herring family of fish.

All bones are made up of three main parts: soft collagen fibrils, proteins and a hard mineral phase. The strength and functioning of bone depend on how these three components pack together during growth, particularly at the molecular level.

Herring bone tissue contains mostly collagen and other proteins that form a rod-like matrix. Calcium phosphate mineralizes around the collagen fibrils to form a tough composite material.

Scientists would like to understand better how the mineralization nucleates and evolves with time; however conventional visible light microscopes cannot image this process with sufficient structural detail. The research group therefore used an x-ray technique called 'lensless imaging'. A bone sample is illuminated with a beam of coherent x-rays. (Coherent x-rays have the same wavelength and travel in phase, similar to the light from a laser, but with a much shorter wavelength). When the x-rays scatter from the sample, they form an interference pattern that can, in principle, be 'inverted' to reveal the real image.

The inversion is a complex procedure, but the final images reveal a surprising amount of structural detail. By studying the herring bone at various stages in the mineralization process, the research group has shown that mineralization first occurs in the spaces between the collagen fibrils, ultimately expanding along the length of the fibrils. As more minerals form, the collagen expands and distorts.

The group suggests that bone strength comes mainly from those minerals that form first, since they can mix well with body fluids and have a relatively large volume in which to grow.

"These findings will enable us to obtain a better understanding of the complex structure of bone at the nanometer scale, and provide important design principles for hard tissue engineering and the development of biocompatible materials", says team-member Tetsuya Ishikawa from RIKEN.

Beyond their specific findings, Ishikawa and colleagues expect that x-ray imaging will be an attractive alternative to electron microscopy for studying biological materials. ■

1. Jiang, H., Ramunno-Johnson, D., Song, C., Amirbekian, B., Kohmura, Y., Nishino, Y., Takahashi, Y., Ishikawa, T. & Miao, J. Nanoscale imaging of mineral crystals inside biological composite materials using x-ray diffraction microscopy. ***Physical Review Letters* 100,** 038103 (2008).

Porous networks in an instant

The scope for materials with internal cavities widens—with a fast synthetic route and accurate structural characterization

Researchers at the RIKEN Advanced Science Institute, the formerly Discovery Research Institute in Wako, and the University of Tokyo report in the international edition of *Angewandte Chemie*[1] that they have synthesized a kinetically controlled porous three-dimensional network, known as a coordination network, and determined its structure using the SPring-8 synchrotron in Harima. The finding should extend the range of physical properties and applications of these porous materials.

Three-dimensional porous frameworks are comprised of an ordered assembly of metal ions and ligands and have many applications in science. Synthesizing porous coordination networks is difficult, however, as non-porous networks often result.

The networks can be produced under thermodynamic or kinetic control, which result in products of varying stability. The so-called thermodynamic product is the most stable of multiple products formed in a reaction, whereas the kinetic product will form the fastest but will not be the most stable.

By controlling the rate of complexation of the starting materials, the researchers produced two different types of porous network. Using a slow crystallization process under thermodynamic control, taking about one week, they produced a network that has very large one-dimensional channels formed from weak interactions between the ligands. However, at a faster rate under kinetic control, taking less than 30 seconds, they produced porous network with smaller holes.

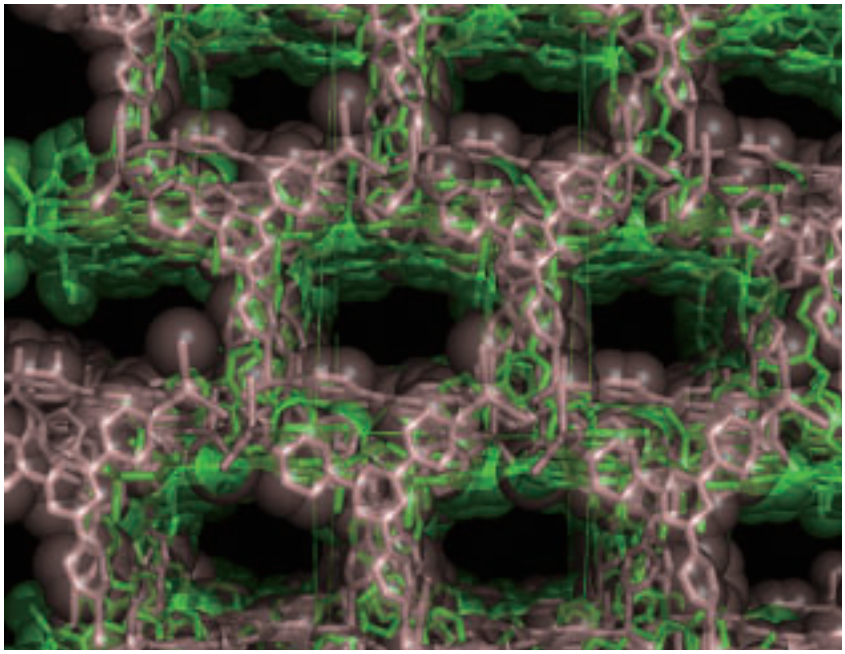

Figure 1: The crystal structure of the network synthesized under kinetic control.

As the latter product is formed almost instantaneously, there is insufficient time for a single crystal to grow, which is needed to determine the structure of these frameworks using conventional x-ray diffraction studies. Instead, the team isolated a uniform microcrystalline powder but found that its structure could be determined by synchrotron powder x-ray diffraction (Fig. 1). According to the researchers, this is the first time a kinetically controlled network with large cavities has been successfully characterized using this technique. Determining the structure of these frameworks is crucial for advancing the applications of these networks.

The researchers believe that this instant synthesis, coupled with the ability to characterize the microcrystalline product, could lead to advances in the area of coordination network chemistry. For example, as the pore size can be tuned by changing the ligands, it may be possible to make porous materials that achieve a larger amount of gas adsorption.

"The results suggest that more unexplored kinetic networks can be prepared and characterized by synchrotron powder x-ray diffraction," says team-member Masaki Kawano from the University of Tokyo. ■

1. Kawano, M., Haneda, T., Hashizume, D., Izumi, F. & Fujita, M. A selective instant synthesis of a coordination network and its ab initio powder structure determination. ***Angewandte Chemie International Edition*** **120,** 1289–1291, (2008).

Particle accelerators go back to basics

Scientists obtain strong evidence that particle accelerators can split protons and neutrons into a quark–gluon plasma

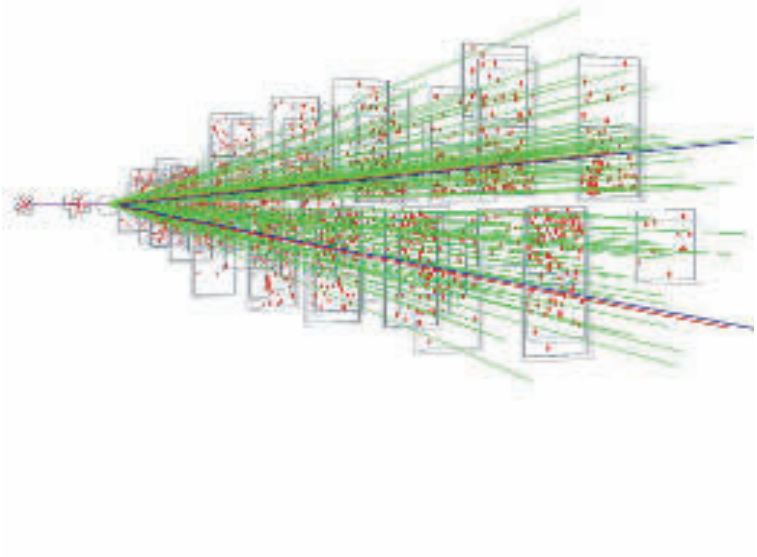

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Figure 1: Typical event for indium–indium collisions seen in the Super Proton Synchrotron. Green lines are particle tracks and red lines are tracks identified as muons.

Common nuclear particles such as protons or neutrons—collectively known as hadrons—are made up from even tinier building blocks called quarks and gluons. Usually quarks and gluons are confined inside hadrons, but scientists believe that the hot dense fireball formed in high-energy nuclear collisions can break down the hadron structure. Now Hiroaki Ohnishi at RIKEN Nishina Center in Wako and his European co-workers may have recorded the first evidence of hadrons breaking down inside a particle accelerator to form a new state of matter called a quark–gluon plasma[1].

"Quantum chromodynamics predicts that under extreme conditions such as high temperature and/or high density, quarks and gluons will no longer be confined in hadrons," explains Ohnishi. "These conditions are expected just after the big bang or in the core of a neutron star."

To recreate such conditions on Earth, the researchers collided heavy ions of indium inside the Super Proton Synchrotron at CERN in Switzerland. Such explosions give rise to pairs of elementary particles called muons, which can freely escape because they do not experience the strong nuclear force that holds quarks and gluons together. Therefore the momentum of the muons provides key information on the temperature and outward flow of the expanding fireball. Ohnishi and co-workers monitored 430,000 pairs of muons that were emitted during the collisions (Fig. 1).

As the fireball expands, the flow of muon pairs is expected to increase. However the latest experiment revealed an initial increase in muon flow, followed by a sudden decline. The researchers suggest that their result is the first direct evidence of a transition from hadron-based matter to a quark–gluon plasma.

At these extreme conditions, the wavefunction that predicts the possible positions of a quark becomes so wide that it overlaps with other particles. In other words, the quark does not belong to a single hadron, and the hadron no longer has any meaning. By understanding this quark–gluon plasma, scientists can begin to understand the mechanisms by which quarks stay confined within hadrons.

"The search for quark–gluon plasma and the investigation of matter at high temperatures are now very hot topics, and new results will soon come out from the CERN Large Hadron Collider [due to be completed this year]," says Ohnishi. "Those researches will be directed towards answering the question of what really happened just after the big bang." ■

1. Arnaldi, R., Banicz, K., Castor, J., Chaurand, B., Cicalò, C., Colla, A., Cortese, P., Damjanovic, S., David, A. & de Falco., A. *et al.* Evidence for radial flow of thermal dileptons in high-energy nuclear collisions. ***Physical Review Letters* 100,** 022302 (2008).

Stringing it together

Superstring theory applied to the interior of a black hole is revealing the links between gravitational and quantum theory

Scientists have spent many years searching for a 'theory of everything' linking the standard model of particle physics—which explains electromagnetism and the weak and strong nuclear forces—with Einstein's theory of general relativity for gravity. One of the most promising candidates to provide the link is superstring theory, in which all particles and forces are represented as vibrations of strings.

Now, Masanori Hanada at the RIKEN Nishina Center in Wako and co-workers have studied the interior of a black hole (Fig. 1), where string theory simplifies to the Super-Yang-Mills theory—a quantum mechanical gauge theory for interacting fields. Their work shows that string theory can reproduce the known gravitational properties of a black hole[1].

Superstring theory involves a concept of particle physics called supersymmetry, which links different types of particles in pairs. "Some black holes are well-approximated by both the Super-Yang-Mills theory and supergravity, which is a supersymmetric generalization of Einstein gravity—so the theories are equivalent," says Hanada. This so-called gauge/gravity duality is especially likely at low temperatures. Hanada's group set out to find further evidence of gauge/gravity duality by directly analyzing the Super-Yang-Mills theory.

"Analyzing Super-Yang-Mills theory is very difficult … and we need to rely on numerical simulation," says Hanada. In such simulations, space is usually divided into a discrete lattice—and the larger the number of lattice points, the more accurately the calculations represent real continuous space. The researchers invented a more powerful 'non-lattice' method and used supercomputers to perform a Monte-Carlo simulation (repeated computation with random sampling) on near-continuous space. They found strong agreement with supergravity.

