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The importance of fundamental measurements

Newly available data on rare, neutron-rich isotopes reveal shortcomings of models describing the synthesis of elements

At the Radioactive Isotope Beam Facility (RIBF) of the RIKEN Nishina Center for Accelerator Science in Wako, a research team has measured the time it takes for 38 extremely rare isotopes to decay by half[1]. This is the first study of half-lives for 18 of the isotopes. The data provide a long-awaited test of theoretical predictions of the rate at which these isotopes decay, and will help nuclear physicists to understand a fundamental source of many of the atomic elements and their isotopes. The results also mark an early achievement for the RIBF, which came online in 2007, and currently has "the highest production yield of heavy radioactive isotopes in the world," according to team member Shunji Nishimura from the Radioactive Isotope Physics Laboratory, headed by Hiroyoshi Sakurai.

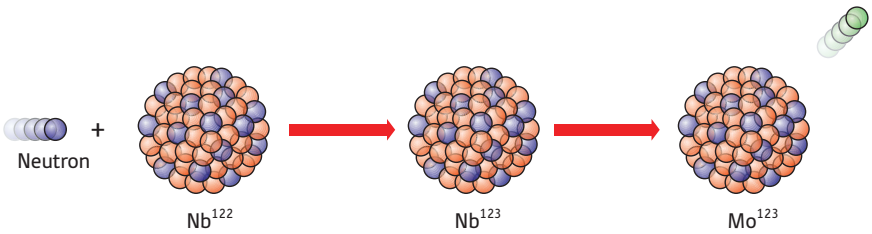


Figure 1: A schematic showing the steps in a key form of nucleosynthesis that only occurs in stars. When a neutron (blue, left) is captured by the element niobium (Nb^{122}), it converts to a proton (Nb^{123}) before decaying to molybdenum (Mo^{123}) by emitting an electron (green, right).

Making the stuff of stars

Most stable isotopes contain slightly more neutrons than protons, which balances the repulsive force between the like-charged protons. To learn more about an important form of astrophysical nucleosynthesis—the generation of new isotopes and their elements in stars—nuclear physicists are interested in creating and studying highly neutron-rich isotopes that are far from this stable balance. However, this cannot be done in the laboratory.

Half of the elements heavier than iron are thought to be produced only in the hot, dense environment of an exploding star by the so-called 'rapid neutron capture process' (r process), in which a seed nucleus—typically a light element—captures neutrons faster than it can decay to stability. The r process continues until the nucleus reaches a so-called 'waiting point' at which the nucleus undergoes beta decay such that a neutron is converted to a proton, an electron is emitted and another neutron can be captured (Fig. 1). This series of captures and emissions continues until a stable isotope is reached.

Since the neutron densities and energies required for nucleosynthesis via the r process to occur are so extreme, physicists are still trying to piece together a complete picture of its path. To this end, they simulate the process, using the relevant isotope masses and half-lives as inputs, and then test the output of the simulations against actual isotope abundances.

A lack of information about many of the neutron-rich isotopes that may exist along the path of the r process meant that simulations have either over- or under-estimated the abundance of the end-product isotopes. Using the measurements from the RIBF, the RIKEN team is filling in key missing information needed to simulate the r process. The measurements include the half-lives of neutron-rich isotopes of krypton, strontium, yttrium, zirconium, niobium, molybdenum and technetium, all of which lie near the r-process path.

"Our results are providing the first hints as to why we observe a higher abundance of certain isotopes—particularly those in the heavy mass region—than what theory predicts," says Nishimura.

Over the course of an eight-hour experiment, the team sorted through fragments produced by the collision of a relativistic beam of uranium ions colliding with a beryllium target. The fragments were identified as they passed through two stages of the RIBF's 'BigRIPS' separator (Fig. 2), the second of which contains superconducting magnets that sort the elements by mass and charge. Finally, a highly specialized silicon detector, which signals when it is implanted with a particular isotope and the time that lapses until this isotope emits an electron (via beta decay), allowed the team to determine the isotopes' half-lives.

The rare, neutron-rich isotopes created in the collisions typically survive for less than a tenth of a second. The

Figure 2: The first stage of the BigRIPS separator at the RIBF uses superconducting magnets to sort short-lived isotopes by mass and charge.

RIBF facility, however, has the world's highest intensity uranium beam and a separator at the cutting edge for discriminating short-lived isotopes, which make it a one-of-a-kind place for such measurements.

