

RIKEN RESEARCH

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Dr. Wolfgang Knoll (Director, Max-Planck-Institut für Polymerforschung, Germany)

Nucleus demonstrates its independence

New view of how cells move to form the brain

A RIKEN-led research team has shown that the nuclei of migrating nerve cells in the mouse brain move independently of the centrosomes, the organelles previously thought to pull them along. The work is significant because of the key role nerve cell migration plays in the development of the brain. Any disruption to migration is likely to have an impact on the final position and integration of the cells. This can lead to serious disorders such as lissencephaly or smooth brain syndrome, and has also been implicated in conditions such as epilepsy, schizophrenia and bipolar disease.

Neural migration

Nerve cells or neurons are generated on the brain's inner surface and migrate radially outwards to where they end up functioning. Although neural migration is most evident in young animals during brain development, it continues throughout adult life.

Neurons differ from other migratory cells in the long, thin projections extending from their cell bodies known as processes. During migration, the neuron extends such a process in the direction of movement. Then the cell body with all its organelles—the largest of which is the nucleus—moves down that leading process.

In previous studies, researchers observed that the centrosome was nearly always positioned ahead of the nucleus during migration. The centrosome is the main organizing center for the strings of

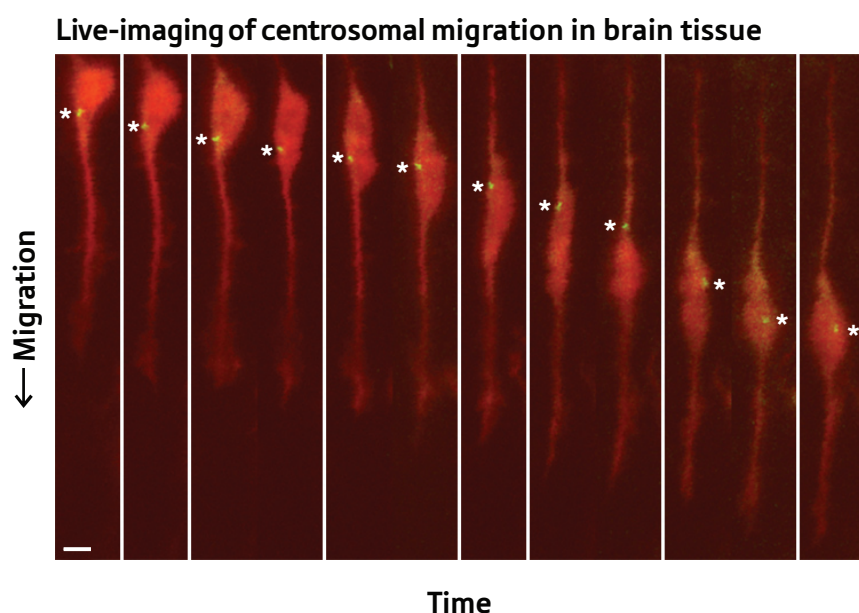


Figure 1: Micrographs showing independent movement of nucleus (large orange body) and centrosome (asterisk spot).

structural proteins called microtubules which form the internal skeleton of the cell. It was therefore suggested that the nucleus was connected by microtubules to the leading process via the centrosome, and was thereby dragged along.

But in a paper published recently in the *Proceedings of the National Academy of Sciences*¹, researchers from Kyoto University and the RIKEN Brain Science Institute in Wako have shown otherwise. In mouse brain slices, using time-lapse photography under a confocal microscope, they observed the migratory movement of granule cells in which the centrosomes and

nuclei had been stained different colors (Fig. 1). The nuclei exhibited a jumping motion, alternating fast movement where they took on an elongated form, with slow 'resting phases' where they returned to a more rounded shape. At times the nuclei moved ahead of the centrosomes.

Microtubular connections

The researchers then stained for different forms of microtubules—the stable form, rich in acetyl groups, and the dynamic form, rich in tyrosine. They found the nucleus was connected to the leading process directly (Fig. 2) by a

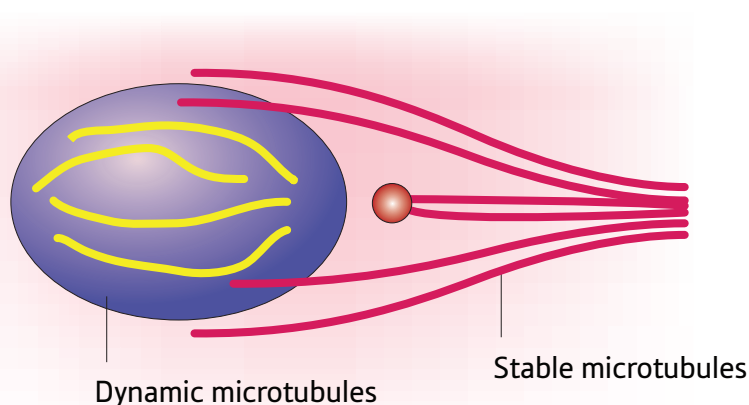


Figure 2: The new model of microtubule connections in brain cell migration. The nucleus is the purple oval and the centrosome is the red circle.

whisk-like structure composed of stable microtubules—there was no intervening link to the centrosome, which is separately bound to the leading process. In addition, the nucleus was encased in a cage-like structure of dynamic microtubules.

The stable microtubules, in particular, appear to be critical to nuclear movement. Migrating cells were treated with different doses of a compound that is known to disrupt dynamic microtubules at a low level and stable microtubules at a higher level. Only the higher dose, however, halted nuclear movement. Another compound which boosts the formation of stable microtubules also disrupted nuclear movement.

The researchers found that inhibiting LIS1—a gene product which binds with the protein dynein—could stop nuclear movement, but not that of the centrosome. Dynein acts as a motor which walks along microtubules in a rack and pinion motion pulling attached compounds with it. LIS1 binds dynein to the microtubule bundle, and has previously been associated with a neural migration disorder.

Piecing together the whole picture

Pulling all this evidence together, the researchers say it is clear that in mouse granule cells the centrosome and nucleus move independently. And while dynein is an integral part of the nuclear movement process, the centrosome seems to move by some different mechanism.

Project coordinator Mineko Kengaku of the Brain Science Institute suggests it is possible that stable microtubule bundles act as guiding rails connecting the nucleus with the end of the leading process, and down which it is dragged. “Dynein functions like a truck carrying its nucleus cargo along the microtubules.”

She also thinks that the dynamic bundles may simply be a younger form of microtubule, which may well be converted to the stable form at a later time. Dynamic microtubules appear to be generated or prepared by the centrosome, she says. They have been observed radiating from the centrosome like a comet’s tail.

In fact, the role of the centrosome in neuronal migration is the next question the research group hopes to unravel. “We

want to uncover the complete mechanism of nuclear and centrosomal movement,” Kengaku says. ■

1. Umeshima, H., Hirano, T. & Kengaku, M.

Microtubule-based nuclear movement occurs independently of centrosome positioning in migrating neurons. *Proceedings of the National Academy of Sciences USA* **104**, 16182–16187 (2007).

About the researcher

Mineko Kengaku was born in Chigasaki, Japan, in 1966. She graduated from the University of Tokyo in 1989 and in 1995 received her PhD degree at the same institution. She completed a postdoctoral fellowship at Harvard Medical School, and became Assistant Professor at Kyoto University in 1998. She was made laboratory head at RIKEN Brain Science Institute in 2003.

Kengaku studies how neuronal circuits in the brain are formed during development. She has revealed molecules involved in the control of cell shape and positioning during neural circuit formation, primarily in the developing mouse cerebellum. Inappropriate regulation of cell shape and positioning may underlie devastating brain malformation and mental disorders, such as schizophrenia and bipolar disorder. Her research may lead to novel strategies for therapy to treat these diseases.



Spin selection

RIKEN researchers are learning how to electrically control spin orientation for data storage technology

Conventional electronics depends on the electrical charges on electrons. The emerging field of spintronics aims to produce devices that also make use of the quantum spin states, or internal angular momentum, of electrons. Researchers at the University of Tokyo, the RIKEN Frontier Research System in Wako and New York University have developed a spintronic technique for accumulating ordered spin states that could have valuable applications in information storage¹.

Spintronics requires 'spin-polarized' non-magnetic materials in which the electron spins all point in the same direction. This has previously been achieved by injecting a spin-polarized current into the material from a magnetic needle. However the direction of polarization can only be changed by rotating the needle, which is not practical at nanometer scales.

The research team has solved this problem by using two injection needles, allowing them to control the polarization direction simply by varying electrical currents. Their experimental device, called a lateral spin valve, consists of a copper strip in contact with two 80-nanometer-wide injection needles at right angles to one another, made of Permalloy—a magnetic alloy of nickel and iron (Fig. 1).

Electrons can only have spins in 'up' or 'down' states. In magnetic materials, spins can align so that when the material is observed from the 'polarization direction', we observe only one type of spin. "Permalloy is a strong ferromagnet that provides spin polarized electrical currents because the population[s] of

up and down spins are spontaneously different," explains RIKEN scientist YoshiChika Otani.

The researchers found that by changing the electrical currents in the Permalloy needles, they had complete control over the angle of spin polarization in the copper strip. Furthermore, the number of polarized spins accumulated in the copper strip obeyed a simple cosine relationship with the angle of polarization.

"Normally spin polarization is along the magnetization direction," says Otani. "By combining spin polarized currents with two different quantized axes, we can rotate the resultant quantized axis."

The technique could be used to reverse the magnetization of certain materials.

"We believe that our electrical means of controlling the spin polarization is important for realizing efficient spin-injection-induced magnetization reversal," explains Otani.