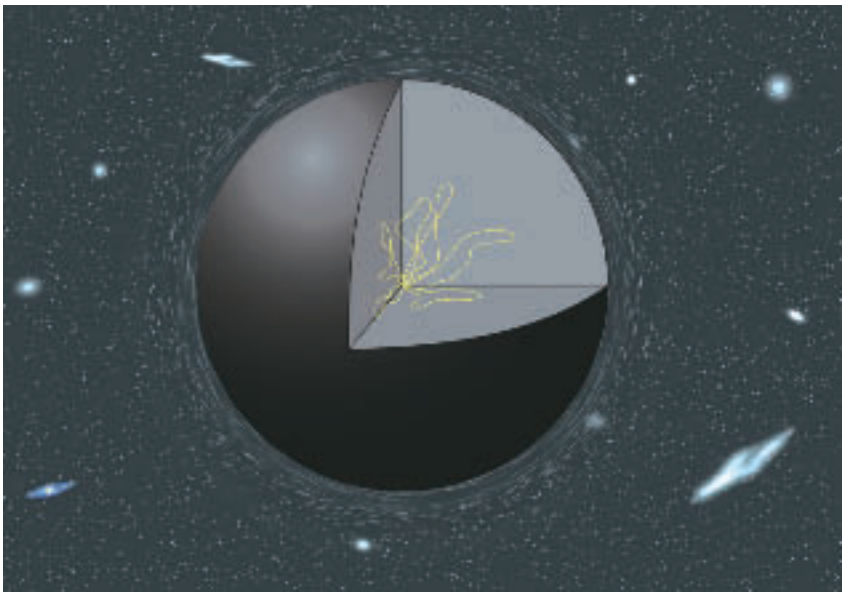

Figure 1: Superstring theory can be used to understand the region of space inside a black hole.

"Our result provides a very non-trivial check for gauge/gravity duality," says Hanada. "Also, because Super-Yang-Mills theory provides a stringy description of a black hole, our results can be regarded as evidence that a black hole is a stringy object."

The black hole they studied is defined in ten dimensions, but has many things in common with black holes in our four-dimensional world (three spatial dimensions plus time). The work suggests that realistic black holes can also be described by string theory.

The next step in the group's research will be to study lower temperatures under even more accurate simulations. "Then we can check the gauge/gravity duality more rigidly, and better understand the nature of black holes," says Hanada. ■

1. Anagnostopoulos, K.N., Hanada, M., Nishimura, J. & Takeuchi, S. Monte Carlo studies of supersymmetric matrix quantum mechanics with sixteen supercharges at finite temperature. ***Physical Review Letters*** **100,** 021601 (2008).

Superfluidity in one and three dimensions

The onset of superfluidity in helium-4 adsorbed within a network of nanoscopic pores depends on the dimensionality of these pores

Thermal and quantum mechanical fluctuations usually have little effect on the behavior of a system when its constituent particles are free to move in all three dimensions. Consequently, theoretical models for describing the transition of a bulk 3-D system from one phase to another usually ignore these fluctuations. But as the dimensionality of a system is reduced, fluctuations become increasingly important.

To better understand such effects a team of Japanese researchers, including Hiroki Ikegami of RIKEN's Advanced Science Institute (formerly the Discovery Research Institute) in Wako, has investigated the behavior of helium-4 in two different nanoporous materials[1]—one consisting of an unconnected array of 2.8 nm-wide 1-D channels, and the other of a periodic network of 2.7 nm-wide pores connected in 3-D (Fig.1). Significantly, the team made the size of the pores smaller than the characteristic wavelength of thermal vibrations, known as phonons, in the liquid.

The transition of a 3-D liquid to superfluid behavior, as it is cooled below its critical temperature, is usually accompanied by the appearance of superfluid density and an abrupt change in heat capacity characteristics. But for helium-4 adsorbed within a 1-D porous network, the team has found that the superfluid density appears at a much lower temperature than the kink in its heat capacity. The team believes this is caused by thermally excited vortices that induce breakdown of long-range order in helium-4, as has previously been seen in superfluids in 2-D.

"The helium atoms adsorbed on the walls of our nanopores act like a cylindrical 2-D system," explains Ikegami. "In a 2-D superfluid, fluctuations are significant, and destroy the macroscopic order. So, the temperature at which the macroscopic order appears, indicated by the appearance of superfluid density, is much lower than the one at which the local order appears, indicated by the heat capacity kink."

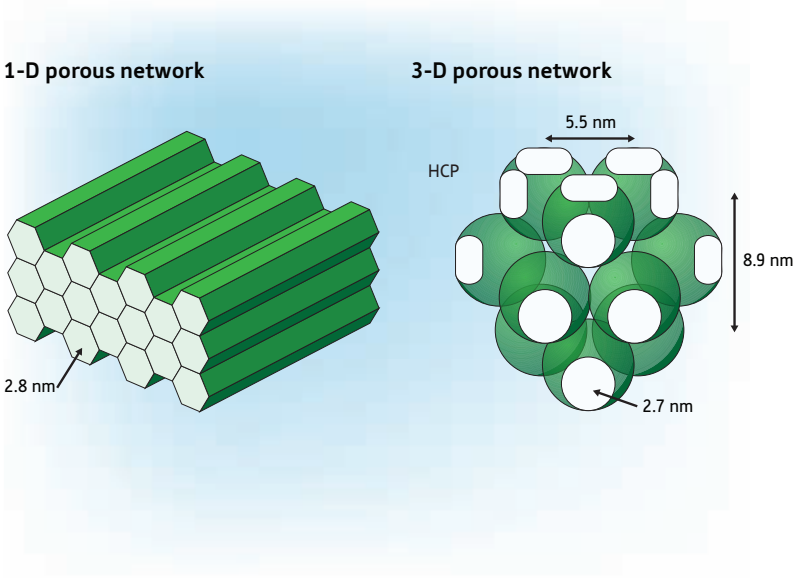

Figure 1: Illustration of the structure of the 1- and 3-D nanoporous networks used to explore the role of dimensionality on a superfluid phase transition.

More surprising, is that in the team's 3-D nanoporous network, the kinks in superfluid density and heat capacity occur at the same temperature, similar to a bulk 3-D liquid despite the fact that at a nanoscopic level its shape is essentially 2-D. The team suggests that the similar behavior arises because the network hinders the phonons that might otherwise destroy long-range ordering. Yet there is still work to be done, says Ikegami. "Although our results are very well described by the ideal 3-D theory, we have no basis, at present, to explain why they are described so nicely." ■

1. Toda, R., Hieda, M., Matsushita, T., Wada, N., Taniguchi, J., Ikegami, H., Inagaki, S. & Fukushima, Y. Superfluidity of ^{4}He in one and three dimensions realized in nanopores. *Physical Review Letters* **99,** 255301 (2007).

Current pulses make the switch

The magnetic reversal in ferromagnetic nanowires by current pulses opens the way to novel spintronics applications

Researchers at the RIKEN Advanced Science Institute, formerly the Frontier Research System in Wako, in collaboration with Hitachi High-Tech Fielding Corporation, have demonstrated how to reverse the magnetization in ferromagnetic wires using current pulses[1]. The result could be an important step for the development of the next generation of magnetic storage devices.

The ability to control the magnetization direction in ferromagnetic elements is critical to magnetic storage. In present devices, an external magnetic field is used for this purpose.

The use of currents is a promising alternative to magnetic fields. According to Yoshihiko Togawa of RIKEN, magnetic storage devices with high recording densities require a large magnetic field to reverse the magnetization, which causes undesirable interference with neighboring magnetic bits and degrades the device performance. "Spin-polarized current induces the magnetization reversal just in the magnetic bit where the current flows," he explains.

It is well known that when a spin-polarized current flows through a wall, which separates two domains with opposite magnetization, the flowing electrons can affect the magnetization by the so-called spin torque effect. This results in moving the domain wall and consequent reversing the magnetization in one of the domains. In addition, scientists have predicted that even when magnetization is uniform, current pulses can nucleate domain walls, move them and eventually reverse the magnetization direction. However, few experiments in wires have been done.

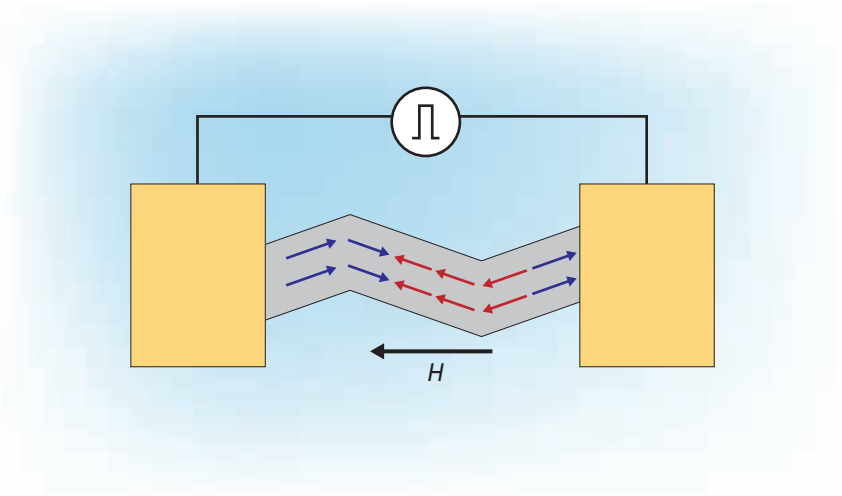

Figure 1: Schematic illustration of the experimental zigzag permalloy wire (grey) attached to electrical contacts (yellow). When the ferromagnetic wire is subjected to a small magnetic field (*H*) and a current pulse is introduced, the magnetization in the central part (blue arrows) is reversed (red arrows).

Now, Togawa and colleagues have studied a zigzag permalloy nanowire attached to large pads used as electrical contacts. They verified that when no external magnetic field is applied, the probability for a current pulse to switch the magnetization is very low. However, as soon as a small field is applied in the direction opposite to the magnetization, the probability rapidly increases and reaches 100% for a magnetic field of just 3.8 Oe.

The researchers have found that the right combination of current and magnetic field is needed for the reversal to occur (Fig. 1). For example, if the field is applied parallel to the magnetization the reversal probability is extremely low.

Although a magnetic field is still necessary for the reversal to occur, this is much lower than the field needed to reverse the magnetization without the use of current pulses. "We can perform magnetization reversal in [targeted] bits using current, which is free from any interference … due to large magnetic field," says Togawa. "We believe that [our] method is effective and advantageous [for] storage device integration." ■

1. Togawa, Y., Kimura, T., Harada, K., Matsuda, T., Tonomura, A., Otani, Y. & Akashi, T. Current-excited magnetization reversal under in-plane magnetic field in a nanoscaled ferromagnetic wire. ***Applied Physics Letters*** **92,** 012505 (2008).

The pairing habits of electrons

A process that makes a material become superconductive has been discovered in anion radical salts

Researchers at RIKEN's Advanced Science Institute in Wako, formerly the Discovery Research Institute, have discovered a novel mechanism by which an anion radical salt becomes superconductive at high pressures. Their discovery may help physicists to understand the transition between different quantum states in a broad class of materials.

Mott insulators are materials where constituent electrons cannot move due to the strong electronic repulsion between them, thereby impeding the flow of electrical current. Under external pressure, the electrons can be 'set free' and these insulators become conductive through a process known as Mott transition.

Reporting in the journal *Physical Review Letters*[1], the researchers have studied the Mott transition in the anion radical salt $EtMe_3P[Pd(dmit)_2]_2$. The anions of this salt form a triangular lattice, where each anion dimer occupies one of the corner positions (inset of Fig. 1). At low pressures and low temperatures, the electrons of the Mott insulator pair with a neighboring electron to form a rare quantum state: the valence-bond solid (VBS) state. This state contrasts with the antiferromagnetic state of conventional Mott insulators, where pairing does not occur. The researchers have now studied how this VBS state evolves at higher pressures.

In measuring the electrical resistance of the salt, the researchers mapped its phase diagram (Fig. 1). Importantly, they observed that at higher pressures, a Mott transition occurs from the insulating VBS state to either a superconducting or a metallic state. The transition from a VBS to a superconducting state, in particular, is of fundamental interest, and physicists have sought to observe it for decades, according to Yasuhiro Shimizu from the RIKEN team.

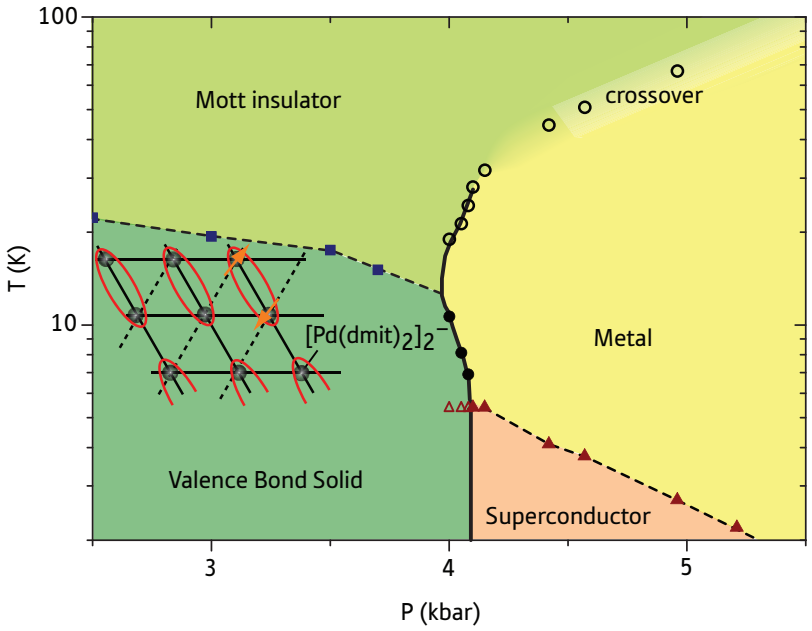

Figure 1: Phase diagram of $EtMe_3P[Pd(dmit)_2]_2$ (Et, ethyl; Me, methyl; dmit, 1,3-dithiole-2-thione-4,5-dithiolate). The inset shows the triangular arrangement of the $Pd(dmit)_2$ dimers. Of particular interest is the Mott transition from a valence bond solid insulator state to the superconducting state as pressure (P) increases at low temperatures (T).

Owing to the rarity of VBS states, previous Mott transitions to superconducting states had been found only in materials where electrons do not form a VBS. Further, this first observation of a transition from the VBS state by the researchers is significant because electrons not only pair up to form the VBS state, but also the superconducting state. However, there are crucial differences between the electron pairs: in a VBS they sit tight at the anions, whereas in a superconductor they are free to roam the crystal.

In future work, Shimizu suggests that it will be important to study this transition in electron pairing in further detail, as "this will help to understand the electron pairing mechanism of superconductivity." The unique properties of this anion radical salt certainly provide an exceptional platform from which to study the physics of quantum states like VBS and superconductivity. ■

1. Shimizu, Y., Akimoto, H., Tsujii, H., Tajima, A. & Kato, R. Mott transition in a valence-bond solid insulator with a triangular lattice. *Physical Review Letters* 99, 256403 (2007).

Molecular cables get insulating sheath

Good insulation for nanowires provided by self-assembling molecular-scale sheaths

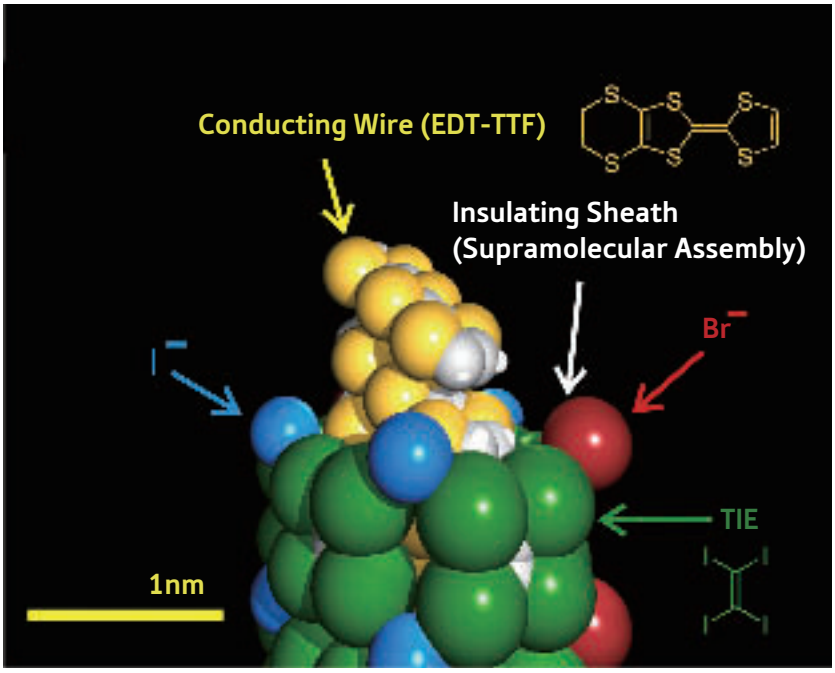

Figure 1: The conducting nanowire is sheathed in insulating molecules containing bromine and iodine.

Japanese scientists have developed a range of insulating materials that should allow computer circuits to be built from nanowires that are tens of thousands of times thinner than a human hair.

The strategy could help to pack much more processing power into the computers of tomorrow—not least because it would allow conventional, two-dimensional circuit boards to expand into the third dimension.

Scientists have already shown that nanowires can be connected together to make logic circuits that perform simple calculations. But the bare wires are prone to short-circuits. Like any electrical cable, they operate much better if they are insulated by a non-conducting material.

Now, Hiroshi Yamamoto, Reizo Kato and colleagues of RIKEN's Advanced Science Institute, formerly the Discovery Research Institute, Wako, along with several other Japanese research centers, have created molecular-scale insulating sheaths for nanowires[1] (Fig. 1).

The team created different examples of conducting nanowires based on stacks of molecules called tetrathiafulvalenes (TTFs). Their arrangement of carbon, hydrogen and sulfur atoms means that under certain conditions electrons can travel easily from one molecule to the next, so that a current flows through the wire. The properties of the wire can be fine-tuned by using similar molecules that contain selenium instead of sulfur.

In one such example, called (TSF)Cl(HFTIEB), a selenium-based conducting wire is surrounded by a relatively thick layer of molecules that incorporate iodine and fluorine atoms. This barrier—just one billionth of a meter thick—has a resistance some 100 million times greater than the wire it protects. This is the highest difference in resistivity within a single chemical substance ever recorded and comparable to the insulating power of epoxy resin, the scientists say, suggesting that HFTIEB provides good insulation for molecular conducting wires.

One of the most exciting parts of the scientists' technique is that these insulated wires 'self-assemble', spontaneously growing into the desired arrangement from their component parts. In the latter case, iodine is a crucial linchpin in holding the wire together.

All the examples created by the team were simple one-dimensional wires. However, it should be possible to achieve similar results using molecules that tend to grow into two- and three-dimensional networks. "Nanoscale wiring in 3D space could potentially realize very high-density and large-scale memory or logic circuits in the near future," the scientists say.

The next important challenges include reducing the number of molecular defects in the wires, and developing thicker, higher-resistance sheathing. ■

1. Yamamoto, H. M., Kosaka, Y., Maeda, R., Yamaura, J., Nako, A., Nakamura, T. & Kato R. Supramolecular insulating networks sheathing conducting nanowires based on organic radical cations. *ACS Nano* **2,** 143–155 (2008).

Copper helps carbon compounds get connected

Medicinal and materials chemists likely to benefit from the development of a reaction to modify benzene-based compounds

Figure 1: Crude oil can be turned into medicines and useful materials with the help of cunning chemistry that replaces hydrogen atoms.

A new chemical reaction developed by RIKEN scientists could speed the process of stitching together the molecules that make our medicines and pesticides. The technique allows benzene-based compounds to be precisely modified, allowing chemists to fine-tune their properties.

The scientists' reaction breaks a chemical bond between a carbon and a hydrogen atom, and then substitutes the hydrogen with a different atom or molecular fragment.

It may sound simple, but this is one of the most important—and tricky—types of reaction in chemistry. Many of the world's medicines and plastics are derived from oil, which is largely made up of simple chains of carbon atoms bristling with hydrogen atoms. These molecules participate in relatively few chemical reactions—yet substituting hydrogen atoms for nitrogen, oxygen or chlorine can completely change their chemical activity (Fig. 1).

These substitutions must be made at precisely the right spot on the molecule to create a compound with the desired properties for a particular application. But all the carbon–hydrogen bonds have very similar chemical activity, so it is often difficult to make the correct substitution, or to avoid making multiple substitutions.

In benzene (C_6H_6), a molecule with a hexagonal ring of six carbon atoms at its heart, each carbon atom is bonded to a hydrogen atom. Replacing any of these identical hydrogen atoms creates the same product. But a second substitution must be made in the correct position relative to the first.

Shinya Usui and Masanobu Uchiyama of RIKEN's Advanced Science Institute (formerly the Discovery Research Institute) in Wako, along with colleagues at the Universities of Tokyo and Cambridge, have developed a reactive chemical that can make sure that second substitution hits its mark[1].

Their organocuprate compound unites an atom of copper with organic (carbon-based) molecules, including a bulky nitrogen-containing group called tetramethyl piperidine.

The scientists found that the organocuprate compound always replaced the hydrogen atom closest to the substituent already attached to the benzene ring, forming a new carbon–copper bond. The copper-based group could then be easily swapped for a variety of other atoms.

The reaction worked on a wide range of different benzene-based molecules, and almost always converted more than 90% of them into the product the scientists wanted. The method could even connect two benzene-based molecules together, providing a useful way to build up large molecules very quickly.

Uchiyama says that this flexible method for constructing such compounds will be of interest to medicinal and materials chemists. ■

1. Usui, S., Hashimoto, Y., Morey, J. V., Wheatley, A. E. H. & Uchiyama, M. Direct ortho cupration: a new route to regioselectively functionalized aromatics. *Journal of the American Chemical Society* **129,** 15102–15103 (2007).

Mimicking molecules

Analogue of a biologically vital molecule will help medical studies

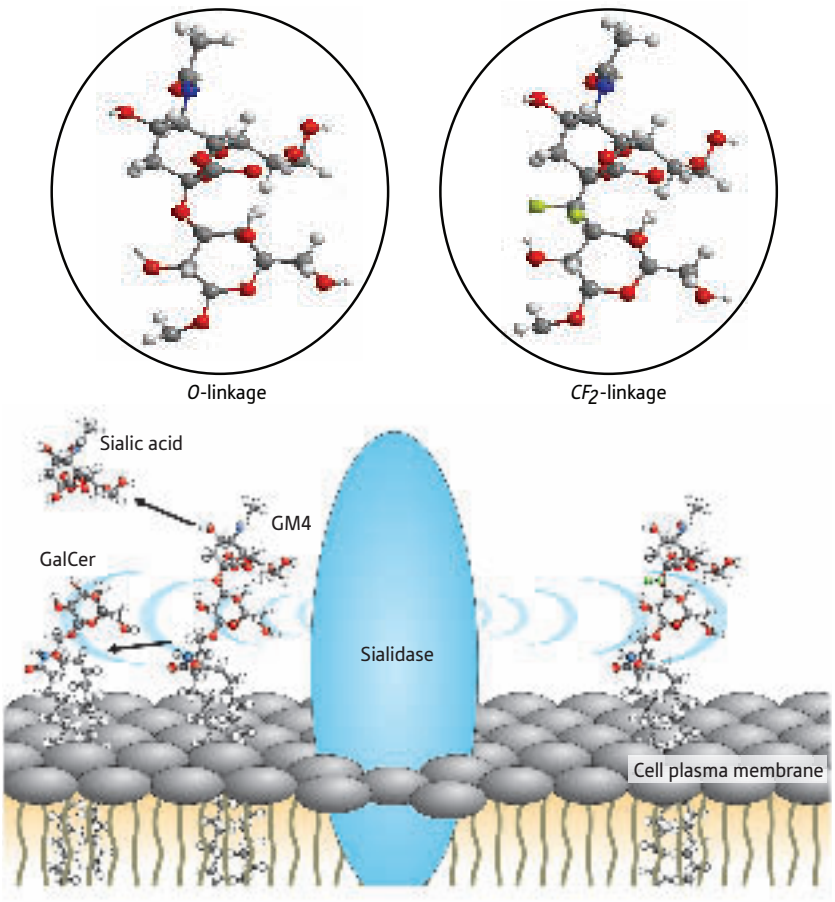

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Fig 1: Sialidase splices natural gangliosides at their oxygen linkage but analogues made with a difluoromethylene (CF_2) linkage are stable.

Japanese chemists have synthesized a robust version of a biologically important molecule that is naturally unstable so difficult to use experimentally. The natural form of the sugar- and lipid-based molecule, called ganglioside GM4, is found abundantly in the body, but without a chemically and biologically stable analogue of the molecule, researchers are yet to fully clarify its physiological roles.

One of over 40 known gangliosides, GM4 sits in the cell plasma membrane and is thought to be involved in cell recognition and transmission of chemical messages across the cell surface. Medically it is of great interest as gangliosides appear to be attacked in patients with certain autoimmune neurodegenerative disorders, such as Guillain Barré syndrome, and seem to be metabolized at a higher rate in cancer cells.

Researchers have grappled with studying the molecule because it is broken down very quickly to sialic acid and the molecule named GalCer by an enzyme called sialidase. Sialidase cleaves the natural ganglioside molecule at a point where an oxygen atom links two parts of the structure together (Fig. 1). Carbon attached to two fluorine atoms (CF_2) offers a good substitute for oxygen however and can easily sit in the oxygen's place, making this linkage point resistant to the enzyme's splicing action.