The magnetization reversal process could lead to new types of random access memory for computers. In future the researchers also hope to apply their technique to induce a quantum spin version of the Hall Effect which is exploited in several types of sensors. ■

1. Kimura, T., Otani, Y.-C. & Levy, P.M. Electrical control of the direction of spin accumulation. *Physical Review Letters* **99**, 166601 (2007).

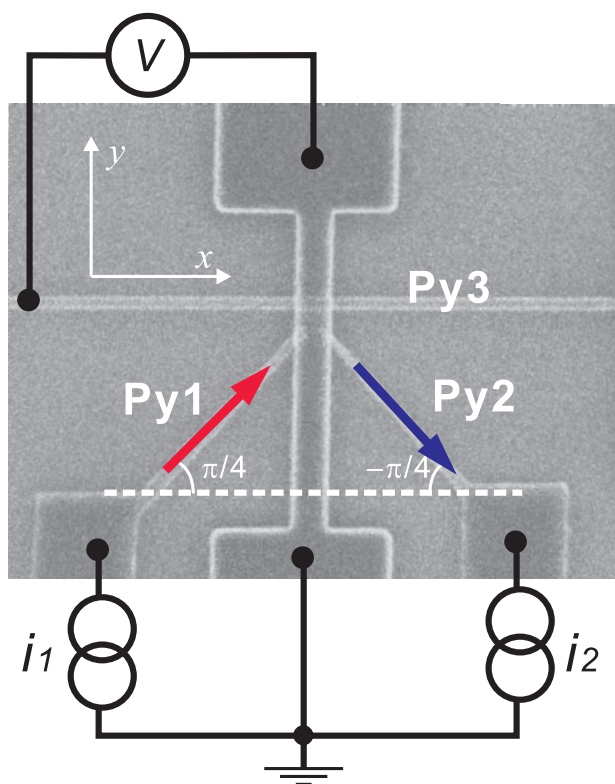


Figure 1: The lateral spin valve device constructed by Otani and co-workers. In the center is a copper strip 280 nanometers wide. Two different spin-polarized currents (i_1 and i_2) are injected via Permalloy needles (Py1 and Py2), providing complete control over the resultant spin polarization in the copper strip (measured using Py3).

Sketching on silicon

Two different chemical compounds can be used to draw perpendicular molecular lines on the surface of silicon substrates

Silicon is the workhorse material of the semiconductor industry because it is on this element that the integrated circuits of modern microprocessor devices are built. In order to satisfy the ever-increasing speed and power demands of computing, the miniaturization of such electronic components is the focus of much research.

So-called top-down methods used to carve ever-smaller features into the surface of silicon wafers will result in performance benefits for a little longer, but there are size limits to which these structures can be practically reduced. An alternative fabrication approach, however, relies upon the bottom-up assembly of molecular building blocks to form nanoscale electronic components.

Now, Maki Kawai and colleagues from RIKEN's Discovery Research Institute in Wako, have discovered a way to 'draw' perpendicular lines—made from different molecules—on silicon surfaces that comprise pairs of atoms, known as dimers, aligned in parallel rows¹. Writing in the *Journal of the American Chemical Society*, they found that acetone—a small organic compound—readily forms straight molecular lines along the rows of silicon dimers on these substrates.

The silicon substrate was first exposed to atomic hydrogen, resulting in the formation of silicon–hydrogen bonds. A small number of the silicon atoms do not react, however, and these so-called 'dangling-bond sites' are quite reactive and can form bonds with organic molecules. When an acetone molecule becomes fixed to the surface by reacting with a dangling-bond site, a new dangling-bond site is

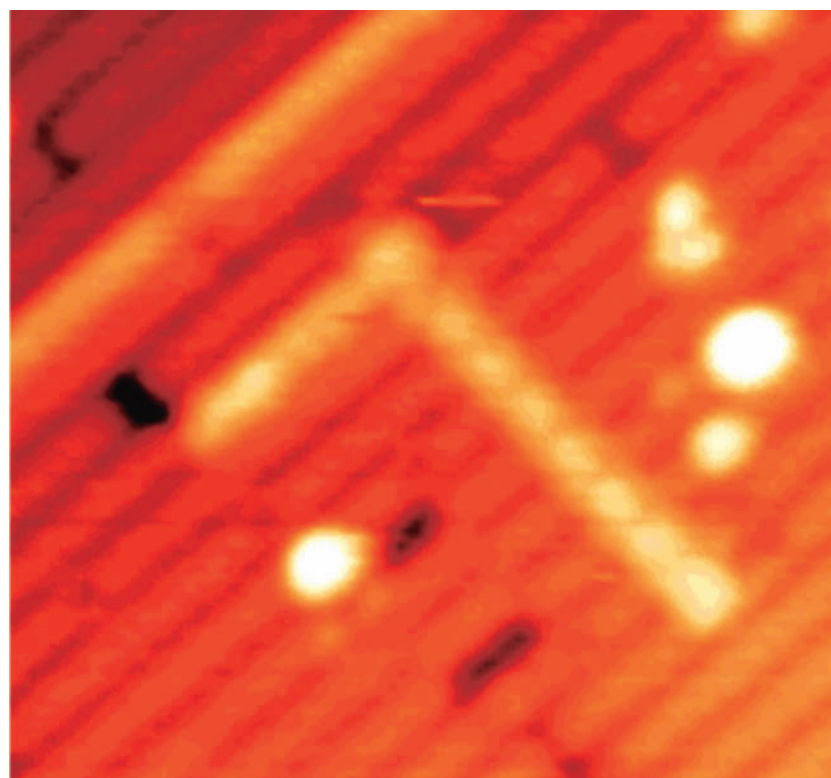


Figure 1: Continuous molecular lines with perpendicular geometries can be drawn on silicon substrates using two different compounds that grow in different directions when they react with the surface atoms.

created in the adjacent silicon dimer in the row, setting off a chain reaction in which more acetone molecules bond to the surface to form a molecular line.

Kawai and co-workers went on to show that acetone lines can be grown from the ends of lines formed from other molecules on the same silicon surface. In contrast with acetone, molecules of a compound called allylmercaptan form lines in a direction perpendicular to the rows of silicon dimers (Fig. 1). In this way, mutually perpendicular lines can be formed on these silicon surfaces, since their direction can be simply controlled by changing the gas feed to the surface.

Because dangling-bond sites can also be produced at predefined positions on

the surface with a scanning tunneling microscope, the origin of the lines can be precisely controlled. The ability to form molecular arrays with carefully controlled geometries on a material around which the semiconductor industry revolves could have significant implications for the rapidly developing field of molecular electronics.

1. Hossain, Md. Z., Kato, H. S. & Kawai, M. Selective chain reaction of acetone leading to the successive growth of mutually perpendicular molecular lines on the Si(100)-(2x1)-H surface. *Journal of the American Chemical Society* **129**, 12304–12309 (2007).

JACS

Rattling the cages of superconductivity

The strong rattling motion of potassium in its atomic cage strongly affects the superconducting state

Physical Review B

A strong interplay between the oscillations of a potassium ion in the crystal structure of KOs_2O_6 and this material's superconductive properties has been discovered by a collaboration of researchers from the University of Tokyo, the Tokyo University of Science and RIKEN's SPring-8 Center in Harima.

KOs_2O_6 is one of a number of compounds with a crystal structure that contains cage-like motifs (Fig. 1). The relatively small size of the potassium ion compared to the cage allows for strong oscillating or 'rattling' motions of the ion within the cage. Materials closely related to KOs_2O_6 are RbOs_2O_6 and CsOs_2O_6 . Of these three, KOs_2O_6 is the compound with the strongest rattling motion. Importantly, all three 'rattler' compounds show superconductivity, which is a rare combination.

This rarity makes these materials very interesting systems for physicists to study the influence of the rattling motion on the superconducting state. In principle, a relation between these two properties is not entirely unexpected, as superconductivity is facilitated by the interaction of superconducting electrons with the atoms of the crystal lattice.

Unfortunately, however, superconductivity in these rattler compounds is relatively weak such that the expected influence of the rattling on the electronic states of the material is very small and observable only at low temperatures. Consequently, detailed investigation into the correlation of the rattling motion and superconducting properties has been a formidable task. As such, the researchers first had to develop a

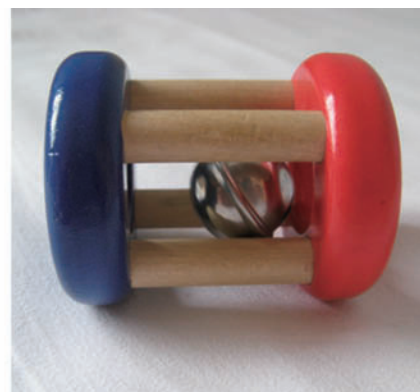
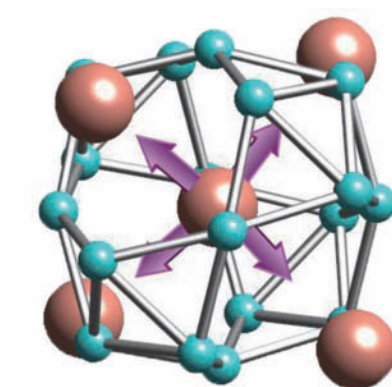


Figure 1: Superconducting 'rattlers'. The crystal structure of KOs_2O_6 consists of a cage that allows for a strong oscillatory motion of the potassium (K) ion (left). This motion is similar to that made by a baby rattle (right).

laser spectrometer to probe the materials' electronic states that, according to Ashish Chainani from the RIKEN team, "has the highest energy resolution and the lowest operating temperature in the world."