The team of chemists from several Japanese institutes, led by Mikiko Sodeoka from the Advanced Science Institute, formerly the Discovery Research Institute in Wako, set out to synthesize a biologically active, but sialidase-resistant analogue of GM4, using this CF_2 substitution as the basis for the structure of the mimic. The team developed a strategy to synthesize the sialidase-resistant molecule that involves the Ireland–Claisen rearrangement, a reaction that breaks carbon–oxygen bonds and forms carbon–carbon bonds simultaneously.

Published recently in the *Journal of the American Chemical Society*[1], the new method offers a high level of stereoselectivity, which is the ability to choose specific arrangements of atoms. This was important because using CF_2 instead of oxygen means a very specific orientation of the molecule is required in order for the atoms to fit together correctly in space. Efficient and controllable production of the imitation ganglioside was enabled by this method of synthesis.

Biological experiments using the new molecule are already underway to determine why gangliosides are degraded more quickly in cancer cells. The strategy used to synthesize GM4 promises to allow other forms of ganglioside to be copied. The team wants to produce a CF_2 linked analogue of ganglioside GM3 next, which may prove even more useful in determining the role of these molecules, says Sodeoka. ■

1. Hirai, G., Watanabe, T., Yamaguchi, K., Miyagi, T. & Sodeoka, M. Stereocontrolled and convergent entry to CF_2-sialosides: Synthesis of CF_2-linked ganglioside GM4. *Journal of the American Chemical Society* **129,** 15420–15421 (2007).

Mapping disease progression

A protocol to form imaging molecules paves the way to new methods of detecting disease *in vivo*

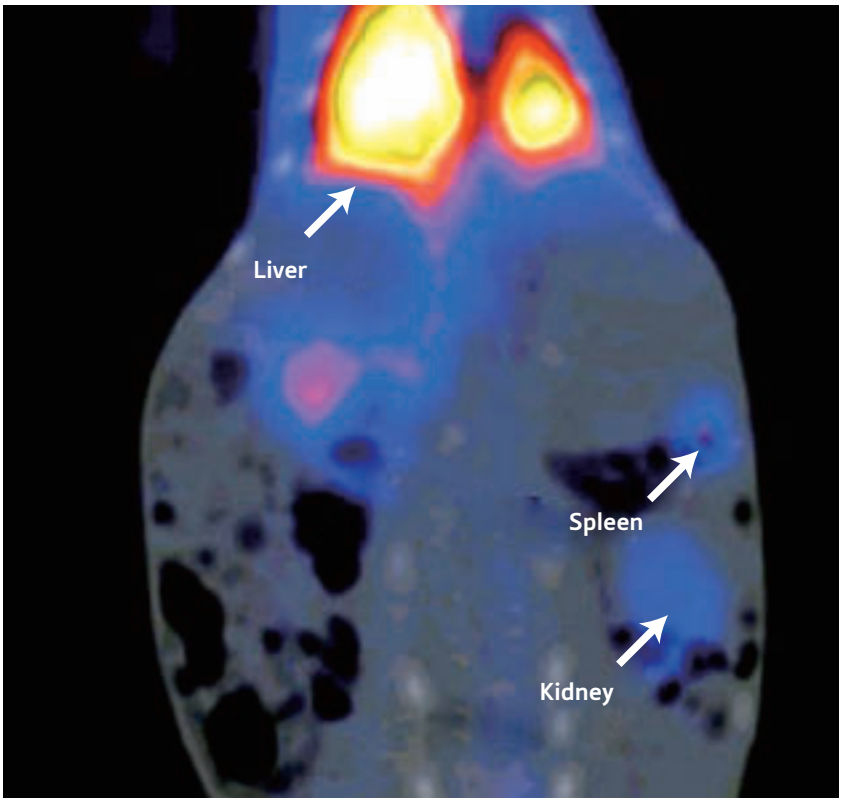


Figure 1: A picture of a new Gallium-containing imaging compound accumulating in several organs of a rabbit.

A team of scientists from Japan has developed a new type of bio-label that can be used to detect and image unusually large molecules in experimental animals and non-human primates. The technique could lead to similar methods for being developed for use in humans.

Tracking diseases or monitoring disease progression in a patient is an important factor in deciding the best form of treatment. While biopsies—taking a small sample of tissue from a patient—remain standard hospital practice, more patient-friendly techniques are sought. Non-invasive techniques, such as imaging, can detect and monitor disease in the living body without the risks associated with surgery.

Now, Yasuyoshi Watanabe from the RIKEN Molecular Imaging Research Program, Kobe, as part of a large collaborative project with Koichi Fukase from Osaka University, has developed a new way of labeling biological molecules to make them suitable for imaging using the nuclear medicine technique of positron emission tomography (PET)[1].

"Previously, PET imaging methods have mostly focused on probing only low molecular weight compounds," explains Watanabe. He hopes to develop methods suitable for larger macro-molecules, such as peptides, nucleic acid sequences, glyco-conjugates and proteins that make up antibodies and drive his research.

When labeling macro-molecules it is important that biological activity is not lost; the antibody must continue to recognize and bind to an antigen—such as the surface molecules of specific cells including cancer cells, bacteria or viruses—and stimulate an immune response. As macro-molecules are often damaged or destroyed during the labeling process, the chemical protocol developed by Watanabe and colleagues uses only mild temperatures and aqueous solutions.

The researchers chose lysine, an amino acid residue, in the macromolecule as the group onto which the label would be attached. They attached the label, a small organic compound, specifically onto the lysine residue under the mild conditions. Next, they added Gallium, a radioisotope element, to form adducts with the label. The resulting derivatives, detectable using PET, were then tested for biological activity. Results obtained from rabbits showed that the label was easily detected and was found in the major organs of the rabbit as expected (Fig 1).

Watanabe and team are now investigating alternative strategies for labeling other macro-molecules, such as F-18, the radioisotope of fluorine, which is also widely used for PET imaging. Through continued research in this area the team hopes to develop better and more efficient ways to label molecules and extend the range of molecules that can be labeled. ■

1. Tanaka, K., Masuyama, T., Hasegawa, K., Tahara, T., Mizuma, H., Wada, Y., Watanabe, Y. & Fukase, K. A submicrogram-scale protocol for biomolecule-based PET imaging by rapid 6 π -azaelectrocyclization: visualization of sialic acid dependent circulatory residence of glycoproteins. ***Angewandte Chemie International Edition*** **47,** 102–105 (2007).

Landmark genome contains wealth of data

Moss provides clues as to how plants came ashore

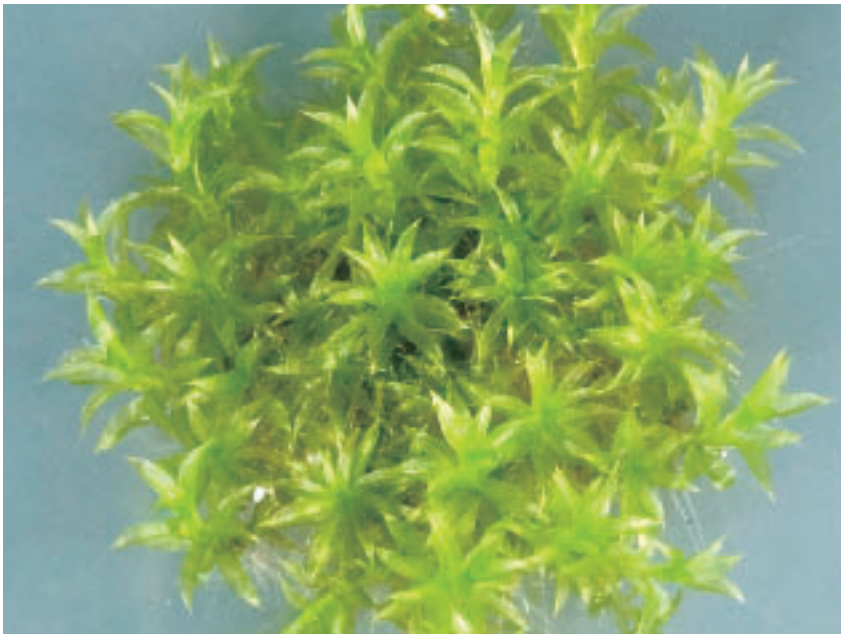


Figure 1: The moss *Physcomitrella patens*—about two centimeters in diameter.

Molecular biologists from RIKEN's Bioinformatics And Systems Engineering division, formerly Genomic Sciences Center and Plant Science Center in Yokohama are among 70 researchers from more than 40 institutes, including Japan's National Institute for Basic Biology (NIBB), who recently published the draft genome of the moss, *Physcomitrella patens*[1]. The genetic information contained in the draft will provide insight into the development of plants and their ability to survive on land, particularly their drought tolerance.

Physcomitrella, a small, delicate moss often found along the edges of lakes and rivers (Fig. 1), is a modern relative of the plants which first colonized land and a key evolutionary link between ancient aquatic single-celled algae and terrestrial flowering plants. The species has already become an important experimental organism, because its genetic material can be manipulated efficiently, it reproduces rapidly, and its simple structure allows it to be observed and imaged easily. The ability to study drought tolerance and the synthesis of plant walls in *Physcomitrella* should increase the capacity to groom crops against water shortages and lead to more effective ways of decomposing cellulose in biofuels.

It is clear from the draft, the researchers say, that *Physcomitrella* underwent at least one large-scale duplication of its genome, possibly more. Such genetic upheavals are evolutionarily important, because copies of genes can subsequently be modified while the organism retains the originals with all the information to form a viable individual.

The mosses are bryophytes, plants which require access to water to reproduce sexually, and which branched off the line leading to flowering plants about 400 million years ago. Hence, by comparing the moss genome to those of three well-known unicellular green algae and three flowering plants, the researchers have already begun to identify broad genetic trends in the evolution of characteristics which allowed plants to survive on land.

They have concluded that among the genes associated with terrestrial survival there are genes for the development of systems for transporting water and for signaling systems that coordinate growth and the response to dehydration. The genes associated with terrestrial survival were gained by the last common ancestor of all land plants.

The mosses also evolved elaborate DNA repair mechanisms to combat the greater impact of radiation on land.

Mitsuyasu Hasebe and colleagues at the NIBB have made a major contribution to all phases of the genomic study. The RIKEN researchers helped determine end sequences of DNA segments used to puzzle out the genome, says contributor Atsushi Toyoda. "We will continue to work at completing and verifying the genome sequence and identifying functional genes," he says. ■

1. Rensing, S.A., Lang, D., Zimmer, A.D., Terry, A., Salamov, A., Shapiro, H., Nishiyama, T., Perroud P-F., Lindquist, E.A., Kamisugi Y., *et al*. The Physcomitrella genome reveals evolutionary insights into the conquest of land by plants. *Science* **319**, 64–69 (2007).

Dampening dangerous inflammation

Immune therapy using unique immune cells significantly reduces inflammation in mouse models of human disease

A team of Japanese researchers is working to find better treatments for chronic inflammation. New work by the team demonstrates that conditions such as lethal disease associated with tissue and organ transplantation[1], and asthma[2], can be successfully treated with specialized immune cells to reduce inflammation.

Led by Katsuaki Sato at the RIKEN Research Center for Allergy and Immunology in Yokohama, the team studied dendritic cells of the immune system, so called because of the many 'dendrites', or branched projections, on their surface. Dendritic cells initiate immune responses by directly communicating with other immune cells. One outcome of such communication is the production of 'guardian' lymphocytes that keep the immune system in balance; referred to as 'regulatory T cells', these lymphocytes are increasingly seen as critical players in a myriad of diseases.

Sato's team has demonstrated that therapeutic treatment of mice with specially conditioned dendritic cells significantly reduces inflammation. Referring to such dendritic cells as 'regulatory dendritic cells' (or simply 'DC_{regs}'), the team—in a series of articles in the past few years—has described the protective effect of immunotherapy with DC_{regs} in mouse models of human disease.

As Sato explains, "to exploit a novel immunotherapeutic strategy using dendritic cells for immuno-pathogenic diseases, we have tried to establish use of DC_{regs} with a potent immuno-regulatory property even under inflammatory conditions." By focusing on ameliorating inflammation when it is chronically present and especially difficult to treat, the team's work is different from other attempts to maximize the efficacy of immune therapy.

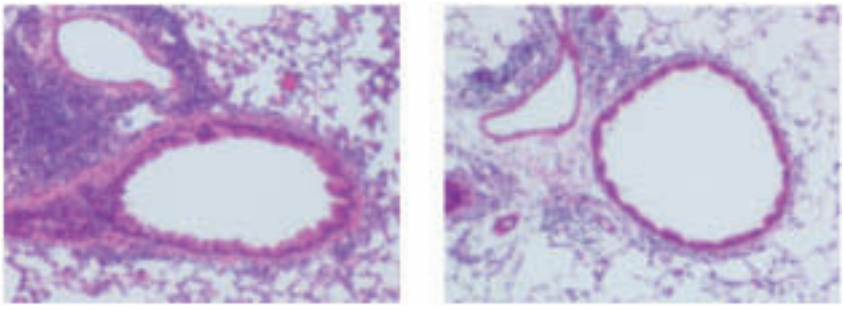


Figure 1: Treatment with dendritic cells clears the airways. A section of an inflamed mouse lung shows numerous immune cells stained in purple that lead to airway constriction (left). Treatment with regulatory dendritic cells significantly reduces the inflammation, leading to open airways (right).

Using mouse models of human disease, Sato's team studied bone-marrow transplantation rejection for graft-versus-host disease (GVHD) and lung-airway inflammation for asthma. DC_{regs} produced in the laboratory and then injected into mice with these diseases demonstrated significantly reduced inflammation (Fig. 1). Looking closely at the recipient mice, the team noted that the treatment was associated with increased numbers of regulatory T cells—key suppressors of inflammation.

According to Sato, the next key step is to clarify the molecular mechanisms responsible for the production of regulatory T cells by DC_{regs}. Longer term, Sato is clearly set on the goal of treating human diseases with DC_{regs}: "we have recently established the methods to prepare a large number of human DC_{regs} for clinical application."

Although not yet ready for the clinic, immunotherapy with DC_{regs} has clear potential thanks to the work reported by Sato and his team that demonstrates the unique power of regulatory dendritic cells to reign in lethal inflammation. ■

1. Fujita, S., Sato, Y., Sato, K., Eizumi, K., Fukaya, T., Kubo, M., Yamashita, N. & Sato, K. Regulatory dendritic cells protect against cutaneous chronic graft-versus-host disease mediated through $CD4^+CD25^+Foxp3^+$ regulatory T cells. ***Blood*** **110,** 3793–3803 (2007).
2. Fujita, S., Yamashita, N., Ishii, Y., Sato, Y., Sato, K., Eizumi, K., Fukaya, T., Nozawa, R., Takamoto, Y., Yamashita, N., Taniguchi, M. & Sato, K. Regulatory dendritic cells protect against allergic airway inflammation in a murine asthmatic model. ***Journal of Allergy and Clinical Immunology*** **121,** 95–104 (2008).

Regulating antibody production

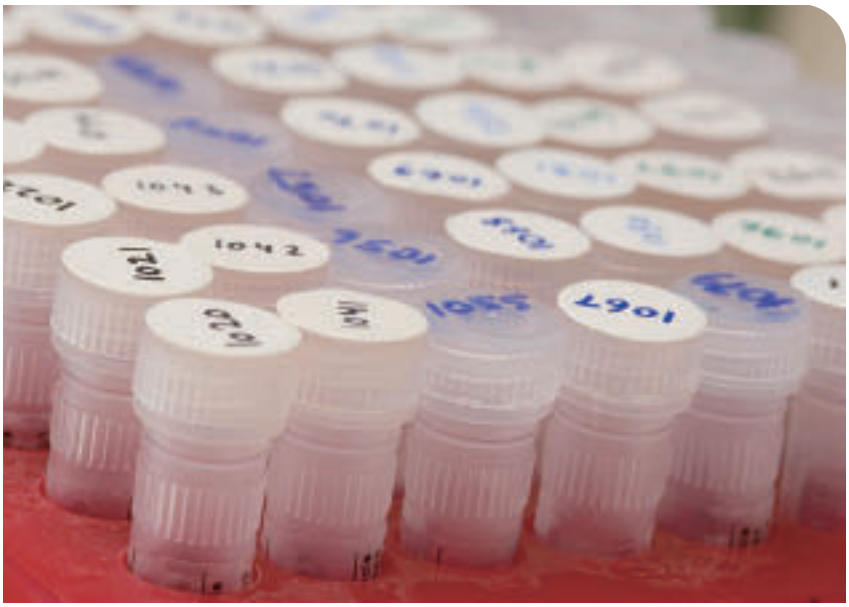
New insight into an important part of the immune response could lead to treatments for immune disorders

A RIKEN research group has puzzled out the molecular details of a key part of the complex communication network that regulates the production of antibodies by the immune system. The findings are an important step towards understanding immune disorders and how some types of tumors are initiated, as well as developing treatments for these conditions.

The work concentrates on the molecular events that occur immediately after an immune system B-cell is stimulated by a foreign body or antigen. From previous studies it is known that antigens bind with a surface protein known as a B-cell receptor (BCR) and that this triggers a complicated cascade of biochemical reactions involved in the immune response and its regulation.

One important biochemical pathway in this response involves two families of proteins called nuclear factor-κB (NFκB) and inhibitor of nuclear factor-κB kinase (IKK). Generally NFκBs are bound in the body of the cell to IKKs. When a BCR is triggered by an antigen, however, one consequence is the phosphorylation or addition of phosphate groups to IKKs which activates them to break up. This liberates NFκBs which can then enter the nucleus and interact with specific genes to trigger the immune response.

In a paper published recently in the *Journal of Experimental Medicine*[1], researchers from RIKEN's Research Center for Allergy and Immunology in Yokohama led by Tomohiro Kurosaki describe work in which they were able to unravel the interactions of these molecules more precisely.



Two of the compounds known to be involved in the phosphorylation of specific amino acids in IKKs are protein kinase C β (PKCβ) and a complex called CBM built of three proteins: CARMA1, Bcl10 and MALT1. Using antibodies engineered to bind to and pinpoint amino acids which have phosphates added, the researchers found that PKCβ not only initiates the addition of phosphates to IKKs, but also adds phosphate directly to CARMA1 and this activates it to build the CBM complex. The researchers also found that one of the components of the IKK complex, IKKβ, phosphorylates CARMA1 as well. IKKβ therefore plays a positive feedback role when the IKK complex degenerates, amplifying the break down process.

"Both prolonged activation and inhibition of NFκBs are able at times to induce tumors," says Hisaaki Shinohara, first author on the paper. "So the molecules included in this feedback loop provide good candidates as cancer drug targets." ■

1. Shinohara, H., Maeda, S., Watarai, H. & Kurosaki, T. I κ B kinase β -induced phosphorylation of CARMA1 contributes to CARMA1-Bcl10-MALT1 complex formation in B cells. *Journal of Experimental Medicine* **204,** 3285–3293 (2007).

Looking beneath the surface

A new imaging technique allows scientists to effectively visualize individual molecules within living cells in real-time

Historically, analysis of the behavior of individual proteins has required the physical destruction of the cells in which they are found. More recently, however, a new generation of microscopy techniques has emerged that make it possible to directly visualize individual fluorescently tagged molecules within the living cell, giving scientists unprecedented capabilities to observe biological processes in their natural context.

"These techniques enable us to visualize molecular dynamics and interactions, to analyze molecular mechanisms quantitatively, and to detect biomolecules with great sensitivity in living cells," explains Makio Tokunaga, an imaging specialist at the RIKEN Research Center for Allergy and Immunology in Yokohama.

One popular technique is total internal reflection fluorescence (TIRF) microscopy, which takes advantage of the physics of refraction to specifically excite fluorescent molecules in the immediate proximity of the microscope objective. Unfortunately, although TIRF is useful for single-molecule visualization, its limited depth of visualization means that it can only observe targets located near the cell surface.

In order to overcome this limitation, Tokunaga's team developed a new variant of TIRF, which they term highly-inclined and laminated optical sheet (HILO) microscopy[1]. HILO makes use of an alternative refraction strategy, in which the laser beam that illuminates the sample is converted into a thin sheet that passes through the center of the specimen. HILO is capable of imaging targets at depths of tens of microns—well beyond the cell membrane—and can be used to generate three-dimensional reconstructions via the computerized assembly of multiple scans into a single image.

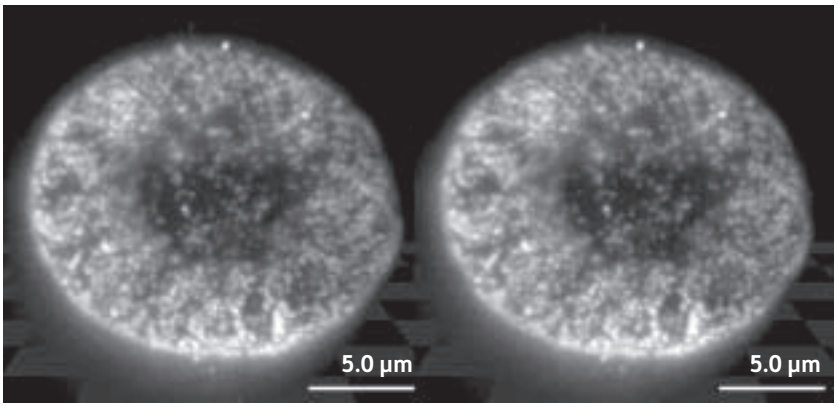


Figure 1: A stereo pair of images demonstrating the three-dimensional reconstruction of the distribution of nuclear pore complexes within the nuclear membrane from a serial set of HILO images. Scale bars = 5.0 µm.

In testing out HILO, the researchers started big—relatively—by imaging nuclear pore complexes (NPCs), the massive multiprotein assemblies that act as the gateway between the nucleus and cytoplasm. The researchers obtained remarkably clear images of these complexes, with virtually no background haze (Fig. 1). They subsequently used HILO to visualize the movement of fluorescently labeled importin β, a protein that shuttles other molecules into the nucleus via the NPCs, generating videos that show the kinetics of nuclear import at high resolution and in real-time.

Tokunaga sees HILO as a promising tool for immunology research. "We intend to visualize signaling pathways from the cell membrane to the nucleus after stimulation using single-molecule microscopy," he says. By combining this real-time imaging data with sophisticated computational modeling strategies, it should be possible to gain unprecedented insight into complex cellular pathways. "We aim to open up new frontiers for understanding immune cells as molecular systems," concludes Tokunaga. ■

1. Tokunaga, M., Imamoto, N. & Sakata-Sogawa, K. Highly inclined thin illumination enables clear single-molecule imaging in cells. *Nature Methods* **5,** 159–161 (2008).

How nerve cells are shaped

Discovery of molecules that sculpt nerve shape will assist in understanding nerve cell function and neurological disease

Molecular biologists at RIKEN's Brain Science Institute in Wako have unraveled details of the genetic controls that determine the distinctive shapes of four classes of sensory nerve cells in the fruit fly, *Drosophila*.

Nerve cell shapes vary according to the number, branching and disposition of their projections or dendrites, collectively known as arborization. This determines their capacity for interacting with their environment and with other nerve cells or neurons, hence their computational ability and roles. Knowing how such shapes are determined is important for understanding nerve cell function and neurological disease.

The shapes of *Drosophila* sensory cells display a progression of increasing branch complexity and symmetry from class I to class IV (Fig. 1). The research, recently published in *Neuron*[1], shows how development of these shapes depends on the levels and interaction of transcription factors, which are proteins that control the information printed off from the DNA.

From previous work by other researchers it was known that only the transcription factor 'Abrupt'—which suppresses outgrowth and branching of dendrites—is active in class I neurons. In the other three neuron classes Abrupt is switched off and the factor 'Cut' is active. Cut promotes growth and branching and is found at low levels in class II neurons, high in class III and intermediate in class IV.

Because class IV neurons have lower levels of Cut than class III, but are much larger and more highly branched, the researchers hypothesized the involvement of a third transcription factor in this biggest neuron class. They subsequently found 'Knot', which encourages dendrite outgrowth and branching primarily through promoting the protein Spastin. By transferring Knot and Cut into cells where they are not normally active, the group found that both regulate development of the cell skeleton, but each controls a different skeletal building block.

Knot and Cut interact in complex ways. In class III neurons, which lack Knot, spikes known as filopodia project from the main dendrite trunks. In class IV neurons where both factors are present, filopodia formation is suppressed by Knot. In contrast, the two factors work together to increase outgrowth and branching.