In experiments with this advanced spectrometer, the researchers have found¹ that the onset of the rattling motion clearly affects the superconducting properties of KOs_2O_6 . In fact, when compared to the expected values obtained from the standard theoretical framework for superconductors, superconductivity appears to be enhanced by the rattling motion.

Intriguingly, of the three rattler compounds, KOs_2O_6 is not only the material that shows the most stable superconductivity, but has also the strongest rattling motion. So does this rattling not only influence, but

also strengthen superconductivity? "It is probably too early to answer this question—but we are planning to do further experiments in this direction," comments Chainani. The investigation into this relation certainly promises to shed light on intriguing aspects of our fundamental understanding of superconductivity. ■

1. Shimojima, T., Shibata, Y., Ishikawa, K., Kiss, T., Chainani, A., Yokoya, T., Togashi, T., Wang, X.-Y., Chen, C.T., Watanabe, S., Yamaura, J., Yonezawa, S., Muraoka, Y., Hiroi, Z., Saitoh, T. & Shin, S. Interplay of superconductivity and rattling phenomena in β -pyrochlore KOs_2O_6 studied by photoemission spectroscopy. *Physical Review Letters* **99**, 117003 (2007).

Electron's magnetism pinned down precisely

Development of a computation system that can accurately predict electron magnetism provides a test of quantum theory

The most precise theoretical calculation of the electron's magnetism to date has been made by RIKEN scientists, providing them with a powerful test of quantum theory.

The electron's magnetic strength is represented by its 'g-factor', which theoretical physicist Paul Dirac—who developed the mathematical foundations of quantum theory in the 1920s—valued at precisely 2.

But experiments have shown that the real value of g is slightly larger. This so-called magnetic moment anomaly is caused by quantum phenomena not included in Dirac's original theory. In an attempt to pin down exactly why the difference arises, physicists improved theoretical predictions that agreed precisely with experimental results—and the g -factor has consequently become one of the most studied quantities in physics both theoretically and experimentally.

Tatsumi Aoyama and colleagues of RIKEN's Nishina Center, Wako, have now developed a computation system that can predict g with an accuracy exceeding that of the latest experimental results¹.

Much of the discrepancy in g is caused by the electron's virtual emission and absorption of photons—a process where the electron behaves as if fleeting packets of light are bouncing between it and its surroundings. This process is described by the theory of quantum electrodynamics (QED).

The RIKEN team has established the effects of four virtual photons around the electron, known as the eighth-order contribution. The photons' effects can be depicted by Feynman diagrams. The researchers' automated computation

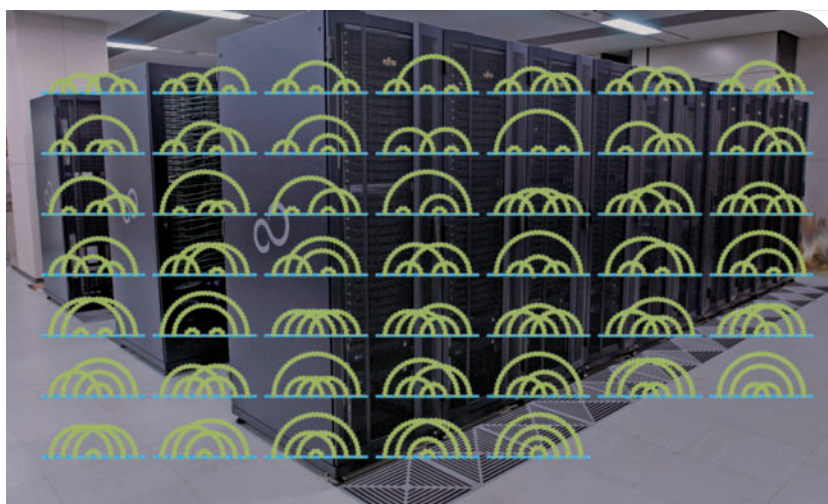


Figure 1: Feynman diagrams that depict virtual emission and absorption of photons (green lines) from/to electrons (blue lines). The numerical calculations of these processes are carried out using RIKEN's supercomputer system.

system has calculated 518 of 891 Feynman diagrams involved in the eighth-order term of the g -factor (Fig. 1), refining the number to astonishing levels of precision. The other 373 diagrams were obtained previously.

A more precise g -factor allows scientists to determine a more accurate value of the fine structure constant, α . This fundamental constant of nature characterizes the strength of the electromagnetic force that governs the interaction between light and matter. Determining α provides a stringent test of QED, and also has strong impact on determining units of electric charge, mass, electric resistance, and many others.

The RIKEN team is now working to calculate the tenth-order contribution to

the g -factor anomaly. "The measurement uncertainty has been reduced to less than one in a trillion, so we are now at the stage where a reliable estimate of the tenth-order contribution is needed," says Aoyama.

The tenth-order term involves 12,672 diagrams, he adds, estimating that the new computer program for integrating these diagrams will need about one hundred million lines of FORTRAN source code. ■

1. Aoyama, T., Hayakawa, M., Kinoshita, T. & Nio, M. Revised value of the eighth-order contribution to the electron $g - 2$. *Physical Review Letters* **99**, 110406 (2007).

Snake-spin

High-energy protons with polarized spin can now be produced in particle colliders, thanks to devices called Siberian snakes

The Relativistic Heavy Ion Collider (RHIC) at Brookhaven National Laboratory (BNL) in the US is the only particle collider in the world that can produce protons with polarized spin. Now researchers at BNL, Indiana University and the RIKEN Nishina Center for Accelerator-Based Science in Wako have improved the quality of these spin-polarized protons. Their work could help to uncover one of the great mysteries of particle physics—the origin of proton spin¹.

The proton contains quarks, however the sum of the quark spins is not equal to the proton spin, explains project-member Junpei Takano. “To find the source of proton spin, we accelerate a polarized proton beam to high energy and analyze data from the collided beam.”

Before entering the RHIC, protons are accelerated in the Alternating Gradient Synchrotron (AGS), which uses magnetic fields to guide a beam of polarized protons around a circuit. However, at the same time, the protons undergo precession, or periodical changes in the direction of their axis of spin. If the frequency of precessions matches the frequency with which the protons encounter magnetic fields, the protons will resonate, causing them to lose their polarization.

To prevent these depolarizing resonances, the researchers have installed magnetic devices called Siberian snakes, which rotate the proton spin. The first snake used in the AGS—a solenoidal snake—removed some resonances but introduced a new ‘coupling resonance’ due to interactions between horizontal and vertical components of the beam.



Figure 1: Helically twisted magnets from the newly installed warm conducting (top) and cold superconducting (bottom) Siberian snake devices in the Alternating Gradient Synchrotron at Brookhaven National Laboratory.

RIKEN researcher Masahiro Okamura, who led the research and is now based at BNL, and Takano built a new type of snake magnet in 2004 that resolves a problem caused by the solenoidal snake².

The new magnet uses a helically twisted coil (Fig. 1). Recently, another helical magnet with superconducting ‘cold’ coils was built at BNL. By carefully positioning the first ‘warm’ snake and the second ‘cold’ snake in the AGS, the researchers managed to accelerate a high energy beam of protons with 65% polarization.

In the RHIC itself, four similar snakes are used to keep high polarization. “The AGS had been the bottleneck of the polarization for the RHIC,” says Takano. “With the installation of the cold snake and the warm snake, the polarization of protons emerging from the AGS is increased.”

In future, the researchers hope to identify and overcome other sources of depolarization to boost the study of the proton spin structure that is producing increasingly intriguing results. ■

1. Huang, H., Ahrens, L.A., Bai, M., Brown, K., Courant, E.D., Gardner, C., Glenn, J.W., Lin, F., Luccio, A.U., MacKay, W.W., Okamura, M., Ptitsyn, V., Roser, T., Takano, J., Tepikian, S., Tsoupas, N., Zelenski, A. & Zeno, K. Overcoming depolarizing resonances with dual helical partial Siberian snakes. *Physical Review Letters* **99**, 154801 (2007).
2. Takano, J., Ahrens, L.A., Alforque, R., Bai, M., Brown, K., Courant, E.D., Ganets, G., Gardner, C.J., Glenn, J.W., Hattori, T., Huang, H., Jain, A., Luccio, A.U., MacKay, W.W., Okamura, M., Roser, T., Tsoupas, N., Tepikian, S., Tuozzolo, J., Wood, J., Zelenski, A. & Zeno K. Helical dipole partial Siberian snake for the AGS. *Journal of Instrumentation* **11**, 11002 (2006).

Junpei Takano

Lasing on the spot

Lasing from 'artificial atoms' is demonstrated for the first time

Researchers from RIKEN's Frontier Research System in Wako, in collaboration with the NEC Nano Electronics Research Laboratory in Tsukuba, have realized the first laser made from 'artificial atoms' based on a superconducting electronic device.

Since their invention almost half a century ago, lasers have always been based on the interaction of atoms with light. Typically, a number of atoms, either a gas or a crystal, are placed between two mirrors that form a cavity. The interaction between the atoms and the light in the cavity then leads to the creation of laser radiation. As the coupling between the atoms and the light in the cavity is generally very weak, many atoms are required to make a laser and lasing only occurs beyond a certain threshold of energy that needs to be pumped into the system.

Reporting in the journal *Nature*¹, the researchers have now demonstrated a laser that is based on a single artificial atom and has no lasing threshold. In contrast to conventional lasers, "the strong coupling between the artificial atoms and the cavity enables a new lasing regime where one atom produces many light particles," notes Oleg Astafiev from the research team.