"We have begun to unravel the complex interactions of the many proteins controlling the characteristic shape of different neuron types," says project leader, Adrian Moore. "But we have a long way to go to understand exactly how these molecular mechanisms translate into the final form of the neuron." ■

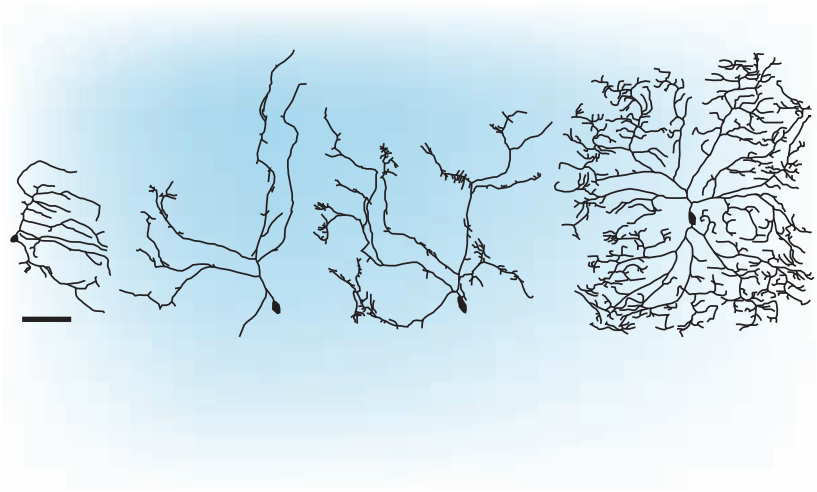


Figure 1: Shapes of the four classes of sensory nerve cells in *Drosophila*.

1. Jinushi-Nakao, S., Arvind, R., Amikura, R., Kinameri, E., Liu, A.W. & Moore, A.W. Knot/Collier and Cut control different aspects of dendrite cytoskeleton and synergize to define final arbor shape. ***Neuron* 56,** 963–978 (2007).

Seeing the essence of chemical reactions

Toshinori Suzuki

Chief Scientist,
Director of Chemical Dynamics Laboratory
RIKEN Advanced Science Institute

"When I was in high school, I was really interested in the first few pages of a textbook on chemistry, in which some molecular structures and chemical formulae were described," says Toshinori Suzuki, Chief Scientist in the Chemical Dynamics Laboratory at the RIKEN Advanced Science Institute. "Why can we understand chemical structures when nobody has ever directly seen them? Why do chemical reactions occur as indicated in the formulae? I wanted to find answers to these questions." Suzuki uses unique methods for visualizing chemical reactions to derive universal rules that commonly govern various chemical reactions, thus contributing to creating new chemical substances or gaining a better understanding of life phenomena.

"I got into the study of chemistry because I was inspired by Professor Yoshito Amako when I took his quantum chemistry course. Then, I was a first-year student at Tohoku University," says Suzuki, looking back on his college years. Quantum chemistry is a field of research that aims to elucidate molecular structures and chemical reactions using quantum mechanics, which is a tool for explaining the microscopic world. "We usually learn quantum chemistry at the junior level," explains Suzuki. "Professor Amako, however, tried to teach quantum chemistry to students who had only just graduated from high school. We had great difficulty in understanding his lectures. It seemed that Professor Amako was trying to see how many students could keep up with his lectures." Suzuki recalls how after class, he would make a copy of his lecture notes in his apartment, and try to add to the notes with what he had found out for himself. "In this way, I managed to decipher the lectures one step at a time. As a result, I noticed, clearly, that chemistry is very logical."

Thus, Suzuki began to pursue the study of elucidating the mechanism of chemical reactions. "Professor Amako told us first-year students that no textbooks were available for us because we should become researchers who explore the frontiers of science and for whom no textbook is available. We should be the ones who write the textbooks for future students. His words are still ringing in my ears."

Bombarding molecules in a vacuum with other molecules

It is difficult even for modern chemists to understand the detailed mechanisms in chemistry.

Suzuki points out, "This is because we cannot directly see the molecular structures or processes of chemical reactions." Molecules are very small, with a size of about 1 nanometer (where nano indicates 10^{-9}). Chemical reactions are phenomena that occur in a very short period ranging from 10 femtoseconds (where femto indicates 10^{-15}) to 10 nanoseconds. Chemical dynamics researchers aim to visualize as many chemical reaction processes as possible to understand the mechanisms involved.

The following rule prevails in many chemical reactions: molecule A bombarded with a molecule B produces molecules C and D. At present, there is no known method that enables the dynamics of this process to be observed as a movie. Such observations would require us to bombard A with B in a very short period of time to within an accuracy of 1 picosecond (10^{-12} seconds), which is the timescale in which most chemical reactions occur. "However," adds Suzuki, "No such techniques are available, anywhere in the world."

In the 1950s, to investigate chemical reaction processes, scientists began to develop the 'crossed molecular beam scattering method', which is a method for observing the direction and speed

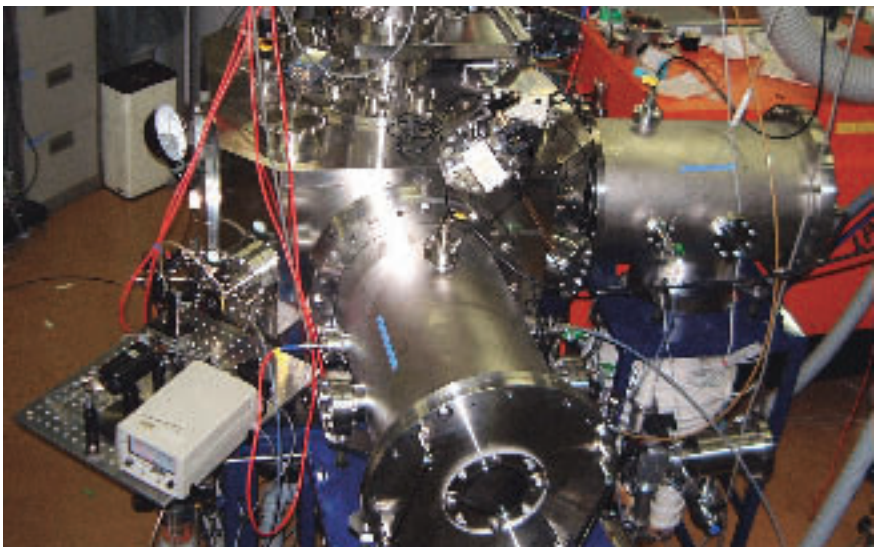


Figure 1 : Crossed molecular beam scattering imaging instrument.
The two cylinders are used to produce two different beams of atoms or molecules (a supersonic molecular beam), which are then crossed causing a chemical reaction between them. The newly created molecules are ionized by a laser beam, and then a voltage is applied so that the ionized molecules collide with a screen for visualization. Selecting a special wavelength allows only the molecules in a special vibrational and rotational state to be ionized and visualized.

of the two new molecules created as a result of one molecule being bombarded by another molecule. In 1969, Dudley Herschbach of Harvard University in the USA and Yuan-Tseh Lee, a member of the RIKEN Advisory Council (RAC—an international RIKEN external assessment committee), completed an apparatus that enabled the measurement of not only the direction and speed, but also the mass of newly created molecules, and to estimate what kind of molecules were created when two molecules bombarded each other. Thus, chemical reactions started to be investigated in detail. They were awarded the Nobel Prize in Chemistry for their work in 1986.

"Chemical reactions mainly occur in liquids and gases," says Suzuki. He adds that, for example, in aqueous solution, there are many water molecules surrounding the molecules that cause the chemical reaction, and these water molecules significantly affect the reaction. "The first step we should take, however, is to eliminate the molecules in 'supporting roles', such as water molecules, and only pay attention to the molecules in 'leading roles', because this could lead to more simplified presentations of chemical reactions." He explains that the crossed molecular beam scattering method is used to investigate how newly created molecules scatter when two leading-role molecules bombard each other in the absence of supporting-role molecules, such as water molecules. This may be compared to 'tracing the memory of chemical reactions', because the procedure is to estimate the chemical reaction that would have occurred at the moment of collision on the basis of how the newly created molecules are scattered.

Conventional crossed molecular beam scattering methods, however, are not available for observing how newly created molecules rotate and vibrate while they are being scattered. Thus, these methods failed to offer sufficient information to elucidate the chemical reactions.

In 1992, Suzuki tried to combine the crossed molecular beam scattering method with laser spectroscopy to develop the 'crossed molecular beam scattering imaging method', which enabled the observation of both the rotation and vibration of molecules. "In 2001, we presented the observation results to the US journal *Science*. We spent nearly 10 years developing the apparatus." (See Fig. 1)

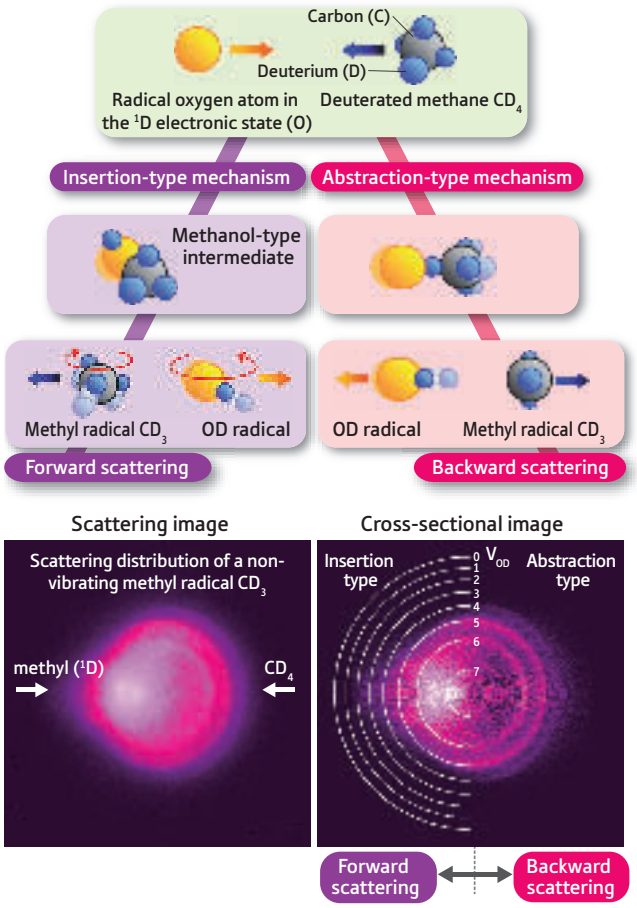
The following shows the results of some observations of chemical reactions between an oxygen atom radical and a deuterated methane molecule. There can be two kinds of channel in this chemical reaction (Fig. 2). One channel is the insertion-type mechanism, in which an oxygen atom is fused with a methane molecule to form a methanol-type intermediate, which is, in turn, separated into a methyl radical and OD (where O is oxygen and D is deuterated hydroxyl radical) radical molecules. The other is the abstraction-type mechanism, in which an oxygen atom pulls a hydrogen atom out of a methane molecule to form a methyl radical, and an OD radical. The chemical reactions in the two channels are reflected in the observed images.

A methane molecule consisting of a single carbon atom and four hydrogen atoms has a tetrahedral shape, whereas a methyl radical, which is a methane molecule minus one hydrogen atom, has a planar shape. "The methane molecule seems to vibrate violently when it is bombarded with a radical oxygen atom, causing a quick configurational change of orbitals and the loss of a hydrogen atom," says Suzuki. "But in reality this is not the case." Observed images showed that the vibration of the methyl radical is very small, and that the majority of the energy is converted into the vibrational energy of the OD radical. Thus, it is possible to physically elucidate chemical reactions only by observing the collision and scattering of molecules in detail, with the use of laser light sources and an imaging technique.

At present the Chemical Dynamics Laboratory at RIKEN is leading the research groups around the world in visualizing the chemical reaction and scattering of molecules and elucidating their dynamics.

Seeing electrons that cause chemical reactions

As another major subject of study, the Chemical Dynamics Laboratory is also conducting research using 'ultrafast photo-electron imaging'. This is a technique that enables us to track, in real time, the motion of electrons caused by chemical reactions. "Although a molecule consists of electrons and nuclei, electrons have a leading role in chemical reactions. Thus, the change in



There can be two kinds of channel in the chemical reaction between radical oxygen atoms O (^1D) and deuterated methane CD_4: insertion type and abstraction type.

The scattering image, observed by the crossed molecular beam scattering imaging method, shows that for the insertion-type channel, the methyl radical CD_3 is injected in the direction of the deuterated methane CD_4 (forward), whereas for the abstraction type, the methyl radical CD_3 is scattered backward.