At the heart of this new laser is the artificial atom that is made from a small superconducting aluminum 'island' (Fig. 1). This island is coupled to a reservoir, which is used to tune its properties and thus optimize the laser. When a small electrical voltage is applied to the island, the pairs of electrons that form the superconducting state are forced

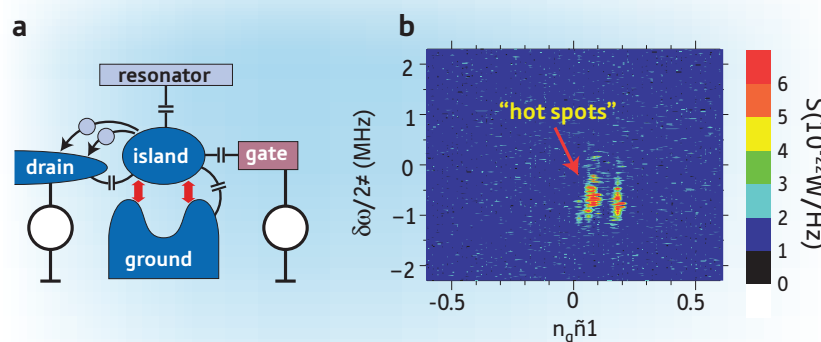


Figure 1: The artificial atom laser. (a) The design of the laser based on a superconducting 'island' made from a small dot of aluminum. The break up of the superconducting electron pairs (blue dots) releases energy into the resonator where laser light is generated. (b) Two spots of laser radiation generated by the device.

to break up and leave the island through the drain.

The energy that is released by breaking up these pairs is converted into light and fed into the resonator cavity. Contrary to conventional lasers, the coupling between the island and the resonator is very strong, so lasing is achieved immediately and without any threshold. This process of light generation can be repeated many times such that a single atom creates many photons for the laser.

The artificial-atom laser offers a number of opportunities. In particular, "this laser may be used to study the fundamental physical properties of this simplest of possible laser systems, consisting of only one atom," comments

Astafiev. Furthermore, the small amount of power required to achieve lasing in this system could lead to the development of arrays of these small and compact lasers on a single computer chip.

1. Astafiev, O., Inomata, K., Niskanen, A. O., Yamamoto, T., Pashkin, Yu. A., Nakamura, Y. & Tsai, J. S. Single artificial-atom lasing. *Nature* **449**, 588–590 (2007).

Sticky spins

Researchers show how spins freeze in a molecular magnet

Most of us are familiar with magnets like iron that are strong enough to pull up a paperclip or scramble the colors on a computer monitor. Molecular magnets, on the other hand, are quite different. Compared to the densely packed and strongly interacting spins in permanent magnets, the spins in molecular magnets—usually contributed by iron or manganese ions—are well separated by organic molecules and a different mechanism is responsible for the magnetic state they form at low temperatures.

Molecular magnets are attractive for studying fundamental magnetic properties, particularly because with chemistry, it is possible to change the length or structure of the organic molecules and therefore, the interactions between the spins on the metal ions. Writing in the *Journal of the American Chemical Society*¹, scientists Isao Watanabe at the RIKEN Nishina Center at Wako and colleagues at Tohoku University and The University of Tokyo present an interesting example of this chemical tuning of magnetic properties in a magnetic molecule called *catena*-[Fe^{II}(ClO₄)₂{Fe^{III}(bpca)}]ClO₄.

This magnetic molecule is a one-dimensional chain consisting of many of the molecular units shown in Figure 1, in which consecutive organic planes twist with respect to one another. The spins on the iron (Fe^{II}) ions minimize their energy when they are directed within the molecular planes—an effect known as ‘easy-plane anisotropy’. However, the twisting of the organic planes along the chain actually causes the spins on the

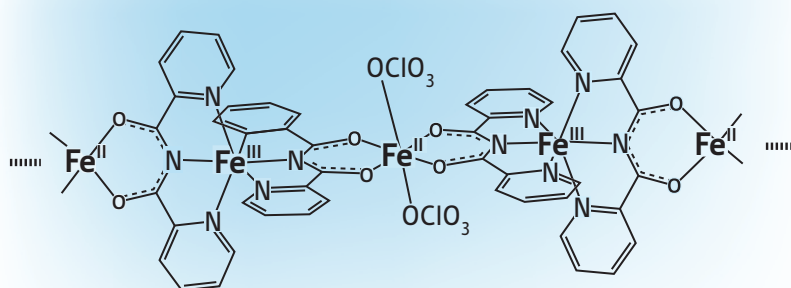


Figure 1: The chemical structure of the molecular magnet *catena*-[Fe^{II}(ClO₄)₂{Fe^{III}(bpca)}]ClO₄ Fe^I. (high-spin ion; Fe^{III}, low-spin ion; O, oxygen; N, nitrogen; Cl, chlorine)

Fe^{II} ions to collectively point along the chain direction, forming a ‘single-chain’ magnet. This is rather unusual because most single-chain magnets are formed from spins that have axial, rather than planar, anisotropy.

To explore magnetic order and dynamics in this molecule, Watanabe and co-workers used muon spin relaxation measurements performed at the RIKEN-RAL Muon Facility. Muons are charged, subatomic particles with the same spin as a proton. By measuring the evolution of the direction of the muon’s spin in a magnetic material it is possible to determine how the spins in the material are distributed or aligned.

With their measurements, Watanabe and his colleagues could observe the

fluctuations of the spins on the Fe^{II} ions slow down and finally freeze at around 6 K (−267.15 °C)—a behavior that is similar to what is seen in a broad class of materials known as ‘spin glasses’. Importantly, their measurements have proved that spins with easy-plane anisotropy can order in a single-chain magnet—similar to spins with easy-axis anisotropy. ■

1. Kajiwar, T., Watanabe, I., Kaneko, Y., Takaishi, S., Enomoto, M., Kojima, N. & Yamashita, M. Direct observation of the ground-spin alignment of Fe(II)–Fe(III) single chain magnet by muon-spin relaxation. *Journal of the American Chemical Society* **129**, 12360–12361 (2007).

Tackling cancer by fishing for trouble

Detecting sequence-specific problems in DNA may help scientists understand genetic disorders that lead to cancer

A team of Japanese scientists has developed a method to 'fish' for specific DNA-base problems that are responsible for causing cancer. The method can also be used to identify the exact site and measure the extent of the disorder.

Akimitsu Okamoto from the RIKEN Frontier Research System, Wako, has been leading this successful team for two years in developing this research aimed at detecting specific changes in DNA that cause ageing and may lead to the onset of cancer.

One of the bases in DNA is cytosine which, during normal biological processes, can react in our bodies by adding a methyl group and result in a compound known as methylcytosine. Whilst this reaction is important for gene regulation, excessive reaction has been shown to be carcinogenic; therefore detecting methylcytosine is of medical significance. Conventional methods exist to detect this target compound; however they all involve long reaction times and large samples—which are often destroyed—with little or no selectivity.

The latest technique by Okamoto and co-workers builds on their previous research to selectively detect methylcytosine, and now facilitates sequence-specific detection within DNA. The technique has reaction times of under an hour¹. The advantage of a sequence-specific approach is that the exact origins of excessive methylation, and consequently carcinogenesis, can be investigated.

Using this conceptually new approach that employs techniques from interdisciplinary areas of organometallic chemistry and DNA physics, the researchers essentially fish for

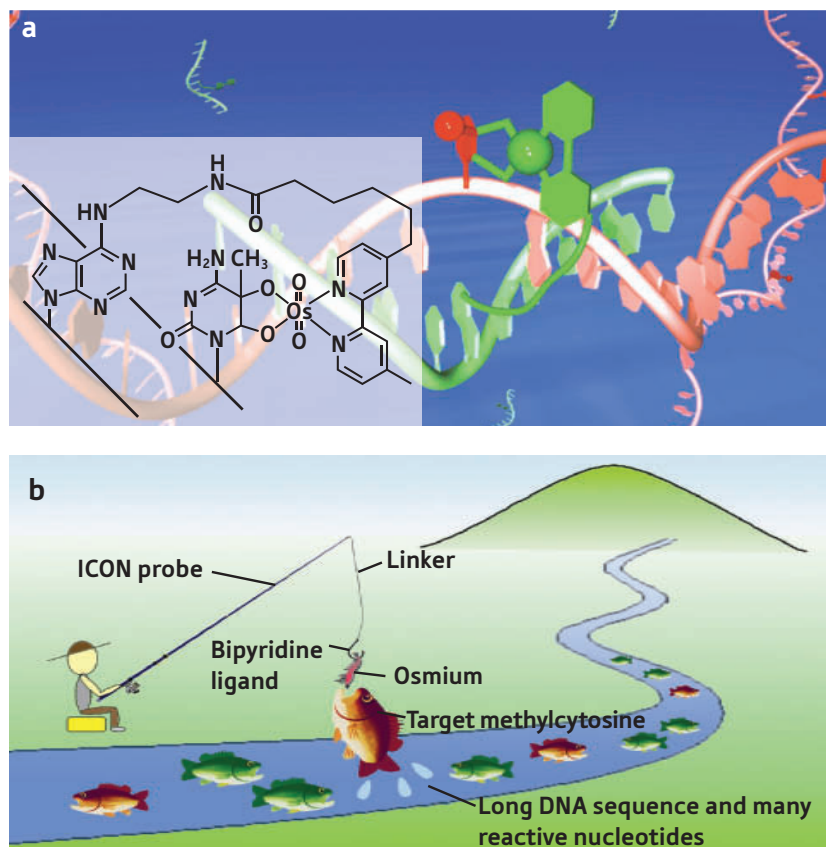


Figure 1: An illustration of how the complex between the osmium-containing DNA strand probe (green strand: fishing rod, hook and bait) would bind the target methylcytosine (red tag) in a biological sample of DNA (pink strand). (a) A biological model and (b) a cartoon of the technique.

methylcytosine within a sample (Fig. 1). The detection probe, named ICON, is a short sequence of DNA that acts as the fishing rod. A ligand, made from bipyridine, acts as the fish-hook. The target methylated cytosine is then caught using a transition metal, osmium, as bait. In the sample, a complex is formed between the osmium, bipyridine and the methylcytosine—this is the fish on the hook. Unmethylated cytosine cannot form a complex with osmium, so the fishing bait is ignored.

The complex that is formed, a cross-linked structure between the two parts, is easily detected. This new technique clearly distinguishes not only between methylated and non-methylated

cytosines, but also quantifies the degree and site of methylation.

Okamoto is confident this research will lead to further improvements and the development of a reliable method for methylcytosine detection. "The reaction conditions need to be optimized to establish the best analyzing system," he explains. "The concept of crosslink formation would be applicable to DNA chips allowing analysis using familiar systems such as fluorescence detectors."

1. Tanaka, K., Tainaka, K., Umemoto, T., Nomura, A. & Okamoto, A. An osmium–DNA interstrand complex: Application to facile DNA methylation analysis. *Journal of the American Chemical Society* **129**, 14511–14517 (2007).

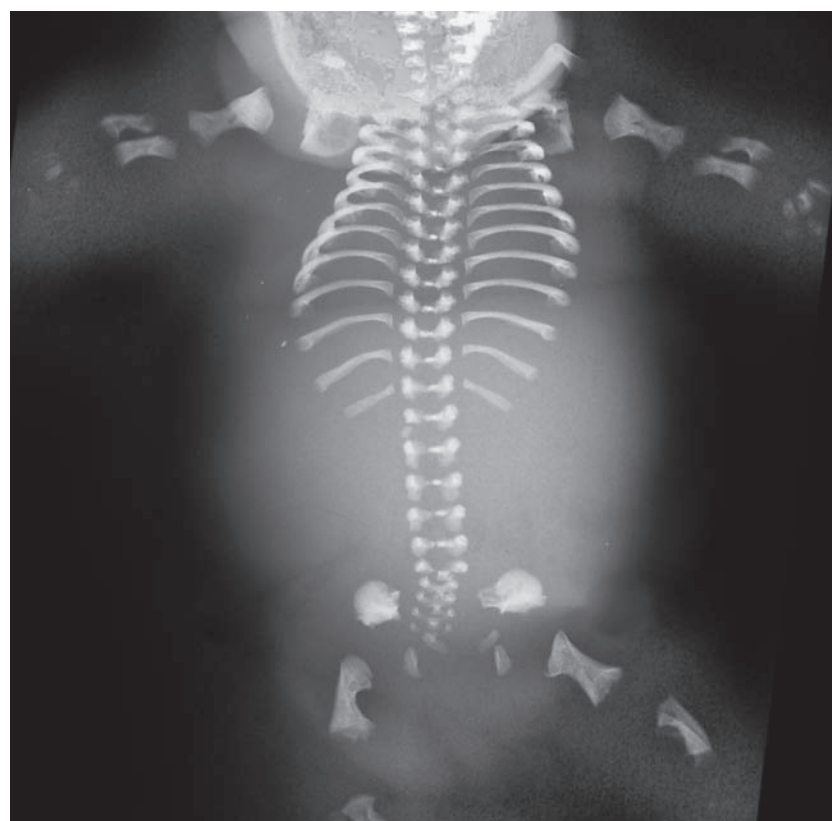
Poor transport cuts to the bone

Researchers link skeletal disorders with sugar chain production

A international research team with strong RIKEN representation has uncovered a molecular basis—and developed a mouse model—for some types of congenital human skeletal disorders, including the rare, lethal Schneckenbecken dysplasia (Fig. 1). The team, led by Shiro Ikegawa of RIKEN's SNP Research Center in Tokyo, has accumulated persuasive evidence that the underlying problem is an inoperative form of the molecule responsible for transporting sugars—critical to the construction of the skeleton—across the membrane of the cellular organelle known as endoplasmic reticulum (ER).

The skeleton is formed from a matrix of compounds secreted by cartilage and bone cells. A family of large molecules called proteoglycan is intimately involved in the process. The proteoglycan molecules consist of a protein core to which long chains of sugars, such as chondroitin sulfate, are attached. Chondroitin sulfate is made in the ER and another cellular organelle, known as the Golgi apparatus, from two different sugar compounds. Its composition reflects, and may even control, the growth activity of the bone. The sugars are moved into the ER by molecules known as nucleotide-sugar transporters (NSTs). More than 10 genes for NSTs are known in humans.

In a recent *Nature Medicine* paper¹, researchers from Japan, the US, Germany and Holland, detailed how they developed a line of mice incorporating a recessive mutation in *SLC35D1*, the gene coding for the NST involved in chondroitin sulfate synthesis. They confirmed that mice in which this mutation is expressed died as newborns, and displayed skeletal



Peter Nikkels

Figure 1: A human skeleton affected by Schneckenbecken dysplasia.

abnormalities, in particular short, thick limbs. The researchers then used cell staining and radioactive labeling to confirm that, at a molecular level, these developmental problems were associated with a severe reduction in the length and number of sugar chains of the proteoglycans.

The mutant mice bore many features in common with humans suffering from Schneckenbecken ('snail pelvis') dysplasia. When the team investigated two human cases of this dysplasia, they were able to show that the NSTs involved in chondroitin sulfate synthesis were inactive. They were also able to trace the problem back to mutations in the human *SLC35D1* gene.

This is the first demonstration of the consequences in humans of such

abnormal biosynthesis of proteoglycans sugar chain. Examples of other human disorders associated with proteoglycans have recently been discovered. "We expect that our results will open many avenues of research in the fields of connective tissue disorders, vertebrate development and glycobiology," Ikegawa says. ■

1. Hiraoka, S., Furuichi, T., Nishimura, G., Shibata, S., Yanagishita, M., Rimoin, D.L., Superti-Furga, A., Nikkels, P.G., Ogawa, M., Katsuyama, K., Toyoda, H., Kinoshita-Toyoda, A., Ishida, N., Isono, K., Sanai, Y., Cohn, D.H., Koseki, H. & Ikegawa, S. Nucleotide-sugar transporter SLC35D1 is critical to chondroitin sulfate synthesis in cartilage and skeletal development in mouse and human. *Nature Medicine* 13, 1363–1367 (2007)..

Regulating a regulator

Researchers identify a mechanism controlling the function of an important cellular protein

New work designates the protein RCN1 as a harness responsible for restraining the protein calcineurin, whose activity is essential for proper regulation of immune, muscle and brain cells. However, as evidenced by links to osteoporosis and Down's syndrome, unleashed or excessive calcineurin function can result in devastating biological consequences. Thus, calcineurin acts as a delicate pivot point on which physiological homeostasis rests.

Prior work aligned calcium 'upstream' of calcineurin, and RCN proteins 'downstream' of calcineurin in intracellular signaling pathways. However, confusing data indicating that RCN proteins can both inhibit and enhance calcineurin activity remained unresolved.

A group led by Tsutomu Kishi, a scientist at the RIKEN Frontier Research System in Wako, set out to understand the molecular process through which RCN proteins influence calcineurin activity. Their findings were published in a recent issue of the *Proceedings of the National Academy of Sciences of the USA*¹.

The researchers hypothesized that RCN proteins might be controlled by SCF^{Cdc4}, a protein complex that binds to and routes substrate proteins for destruction. Conducted in yeast cells, an unbiased screen for proteins interacting with SCF^{Cdc4} confirmed their suspicions. Experiments using mutant yeast cells firmly designated SCF^{Cdc4} as essential for destabilization and degradation of RCN1, and showed that RCN1 destruction is required for calcineurin activation.

As RCN1 is degraded in a dynamic rather than constitutive manner, the team sought to identify the mechanism

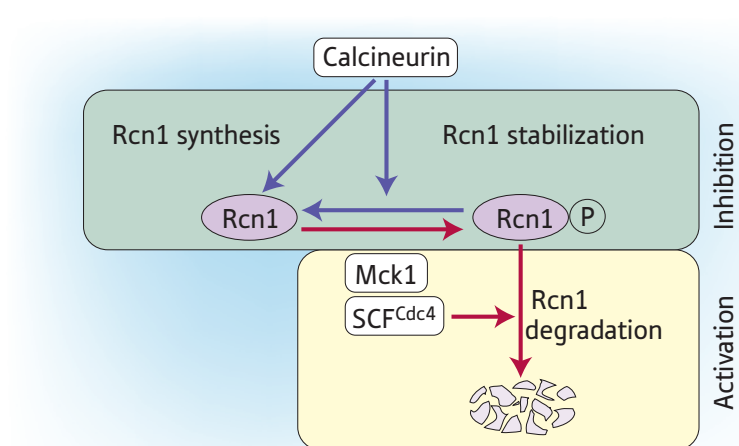


Figure 1: Calcineurin–Rcn1 cross-regulatory loop. Blue and yellow boxes denote processes that suppress and enhance calcineurin activity, respectively.

responsible for 'tagging' RCN1 for destruction. Their focus on Mck1, a protein already established as capable of phosphorylating RCN1, proved fruitful. Mutant RCN1 proteins lacking the serine residues phosphorylated by Mck1 were resistant to SCF^{Cdc4}-mediated degradation.

Adding to the complexity of calcineurin control mechanisms, the researchers noted that calcineurin, a phosphatase capable of dephosphorylating proteins, effectively counteracted Mck1-mediated RCN1 phosphorylation.

Thus it appears that a 'feedback loop' regulates calcineurin activity (Fig. 1). Calcium flux stimulates Mck1-mediated phosphorylation of RCN1. SCF^{Cdc4} targets phosphorylated RCN1 for destruction and releases calcineurin function. By

synthesizing, dephosphorylating and stabilizing RCN1, activated calcineurin then suppresses its own activation.