Figure 2 : Chemical reaction between radical oxygen atoms and deuterated methane.
The scattering image looks like a diamond ring, in which the brighter diamond part corresponds to forward scattering, whereas the ring part corresponds to backward scattering. Backscattered methyl radicals CD_3 move at discrete velocities. This corresponds to the fact that OD radicals occupy discrete vibrational energy levels when they are created in pairs and vibrationally excited.

the motion of electrons is the essence of chemical reactions."

However, as mentioned before, there are no techniques that enable the real-time observation of the whole process in which molecule A is bombarded with molecule B to create molecules C and D. Laser-beam pulses are used to irradiate the combined state of molecules A and B at 100 femtosecond intervals—a timescale shorter than the timescale for chemical reactions—thus initiating the chemical reaction for creating molecules C and D. This process is called 'half-collision', because it only refers to the process following the bombardment of A with B. The laser pulses are used to knock the valence electrons—which are in the outmost orbit of the atoms and play an important role in this chemical reaction—out of the molecule, and to project the valence electrons onto a screen. The change in the motion of the electrons that cause chemical reactions is reflected in the projected electron distribution.

"In the spring of 1998 while I was developing this new experimental idea, I was invited by the Royal Society of Chemistry to a Faraday Discussion that was to be held in July of the following year," says Suzuki. "I was expected to submit my paper to the Discussion in advance, and to deliver a presentation for several minutes on the day, as well as answer a bombardment of questions." He describes how much he wanted to prepare interesting study results for the event. "Thus I finally completed the apparatus by December, and tried to make a thorough measurement of molecules available in the laboratory. I gave up my New Year's holidays to continue the experiments, and finally obtained interesting observation results in March. However, I broke down from overwork immediately after I had obtained the successful results."

It was a molecule called pyrazine that brought about the interesting results. Electrons have a physical property called 'spin angular momentum', which is similar to the spinning of the Earth. In terms of angular momentum, electrons can be in one of two spin states: either in the clockwise or counter-clockwise directions. When pyrazine molecules are irradiated by light, the spin state of the electrons is reversed, for example, from clockwise to counter-clockwise. The energy of the electrons is then reduced, causing the electrons to change their orbits. The reduced energy is converted into the vibrational energy of the molecules. The molecule disintegrates long afterward. Suzuki succeeded in observing the change in the motion of the electrons that occurs only momentarily, over about 100 picoseconds. At present, only Suzuki and members of the Laboratory are capable of conducting such detailed observations. The time resolution is now approaching 10 femtoseconds (Fig. 3).

"When I was in graduate school," he says, "I had a chance to listen to a lecture given by Dr Kenichi Fukui, a Nobel Prize Laureate." Suzuki recalls how after the lecture, a question was asked as to how to conduct good research. In answer to the question, Fukui said, "You should choose your molecules carefully." Suzuki adds, "At the time I wondered why he told us to choose our molecules carefully when we were pursuing universal rules that govern every chemical reaction." Suzuki then points out that in actual research activities, there is an opportunity to find molecules that can clearly provide the information needed or unexpected hints. "Thus we should listen to and try to thoroughly explore what the molecules tell us. In fact, that is the shortest way to detect universal rules in chemistry," he continues. "We should explore, from a breakthrough with a specific molecule, the essence of chemistry located at the core of diversity, because chemistry is the study of science that deals with the

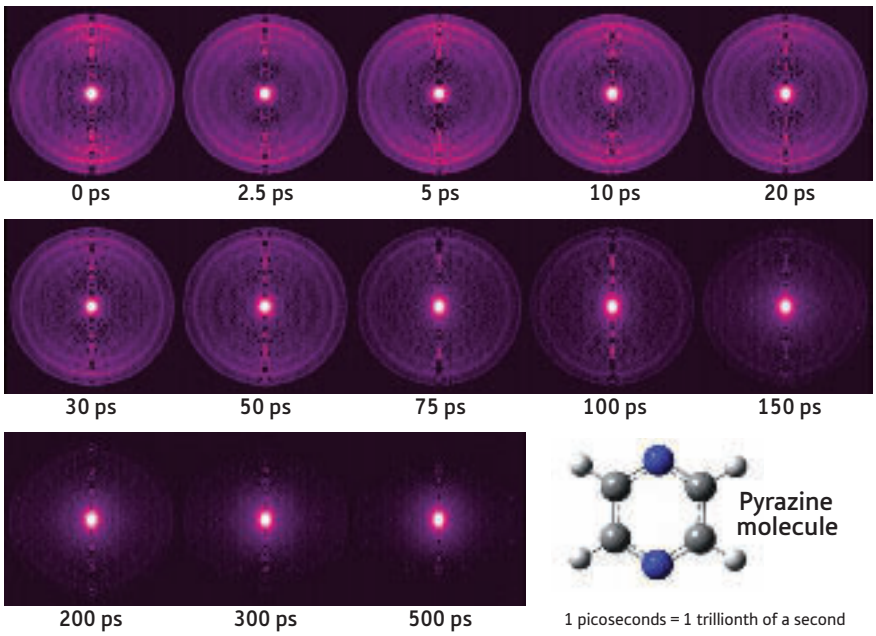


Figure 3 : Ultrafast photo-electron imaging.
When pyrazine molecules are subjected to 320 nm ultraviolet light, an electron is excited. The electron is then spin-reversed within about 100 picoseconds. The energy of the electron is reduced and the electron changes its orbit. The figure shows an observed cross-sectional image of a pyrazine molecule while its electrons are knocked out of the molecule by the light used for observation. The electronic distribution tends to become more concentrated at the center as the time it is exposed to the observation light increases, reflecting the change in electronic-spin motion.

diversity of materials."

In the current ultrafast photo-electron imaging method, the valence electrons in the outmost orbit of atoms are knocked out of the molecules. "The valence electrons play the most important role in chemical reactions. However, we also need to observe electrons that lie deep in the molecule and close to the nuclei, so as to obtain structural information concerning specific atoms in the molecule."

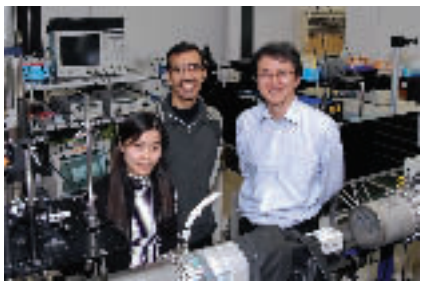


Figure 4 : Suzuki, Chief Scientist (right); Alnama, Contract Researcher (middle); and Liu, Asia Program Associate (left).
The Chemical Dynamics Laboratory, from which 5 out of 10 scientists will be foreign nationals from April 2008, typifies international institutes like RIKEN. The photograph shows an apparatus to observe chemical reactions in solution. This apparatus will be brought into the RIKEN Harima Institute to conduct experiments using the XFEL.

In order to knock deep-lying electrons out of the molecule, an extremely powerful laser beam with a shorter wavelength is needed. The X-ray Free Electron Laser (XFEL), which is now under construction at the RIKEN Harima Institute, would enable such observations. Suzuki and Laboratory members are planning to use the XFEL to extend further the ultrafast photo-electron imaging method.

Understanding how proteins act in water

Suzuki has successfully formed a very small liquid droplet, 10 nanometers in diameter. They have also begun to knock electrons that cause chemical reactions out of the tiny droplet, thus observing in detail the chemical reactions in it.

The above-mentioned observations are all based on chemical reactions in a vacuum environment. However, most research on the development of new chemical substances is based on chemical reactions in solutions. In addition, biological molecules, such as proteins, which build and maintain our bodies, cause various chemical reactions in water. Thus it is essential to explore chemical reactions in water so as to make effective use of research into the mechanism of chemical reactions, for creating new chemical substances and developing life-science technologies. Furthermore, as the chemical reaction is driven by electron motion, we need to capture the motion of electrons in solutions. The measurement can be performed by using a very small liquid droplet.

Suzuki has launched a research project to explore the interaction between water and biological molecules, in collaboration with researchers working in physics, biology, and computer simulation at RIKEN. "We plan to observe, at the electronic level, how biological molecules function in water. Within an organism, water molecules are no longer in supporting roles. The dynamics of chemical reactions blended with solvent molecules is a very hard subject to deal with, but a challenge worth attempting because it affects the basis of life phenomena."

Finally Suzuki related his dream as follows: "Chemistry is an important field of study for establishing our views on the world and the matter that forms it. We would like to give a complete picture of chemistry so that everyone can understand it. Through our research, we would like to rewrite textbooks on chemistry to make them more attractive."

About the researcher

Toshinori Suzuki was born in Yamagata, Japan, in 1961. He graduated from the Department of Chemistry, Faculty of Science, Tohoku University, in 1984, and obtained his PhD degree in 1988 from the same university for stimulated emission spectroscopy of jet-cooled molecules. He then became a research associate at the Institute for Molecular Science (IMS) in Okazaki, Japan, between 1988 and 1990, and a JSPS fellow for research abroad to carry out research on molecular beam scattering at Cornell University and the University of California, Berkeley, between 1990 and 1992. He returned to Japan as an associate professor at IMS, where he started his independent research group on chemical reaction dynamics in 1992. He moved to RIKEN to become a chief scientist and the director of the chemical dynamics laboratory in 2002. He has received the Broida Award from the international symposium on free radicals, the JSPS Award, and the IBM Science Award for his achievements in chemical reaction dynamics.

Pushing boundaries and helping to feed the world

The RIKEN Plant Science Center

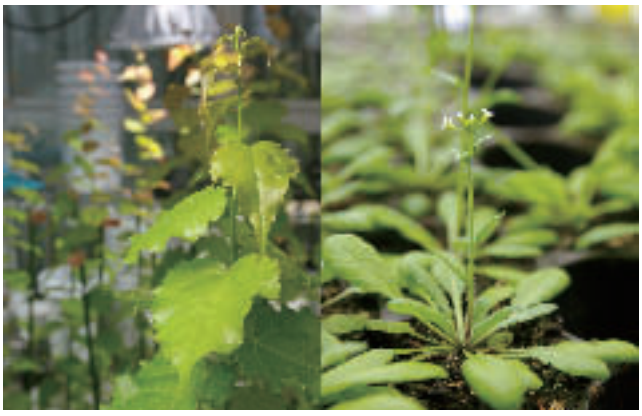
The field of plant science grows more important with every passing year, as increases in human populations and environmental pressures put stress on our ability to feed ourselves and maintain our environment.

The RIKEN Plant Science Center (PSC), located at the RIKEN Yokohama Institute, is at the forefront of this crucial field, as one of the world's leading research centers in plant genomics, metabolomics, and other areas of plant science.

"The primary concept of our research is to promote plant science that is useful for society, mainly agriculture, environment, energy biomass and studies related to human health," notes PSC Director Kazuo Shinozaki. "Of course, our research is basic, using model plants, but the focus is on useful genes for applications."

By any measure, the PSC has been a great success during its eight years in existence. Plant science is one of the top fields at RIKEN, and the PSC is now one of the top research centers in plant science in the world—its researchers publish over 500 articles a year, and the center is ranked number two in the world, based on citations in scientific journals.

Research at the PSC concentrates on four major topics—metabolomics, the study of the complicated plant metabolic network; systems biology, or how plants regulate stress responses, disease resistance and metabolism; gene discovery, in which researchers tease out genes and their functions; and comparative genomics, finding parallels between the genetic data on model plants, such as Arabidopsis and poplar, and other plants, such as crops and trees, to see if the data can be applied to enhance productivity, drought and disease resistance, and other useful traits.



Poplar (left) and Arabidopsis (right) growing in a greenhouse.

"Plants actually have very complex metabolic systems. In the plant kingdom there are 200,000 metabolites, compared with 2,500 in humans, for example," says Shinozaki. "Since we established the metabolomics platform, we have collected a variety of mass spectrometric and nuclear magnetic resonance data and used it to analyze complex plant metabolomics and metabolic networks."

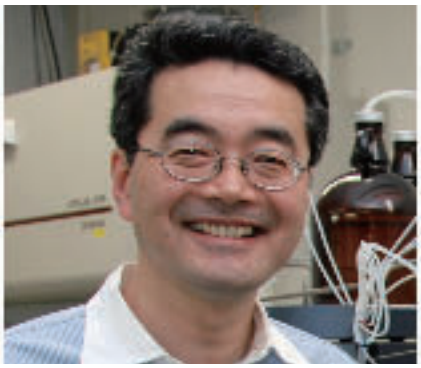
Kazuki Saito, director of the Metabolomics Research Group, the group responsible for setting up the metabolomics research platform, is excited about the possibilities of the new platform, including the ability to investigate hundreds of different metabolites at a time, and to see how they interact with each other. "This is totally new work, metabolite–metabolite correlation—we never considered this before, how these compounds intensify each other," he points out.