Additional work is needed to understand the factors capable of influencing the direction in which this regulatory cycle spins. "We believe that cellular regulation by this feedback loop and the selective degradation of feedback inhibitors might be a fundamental strategy to control cellular signals," says Kishi. ■

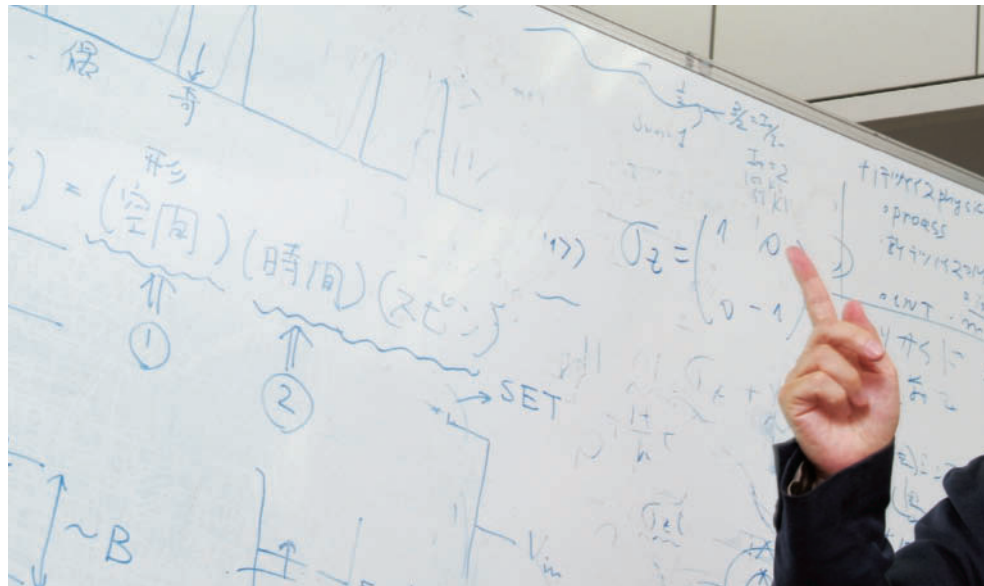
1. Kishi, T., Ikeda, A., Nagao, R. & Koyama, N. The SCF^{Cdc4} ubiquitin ligase regulates calcineurin signaling through degradation of phosphorylated Rcn1, an inhibitor of calcineurin. *Proceedings of the National Academy of Sciences USA* **104**, 17418–17423 (2007).

The creation of nanodevices

Koji Ishibashi

Chief Scientist
Director of Advanced Device Laboratory
Discovery Research Institute

Continued reductions in size and integration of devices, such as transistors used in integrated circuits, have improved the performance of personal computers and mobile phones. However, in the near future, this approach to improving performance may no longer be available as the quantum phenomena that govern the microscopic world are expected to dominate. This means that when devices are reduced to the microscopic level they will fail to function in the conventional classical way. In contrast, the Advanced Device Laboratory (ADL) is rising to the challenge of making use of these quantum phenomena. The laboratory is making efforts to develop nanodevices based on a new principle of operation, defying the boundaries of conventional electronics. The developing research field of 'nanoelectronics' is about to take off.



Phenomena that occur in the microscopic world

"Make things very small and probe the physics." This was the advice given to Koji Ishibashi, now a chief scientist at RIKEN, by his supervisor in the mid 1980s when Ishibashi was taking a graduate course in electronics. "In those days, the word 'nanotechnology' did not exist, and research activities were not as active as today," Ishibashi recalls. "We had no specific ideas, but I was asked to make things very small in the hope that it might lead to finding new phenomena. I think that my former direct supervisor knew in his bones that something new would happen."

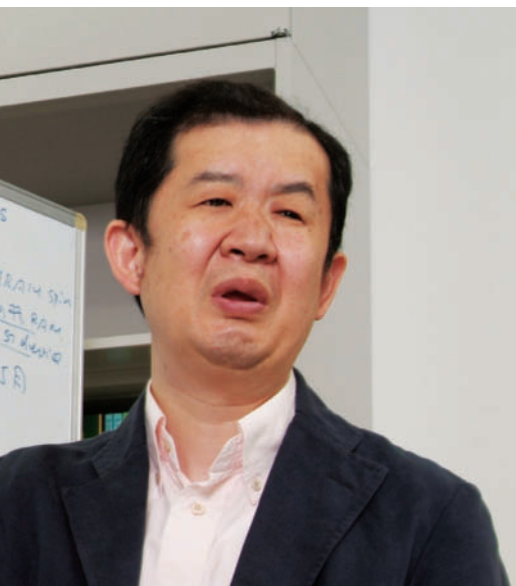
Single-electron transistor

The single-electron transistor is a high-profile nanodevice based on a new principle of operation. A typical transistor currently deals with a flow of about 100,000 electrons. In contrast, a single-electron transistor deals with only a single electron, thus opening up functions that were not possible previously.

When a voltage is applied to the gate of a single-electron transistor, electrons try to jump from the source to the 'quantum

dot' (Fig. 1, left). Note that only a single electron can enter the quantum dot. The reason is as follows: a quantum dot confines electrons within a very small space. When one electron jumps into the quantum dot, the electrons in the quantum dot increase the repulsive force between the negatively charged electrons (Coulomb force), and this blocks one or more additional electrons from jumping into the quantum dot. This is known as the 'Coulomb blockade phenomenon'. Thus, enabling one more electron to jump into the quantum dot requires a voltage to be applied to the gate.

Implementation of the Coulomb blockade phenomenon requires fabrication of an extremely small quantum dot. Furthermore, the Coulomb force between electrons confined within the quantum dot is very small. Thus, devices of the size manufactured by conventional microfabrication techniques can generate the Coulomb blockade phenomenon only at very low temperatures. "In the mid-1990s I launched a study into the single-electron transistor made from a semiconductor," says Ishibashi. However, the Coulomb blockade phenomenon did not occur until the transistor was cooled to a temperature



of 1 K (-272 °C). Under those conditions, there was no hope of finding a practical application. The minimum wire width for semiconductors currently achievable by microfabrication is about 20 nm (1 nm is a billionth of a meter). “Thus,” says Ishibashi, “We need to make further efforts to reduce the size of quantum dots so that the Coulomb blockade phenomenon occurs at higher temperatures, for example, at room temperature.”

In 1996, a research group at Delft University of Technology in Holland successfully made a single-electron transistor using a carbon nanotube 1 nm in diameter as the quantum dot. “I was studying there in those days, working in that research group,” says Ishibashi. At that time, nobody had ever thought of the idea of a single-electron transistor made of a carbon nanotube, but a student in the laboratory just tried out the idea, and acquired data that clearly shows the Coulomb blockade phenomenon. “I thought this was great, and started to conduct research into a single-electron transistor using carbon nanotubes.”

The carbon nanotube is an extremely fine tube made of carbon. “Microfabrication techniques for semiconductors can be

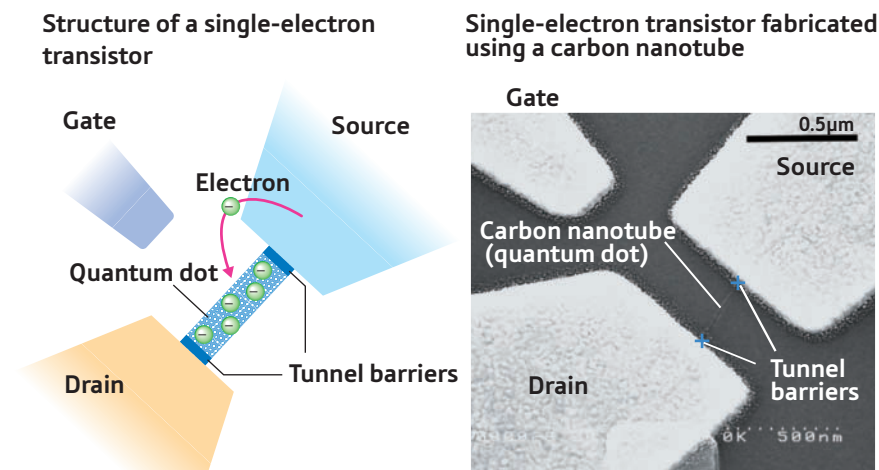


Figure 1 : Single-electron transistor.

Electron tunnel barriers are fabricated between the quantum dot and the source, and between the quantum dot and the drain. When a voltage is applied to the gate, electrons jump over the barriers (tunnel effect), entering the quantum dot from the source on a single electron basis.

used to connect a carbon nanotube to electrodes because, although the diameter is about 1 nm, the tube has a length of more than 1 μm,” says Ishibashi. “In our laboratory, we successfully used a carbon nanotube to generate the Coulomb blockade phenomenon at 20–30 K.” (See Fig. 1, right). Ishibashi adds that one report suggests the Coulomb blockade phenomenon can occur even at room temperature.

In 2003, Ishibashi and members of ADL were successful in using two carbon-nanotube single-electron transistors to make a single-electron inverter similar to the complementary metal oxide semiconductor (CMOS) inverter, which is currently the mainstream of semiconductor devices. They were the first people in the world to get it to work properly (Fig. 2). “The research brought more attention from around the world than we had ever expected,” he adds.

Then, why did the research draw such keen interest? One reason is that they successfully made a device by integrating carbon-nanotube single-electron transistors for the first time, although the device has only two single-electron transistors.

Devices such as transistors have been reduced in size, and more and more devices are integrated into a single semiconductor chip to achieve further improvements in performance. The application of this technique, however, is said to be approaching the limits of

performance improvement.

This is because it is predicted that quantum phenomena will dominate when conventional devices are further reduced into extremely small elements, and thus devices will fail to function under the conventional principles of operation. Besides, further microfabrication of integrated circuits increases the heat consumption per unit area, leading to circuit malfunction. This is another serious problem.

The single-electron transistor can function at temperatures closer to room temperature when its size is reduced. Furthermore, the single-electron transistor, which deals with a single electron, is the ultimate energy-saving device, and so it is capable of solving the problem of heat generation. Ishibashi and other members of the laboratory used carbon-nanotube single-electron transistors to successfully implement the specific function of a CMOS inverter, demonstrating the possibility of defying the boundaries of current electronics.

Using artificial atoms to capture terahertz light

Both an atom and a quantum dot confine electrons within a narrow space. In this sense, a quantum dot can be regarded as an artificial atom. Although the nature of atoms is fixed, artificial atoms can be designed as devices after they have been variously changed and modified.

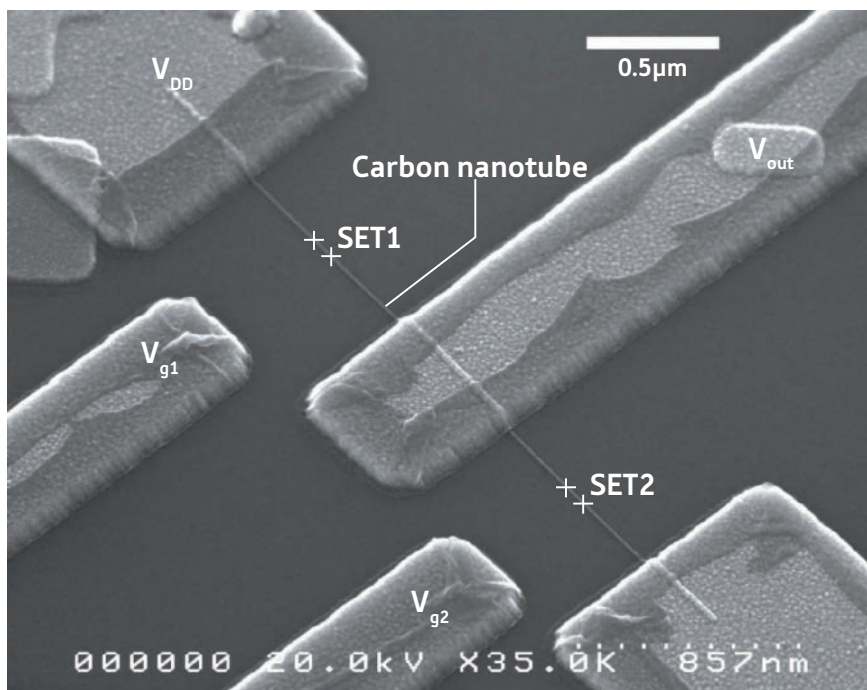


Figure 2: CMOS-like inverter comprising single-electron transistors.

A CMOS inverter acts as a special switch (inverter), in which one transistor is 'on' while the other is 'off'. This function is achieved using two single-electron transistors (SETs) fabricated on a carbon nanotube. V_{out} : out voltage; V_{DD} : drain voltage; V_{g1} : gate1 voltage; V_{g2} : gate 2 voltage

Light is made up of photons. Atoms absorb the energy of photons and emit electrons when high-energy light, such as ultraviolet or X-ray, shines on the atoms. In contrast, carbon-nanotube artificial atoms are designed so that they can emit electrons when photons of low-energy terahertz light are absorbed. In 2006, Ishibashi and laboratory members successfully observed terahertz photon absorption using carbon nanotube artificial atoms (Fig. 3).

Terahertz light—light that has a frequency of about 1 terahertz or a wavelength of 0.3 mm—is between visible light and radio waves in the electromagnetic spectrum. Because terahertz light has moderate permeability and is readily absorbed by materials, it is anticipated to be applied to a number of methods of examination and diagnostics, including how to distinguish normal cells from cancerous ones, or how to detect illegal drugs hidden in envelopes. Conventional optical techniques or radiowave techniques, however, cannot control terahertz light. In particular, the development of highly sensitive detectors has been delayed. Today, a widely used detector called the 'bolometer' can detect a temperature rise in silicon material as

a change in electrical resistance when terahertz light is shone on the material. This principle, however, has limitations in sensitivity. In contrast, the device that Ishibashi and other members of ADL have been studying will be able to detect a single photon, that is, it will be able to achieve the ultimate sensitivity.

"After presenting these findings, we received inquiries from researchers in radio astronomy," says Ishibashi. Terahertz light is an unexplored field of observation even in astronomy. Today, the giant radio telescope 'ALMA' is jointly being constructed in Chile, South America, in collaboration with Europe, Japan, and North America. This telescope, which was designed to observe a certain type of light, namely, electromagnetic waves in the millimeter, or submillimeter wavelength range, will be used to probe the galaxy, planetary systems, and the origins of life. In the future, a detector with built-in carbon-nanotube artificial atoms might contribute to a great astronomical discovery.

Building a quantum computer

"If a single electron can be completely controlled, a quantum computer can be developed," states Ishibashi. The quantum

computer is expected to be capable of completing a prime-factor-decomposed computation in only tens of seconds, whereas current supercomputers require thousands of years to conduct the same computation. The basic element of the quantum computer is called the 'quantum bit'. Current computers allocate '1' or '0' to each bit, and these bits are processed for the intended calculation. In contrast, the quantum bit is represented by a two-state system described like this, for example: a 30% probability of '0' and a 70% probability of '1'. This linear superposition of states that simultaneously enables the two states of '0' and '1' is called 'quantum superposition'.

Today, scientists are conducting research on how to achieve a quantum bit using various materials and ideas. Ishibashi and other members of ADL are advancing research on the use of electron spin states of carbon-nanotube artificial atoms.

Electron spin is the angular momentum of an electron, similar to the rotation of the earth, and there are two electron-spin states: clockwise (spin-up) and anticlockwise (spin-down). For example, '0' can be allocated to spin-up, and '1' to spin-down. By applying a magnetic field to carbon-nanotube artificial atoms, Ishibashi and his laboratory members successfully created both independent states, spin-up and spin-down, from a single electron-spin state. "Next we need to create a quantum superposition for any values of probability, for example, a 30% probability of 'spin-up' and a 70% probability of 'spin-down'. This is a really tough proposition. Only a few groups have succeeded in creating this level of quantum superposition."

One of the few groups that have succeeded in it is the Macroscopic Quantum Coherence Laboratory, according to Jaw-Shen Tsai, the laboratory head of the Single Quantum Dynamics Research Group at RIKEN Frontier Research System. This laboratory successfully used a superconductive device (Josephson device) to produce a

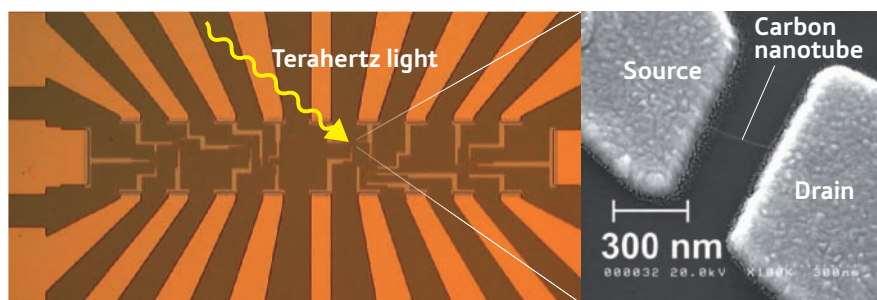


Figure 3 : Terahertz light detector.

The energy of the photons causes electrons to be emitted when terahertz light is shone onto artificial atoms in a carbon nanotube. Terahertz light can be detected by capturing the electrons.

quantum bit, and leads the world in terms of research into quantum computing. “A calculation based on a quantum computer requires many operations of quantum bits,” says Ishibashi. The state of quantum superposition, however, does not last long enough. Even superconductive elements do not give a performance as long as initially expected. Ishibashi says, “Carbon-nanotube artificial atoms are expected to maintain the state of quantum superposition for a longer time.”

I feel as if it were 1948

Having achieved many research results using carbon nanotubes, Ishibashi says, “Different materials may be used instead of carbon nanotubes in five years time.” He adds that microfabrication of carbon nanotubes is really difficult. For example, only one single-electron transistor out of ten prototypes works properly. “This means our single-electron transistors are created only by chance at the moment.”

Ishibashi continues, “I feel as if it were 1948.” This is the year when the transistor

was invented. In those days, the transistor was first predicted to be a substitute for the vacuum tube. The transistor, however, was broken easily, and therefore putting it into practical use was also considered difficult. In the meantime, silicon supplanted germanium as a material for transistors and integrated circuits were invented. Thus nearly 60 years were needed to develop the transistor to the current level. In contrast, the carbon-nanotube single-electron transistor can be compared in performance to the transistor in 1948. “We will also try out other materials such as semiconductor nanowires. Anyhow, we will make things very small using various materials, and see what happens.”

Former direct supervisor, Susumu Namba

In April 2007, Susumu Namba, a pioneer of semiconductor engineering passed away (Fig. 4, RIKEN Honorary Researcher and Professor Emeritus of Osaka University). He was Ishibashi’s former direct supervisor during his graduate course in electronics,

and he was the supervisor who advised Ishibashi to “make things very small and probe the physics”.