For the future, Saito says, "Our next challenge should be to intensify the power of the metabolome analytical platform, and integrate it with bioinformatics." He adds that the group should work toward the advance of system biology, with mathematical models, but based more on holistic data sets, like transcriptome, metabolome and proteome data, to see in finer and finer detail how living organisms behave.

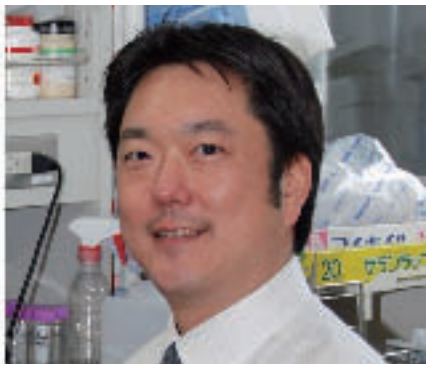
The center has seven groups analyzing plant functions—metabolomics, gene discovery, growth regulation, metabolic function, plant productivity systems, plant immunity and plant functional genomics. "The PSC has some of the best research infrastructure in the world in this area of research in that we can use gas and liquid chromatography and combined mass spectrometry for the analysis," says Saito. "We also have access to four nuclear magnetic resonance machines, which we use for protein analysis."

Plant science, like most scientific endeavors, is a collaborative activity, and joint ventures between scientists and institutes are

Kazuo Shinozaki



Kazuki Saito



Ken Shirasu

crucial. So PSC is actively pursuing collaborations with research institutes both within Japan and overseas, including: the Max Planck Institute at Golm, Germany, with which RIKEN shares a database; the Chinese Academy of Science for work on rice and tree biotechnology; and the University of Pretoria for research concerning pharmaceuticals derived from Artemisia.

In charge of the internationalization effort is Ken Shirasu, leader of the Plant Immunity Research Team. Having spent most of his career doing research overseas, including at the Salk Institute in the US and the John Innes Center in the UK, Shirasu is well aware of the needs and concerns of international researchers.

Among its many international collaborations, his lab is working with the Sudan Agricultural Institute on research into Stryger, a parasitic plant that has infested and destroyed corn crops in large areas of Africa, especially Sudan. "It can be eradicated by brute force, by digging it up with machines, but in Africa farmers can't afford such methods. So an inexpensive genetic solution could improve the lives of thousands of people there," he explains.

One change that Shirasu is insisting on is the use of English in the lab, including seminars, lab meetings, and labels on equipment, even down to the trash cans. "In science you have to have good skills in English. You might have great science, but if you can't present it, nobody will listen."

A perceived language barrier can also discourage foreign researchers from coming here. "If people can't communicate, they can't discuss their work, and this is very important in the world of science," Shirasu says.

As part of its efforts to make itself more foreign-researcher-friendly, the PSC decided to employ two non-Japanese team leaders this year, from South Korea and Vietnam, both with research backgrounds in the US.

"The best way to spread the word about the center is to exchange students—they're the best advertising for us," Shirasu points out. "They may come back someday and do research, and they will certainly talk about their experiences with their colleagues."

Marco Trujillo

In plant immunity, the tagging of proteins with ubiquitin, which can lead to degradation, is emerging as a key regulatory process. German-born Marco Trujillo is investigating the mechanisms by which the attachment of ubiquitin to specific target proteins regulates plant immune responses, which are triggered by the detection of microbial pathogens.

"I focus on a specific kind of E3 ubiquitine ligase," says Trujillo. "These contain a so called u-box domain, and we call them plant u-box proteins or simply PUBs." He adds that by acting as scaffolds, they mediate the binding of ubiquitin to a target protein. "The tagging of a protein with ubiquitin can lead to several outcomes, for example degradation, relocalization to another compartment in the cell, endocytosis, and many others."

Trujillo has employed, among others, a reverse-genetics approach using mutant 'knock-out' lines of Arabisopsis thaliana. "When we analyzed the knock-outs of certain PUBs, we found that they became more resistant to bacteria and other pathogens, and their responses were hyperactivated, but not constitutively, as is typical for most known negative regulators of immunity."

"Knocking out these genes enhanced resistance, indicating that they act as negative regulators," he adds. He explains that plants have both positive and negative regulators to keep their defenses tightly controlled. "A balanced response is needed: too much is deleterious for the plant; not enough makes it susceptible to attack by pathogens."

Trujillo came to Japan in 2006, after working with Ken Shirasu at the Sainsbury Laboratory in England. His experience here has been a valuable one, both personally and scientifically. "RIKEN is well known for having good facilities. You can get anything you want here, any equipment you need, and I've had a lot of liberty to pursue my own research," he says. "I was worried at first about the language barrier, but Dr. Shirasu insists that everyone speaks English in his lab, which allows for free scientific discussions."

Trujillo is heading back to Germany later this year, to continue his work at Julius-Maximilians University, but he plans to continue his close collaboration with Shirasu, and with RIKEN.

New flower, Olivia Pure White, created using heavy ion beams in the RIBF

RIKEN researchers have succeeded in creating a new strain of dianthus flower by bombarding dianthus plants with carbon ions. The new flower, dubbed the Olivia Pure White, features a pure white color, a low 10 cm height and wide spreading stems, and it blooms all year round. It was created in cooperation with Hokko Chemical Industry Co.

Heavy ion beams from the RIKEN Ring Cyclotron (RRC) at the RIKEN Nishina Accelerator Research Center were used to irradiate axillary buds on a wild dwarf white dianthus that has a band of red toward the petal edges, called the Olivia White Eye. The whole process took only three years, compared with the usual breeding period of about 10 years.

Team leader Tomoko Abe of the Nishina Center's radiation biology team joined up with Hokko Chemical's Central Research Laboratories's Biochemical Laboratory to do the research.

Using heavy ion beams induces a higher rate of genetic mutation than other techniques of inducing mutation, such as gamma and X-ray irradiation and chemicals. In addition, the technique causes less damage to the plants, and takes less time to stabilize the mutation because fewer genes are damaged than with other techniques.

The Radiation Biology Laboratory has already used the RRC's heavy ion beams in horticultural breeding with dahlia, petunia, verbena, and torenia, and has already marketed several new varieties. It unveiled a new kind of sakura, 'Nishina Zao', the first variety of cherry in the world bred using heavy ion beams, in October 2007.

After the stability of the mutation had been confirmed, the group applied to the Ministry of Agriculture, Forestry and Fisheries to register the Olivia Pure White as a new strain in December 2007.

The new flower began sales in cooperation with Kaneko Seeds Co. in March. Seeds of the new flower were distributed free of charge on April 19 at an open house at the RIKEN Wako campus during National Science and Technology Week.

RIKEN and Dowa develop moss to clean up heavy metals

The RIKEN Plant Science Center, RIKEN Nishina Accelerator Research Center and Dowa Holdings Ltd. have begun joint research on cleaning up heavy metal pollution using a type of moss that absorbs such metals. With the aim of developing a heavy metal wastewater clean-up technology using *Funaria hygrometrica* protonema, they signed an agreement for the collaboration, on April 1, 2008.

Many heavy metals such as cadmium, mercury and lead have a host of useful characteristics, for example, high electrical and thermal conductivity. Such metals are used for a variety of purposes, including batteries and clinical thermometers, and as pigments for paints.

However, they are also highly toxic to living things, so the use and disposal of such metals are severely restricted. In addition, they are quite rare and very expensive, so an efficient way of collecting and purifying the metals would be a valuable development for industry, as would a cheap and effective method to clean up heavy metal pollution.

The Plant Science Center's Biodynamics Research Team is advancing research into cultivating varieties of moss, and have succeeded in finding a type of moss with an enhanced ability to selectively accumulate lead at high levels of several dozen per cent.

Dowa, for its part, has experience in environmental recycling, and is developing a waste management, soil reclamation and metal recycling business. The company is recognized as an authority in heavy metal purification technology, and set up Japan's first soil purification facilities in 2003. In the joint research, a wastewater clean-up device will be developed incorporating moss at a Dowa facility.

The original technology to create new plant varieties using heavy ion beam irradiation was established at the RIKEN Nishina Accelerator Research Center. Useful variant strains for many kinds of heavy metal processing and collection will be developed from moss plants irradiated by heavy ion beams.

2008 CDB Symposium: 'Turning Neurons into a Nervous System'

May 1, 2008 – The RIKEN Center for Developmental Biology held its sixth annual symposium on the theme 'Turning Neurons into a Nervous System,' from March 24 to 26. The annual symposium series, which was launched in 2002, was established as a forum for addressing diverse aspects of developmental biology and the mechanisms of regeneration and aims to promote the free, timely and borderless exchange of research achievements. This year's event was co-organized by the CDB's Hideki Enomoto, Raj Ladher, and Masatoshi Takeichi, along with Joshua Sanes of Harvard University (USA).

The three-day program featured a broad spectrum of talks ranging from the genetic and molecular activities that guide the morphological and migratory behaviors of individual neurons, to the complex networks that allow huge numbers of neurons to work together in a coordinated fashion to achieve higher brain functions. In addition to the nearly 30 invited talks, each day included a poster session in which more than 80 presenters discussed their work. For more information and photos, visit the 2008 CDB Symposium website at: http://www.cdb.riken.jp/sympo2008/.

The 2009 CDB Symposium on 'Shape and Polarity' will be held from March 23-25, 2009. Check the CDB website periodically for updates.

Mario Capecchi speaking at the CDB Symposium

Dr. Hideki Enomoto
Team Leader
Neuronal Differentiation and Regeneration
Center for Developmental Biology (CDB)
Kobe, Chuo-ku, Japan.

Dear Hideki,

As a post-doctoral research scientist in your laboratory from September 2005 to September 2007, I found the experience to be tremendously enjoyable, with a fantastic set of both material and personal resources. I have fond memories of the many discussions we had on Saturdays in the lab meeting room over *shu-crème*, whether they focused on gene inactivation or US chief-of-state inactivation. I also would like to extend my gratitude to everybody in your lab, who kindly allowed me to express myself in ridiculous Japanese. Their kindness and willingness to share made my transition into the lab very comfortable and also helped me discern that Japan takes its pursuit of art, cinema, music and food very seriously. Specifically, I must also thank your lab manager, Kaori Hamada, who provided unending assistance in professional, financial and even social matters! Likewise I am indebted to Naoko Yamaguchi in the foreign affairs office for her patience and unbelievable efficiency.

Hideki, you were a valuable mentor both professionally and personally, and your generosity extended well beyond your lab: I remember that at my farewell your three children played a small concert on violin and viola. Moreover, we both shared a passion for music, though I still insist that it would be OK if your children pursued fiddle rather than classical violin.

I would also be remiss not to mention the friendship and guidance of Toshi Uesaka in your lab. His advice on work AND wine is equally memorable. There are many more people at CDB I'd like to mention, but one who stands out both as a great friend and a valuable resource is the team-leader Raj Ladher. He takes an awful lot of '*gaijin*-orientation' responsibility for CDB on his shoulders, whether for meetings, visiting lecturers, or lousy postdoctoral punks like me who fear they've taxed their Japanese friends beyond limit and/or repair. Raj also can sell anything to anybody with his unique blend of culture and 'street-smarts', which is why I ate raw chicken more than once.

So in summary it was the people who make me miss Japan so much. Well perhaps the food as well, which basically blows off the map every other place I've visited (about 35 countries), though I've yet to try the hawkers in Singapore or dine in Hong Kong. And finally, where else can you jump on a table and belt out Olivia Newton-John with deep reverence for all things Australian and not be ashamed?

I have attached photos of Samoa, where I am now teaching basic sciences to medical students at a small university for a couple years. Samoa has a diametrically opposed pace of life from Japan, strikingly unmolested land, forest-dwelling pigeons, non-toxic fruit bats and a plethora of colorful fish easily viewed by snorkeling. You won't find *udon*, but the tuna is equally fresh and 10% of the cost. Again, my sincerest thanks to all, including Mr. Roboto, for a wonderful experience in Kobe.

Kind regards,
Tom Gould
Oceania University of Medicine
Apia, Samoa

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RIKEN, Japan's flagship research institute, conducts basic and applied experimental research in a wide range of science and technology fields including physics, chemistry, medical science, biology and engineering. Initially established as a private research foundation in Tokyo in 1917, RIKEN became an independent administrative institution in 2003.

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