“He really was a man of wide vision. He had a keen perception and looked ahead of the times,” says Ishibashi. The study subjects that Namba quickly launched into and explored included light modulation, ruby-laser oscillation, ion implantation into semiconductors, excimer laser lithography, and synchrotron radiation lithography. He used to say to his students, “Study things that I do not understand. Otherwise, nothing new will be created in this laboratory.” He told his students, “Follow this way, but don’t get hung up on the details.” Ishibashi adds, “He was a great lover of sake, and often visited my lab at RIKEN until recently, but”

Ishibashi fails to complete the sentence.

It seems Ishibashi will accept the baton of his supervisor’s pioneer spirit and will continue to conduct research into small things, just as he was advised. ■

About the researcher

Koji Ishibashi was born in Kyoto, Japan, in 1960. He graduated from the Department of Electrical Engineering, Osaka University, in 1983, and received his doctorate in engineering in 1988 from the same university. After postdoctoral work in the Frontier Research Program, at RIKEN, he joined the semiconductor laboratory at RIKEN and became the chief scientist of the Advanced Device Laboratory in 2003. He was a visiting researcher at Delft University of Technology in the Netherlands from 1996 to 1997, and acquired the post of visiting professor at Lund University in Sweden in 2007. He is also a visiting professor at Tokyo University of Science and Chiba University. He has worked on quantum transport in semiconductor nanostructures, and his current interests are the fabrication of very small nanostructures that can be used for single-electron devices, quantum computing, and other new functional devices..



Figure 3 : Susumu Namba (far right).

From left, Gottfried Landwehr (Klitzing’s former supervisor), Koji Ishibashi, Chief Scientist, and Klaus von Klitzing (1985 Nobel Laureate in Physics).

RIKEN BRC plans distribution of mouse iPS cells

Shinya Yamanaka of Kyoto University and RIKEN BioResource Center (RIKEN BRC) are planning to distribute induced pluripotent stem (iPS) cells, which Yamanaka recently succeeded in producing for the first time from the skin cells of a mouse.

Pluripotent stem cells are universal cells that are capable of producing various kinds of body cells. They offer potential in the development of medical treatments for a wide range of diseases that are currently untreatable, including disease and damage to the brain, spinal cord, skeletal muscles and heart.

Until now, research on this type of cell has been performed using embryonic stem (ES) cells. However,

as human ES cells have to be harvested from human embryos, which must be destroyed in the process, there are considerable ethical arguments against using them. Induced pluripotent stem cells are artificially derived from somatic cells by the insertion of certain genes, so they do not raise these ethical issues. Thus Yamanaka's development opens the way for the use of stem cells in medical treatments.

After the announcement of Yamanaka's achievement in producing iPS cells, Yamanaka sent the cells to RIKEN BRC, and the BRC Cell Engineering Division started examination of the culturing conditions. This examination is due for completion

at the end of March, by which time the cells are expected to be ready for distribution.

The key factors that became basis of iPS cell production are also included in the clone database of the RIKEN-sponsored international consortium FANTOM (Functional Annotation of the Mouse cDNA), a project aimed at providing the ultimate characterization of the mouse transcriptome. Yamanaka picked 24 candidate genes from several databases, including FANTOM database. He then introduced four genes into the cells, and succeeded in producing the iPS cells. ■

Center for primary immunodeficiencies opens at the RIKEN Research Center for Allergy and Immunology

On January 15, the RIKEN Research Center for Allergy and Immunology (RCAI) established the RIKEN Jeffrey Modell Diagnostic and Research Center for Primary Immunodeficiencies, with the support of the Jeffrey Modell Foundation. Thirteen Japanese universities and the Kazusa DNA Research Institute will also cooperate in the activities of the center.

Primary immunodeficiencies (PIDs) are a syndrome in which the immune system does not function properly owing to genetic abnormalities. These are extremely serious disorders, causing patients to suffer from recurring infections. At times they are accompanied by autoimmune diseases and allergies, and young patients may suffer from malignant tumors. Delayed diagnosis not only increases complications and medical costs, but also the risk of fatality. In Japan, PIDs are specified as intractable diseases. However, cases of PID have been dispersed, and there has been no central database that could amass clinical and genetic analyses, making it difficult to promptly and accurately identify the causative genes in patients.

In this context, RCAI and the 13 universities in the Clinical Study Group for Primary Immunodeficiency, supported by the Ministry of Labor, Welfare and Health, together with Kazusa DNA Research Institute, launched a PID data repository (PID) database: <http://pidj.rcai.riken.jp/>. The database contains clinical, cytological, and genomic data, which allows Japanese clinicians and specialists a total view of the pathogenesis and the definitive diagnosis of PID via multiple parameters. In addition, the network will expand to the rest of Asia. Sujatha Mohan, from the Institute of Bioinformatics in India, joined RCAI as a unit leader and established an open access Asian PID database. Besides these database networks, a centralized storage system of PID clinical samples at RCAI and a consultation system for clinicians by PID specialists are being instigated.

Because of these highly regarded activities, the Jeffrey Modell Foundation chose RCAI as its 36th Jeffrey Modell Diagnostic and Research Center. "The level of the research facilities is one of the highest amongst those all over the world that I have seen," Fred Modell said.

The Jeffrey Modell Foundation is a nonprofit organization in the USA founded by Fred and Vicki

Modell in memory of their son Jeffrey, who died of pneumonia resulting from PID at the age of 15. Sponsored mainly by the US firm CSL Behring, a leader in the field of plasma protein biotherapeutics, the foundation is dedicated to the support of basic and clinical research, patients and families, education, and promoting public awareness of PID. ■

Hollywood movie shot at RNC

'Jumper', a Hollywood movie directed by Doug Liman, is to be released this spring. A scene for the movie was filmed at the RIKEN Nishina Center for Accelerator-Based Science (RNC) in February last year. Almost 100 members of staff traveled to the center, including Liman, renowned for his film 'Mr. & Mrs. Smith', and actor Hayden Christensen, of 'Star Wars: Episode II—Revenge of the Sith'. Filming started at 7 am and wrapped up at 2 am the next day. Unfortunately, the scenes filmed at RIKEN were eventually cut due to a change in the script. However, the filming of the scene offered an exciting opportunity for people working in scientific research and the movie industry to meet. A reporter on the event told Liman, "Mr. & Mrs. Smith' is the first action movie I ever liked," to which Liman answered, jokingly, "Actually, it should be called a romantic movie."

Over the course of a lunch break during the filming at RIKEN, Liman answered questions about both the

film, 'Jumper', and his interest in science. One of the questions put to Liman was, "Why did you come here [RIKEN] to film this movie?" He replied, "The production company of 'Mr. & Mrs. Smith' offered me the job almost a year ago. The staff of 'Jumper' is almost the same as that of 'Mr. & Mrs. Smith', and we are almost like a big family, loving and hating each other." He was also asked whether this was the first time he had used a research facility in a film. "Yes," he replied. "After we decided to film at RNC, I looked into all the accelerator facilities around the world on Wikipedia. Physics research using accelerators is surely as impressive as an expedition to the moon. The RIBF is an incredible place, and it really inspired me." Finally Liman was asked whether he had an interest in science. His response was:

"In fact, the subject I got best marks in during high school was physics. And I myself have actually built a robot... a cat-shaped one. I considered studying physics at university, but I chose history instead. And I do include some more-or-less scientific factors in my movies, as I did in this one, 'Jumper'.

"And I have a scientist in my family— my sister is a neuroscientist. That makes me feel much closer to science. My heart is always in science, and I am always interested in scientific matters."

When the filming was over, Liman and Christensen left their signatures on top of the RNC Superconducting Ring Cyclotron. ■



Liman and Christensen leave their signatures on top of the RNC Superconducting Ring Cyclotron.

Dr. Masahiko Hara
Laboratory head
Emergent Functions Asian Collaboration Laboratory
Frontier Research System, RIKEN
Wako-city, Saitama, Japan.

Dear Dr Hara,

It's many years back, but the wonderful memories of my time at RIKEN are still very alive—as if it was just yesterday. I remember my first visit in 1989 to the Wako campus—on the occasion of the fourth Langmuir/Blodgett Conference (LB4), in Tsukuba. My colleague Dr. Hiroyuki Sasabe of the nano-photonics laboratory had invited me to spend a few days with his group at the Frontier Research Program. Since it was my first visit to Japan we went to a sushi bar for dinner. It was not love-at-first-sight. Well, that was only at the very beginning—today I'm an absolute sushi and sashimi fan. But my memories of RIKEN do not only revolve around the wonderful food in Japan. For me, as a researcher, it was exciting to be exposed to the country's great science; and it was a unique opportunity to meet so many excellent scientists—many of whom became friends for life.

The most rewarding privilege, however, was to meet Minoru Oda, then the President of RIKEN. Minoru is one of the people who have impressed me the most in my life. He was an outstanding scientist, a great mentor and a wonderful person. We shared unbelievably inspiring times in his office, at the Friday Bar on campus, at scientific meetings and during his visits to Germany. I remember once that I went on a boat trip with him and his wife on the River Rhine along the Loreley... Thank you Minoru for these moments!

I am deeply moved when I think of my time as the Head of Laboratory for the Exotic Nanomaterials at RIKEN with you by my side as the deputy head. We were working on exotic topics such as: coupling neurons to field effect transistors, growing crystalline multilayers by organic molecular beam epitaxy, and assembling biofunctional interfacial architectures and nano-aggregates—long before the wave of the nano-hype hit the world.

I really appreciate what those eight years meant to me as a scientist and as a person. I am grateful for the unique privilege of having worked at the Frontier Research System of RIKEN.

With best regards,
Wolfgang Knoll
Director, Max-Planck-Institut für Polymerforschung
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For further information on the research presented in this publication or to arrange an interview with a researcher, please contact

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