Putting elemental theories to the test

Before the experiments at the RIBF, nuclear physicists relied on theoretical models to determine the masses and half-lives of many of the isotopes along the r-process path. The irony was that with no data available, the accuracy of these models could not be tested. A key component of the work by Nishimura and his colleagues was therefore comparing their measured decay rates with those predicted by several widely used models. "Prior to our work, it was not clear which model should be used," says Nishimura.

In particular, the team showed that two models—called KTUY + GT2 and FRDM + GT2 for short—predicted the measured half-lives of the isotopes fairly well, while the so-called FRDM + QRPA model predicted half-lives that were, in some cases, ten times more or less than what the RIKEN team observed.

"Only by measuring many isotopes in a systematic way could we say that one model is wrong, at least where the total number of protons and neutrons is around 115," says Nishimura.

This new insight may explain why earlier r-process simulations based on certain models underestimated the abundance of heavier elements. For example, a model that overestimates the half-lives of the nuclei contributing to the r-process will overestimate the time for the r process to occur. The team's data suggest that once the seed nucleus reaches a waiting point, it decays fairly quickly, rarely reaching the sizes needed to produce a heavier isotope.

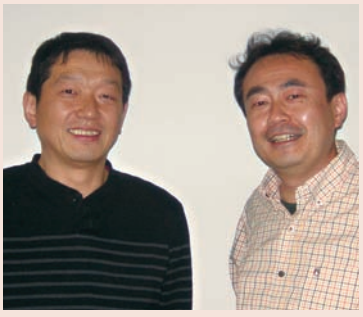
The important new measurements are still "a tiny piece of the big puzzle of how elements like gold and uranium are created," Nishimura says. Using the unique capabilities of the RIBF, the team plans to continue their measurements—by conducting the experiment over longer times using a higher intensity beam of uranium ions. ■

1. Nishimura, S., Li, Z., Watanabe, H., Yoshinaga, K., Sumikama, T., Tachibana, T., Yamaguchi, K., Kurata-Nishimura, M., Lorusso, G., Miyashita, Y. *et al.* β–decay half-lives of very neutron-rich Kr to Tc isotopes on the boundary of the r-process path: An indication of fast r-matter flow. *Physical Review Letters* **106**, 052502 (2011).

About the Researchers

Shunji Nishimura (left) was born in Shimane, Japan, in 1966. He graduated from the Faculty of Science of Hiroshima University in 1989. After obtaining his doctoral degree in 1994 from the same university, he was awarded a Research Fellowship for Young Scientists. He then did postdoctoral work at the University of Tsukuba in 1995, and became a CNS research fellow at The University of Tokyo in 1998 and studied the quark–gluon plasma in heavy ion collisions. In 2000, he became a research scientist at RIKEN where he began a career in radioactive beam science. His research now focuses on the nuclear physics related to nucleosynthesis in extreme conditions.

Hiroyoshi Sakurai (right) was born in Kyoto, Japan, in 1963. He graduated from the Faculty of Science of The University of Tokyo in 1987 and obtained his PhD in 1993 from the same university. Also in 1993, he started his career in the nuclear structure and reactions of exotic nuclei. He was employed as a research scientist by RIKEN in 1995, then as an associate professor by The University of Tokyo in 2000. He later returned to RIKEN as a chief scientist to conduct experimental programs at the RIBF. In 2001, he was appointed as a professor of The University of Tokyo.



Electrons set free

Free-floating electrons on top of liquid helium yield insights into their transport behavior

The multibillion dollar computer industry hinges on the ability to efficiently pass an electric current through a material. However, in any electronic device such as a computer transistor, the influence of the material's atoms inevitably masks the interactions between the electrons. Using a custom-designed system, a research team from the RIKEN Advanced Science Institute, Wako, in collaboration with colleagues from the University of Konstanz, Germany, has completed the first study of the transport of single floating electrons free of external influences[1].

Trapping electrons outside of matter and keeping them in order is difficult, but liquid helium is ideally suited to the task. Electrostatic charges in the liquid can attract electrons towards its surface but, owing to a lack of energy, the electrons cannot penetrate the surface and enter the liquid. Instead, caught between these competing influences, the electrons hover above the liquid helium, forming a two-dimensional electron system. "This is a unique system for studying the fundamental properties of electrons, as the electrostatic interactions between them are effectively unscreened," says team member David Rees.

To measure the transport properties of this liquid-like system of electrons, the researchers fabricated a channel on the surface of a silicon chip that they filled with liquid helium. In one location, they physically narrowed the width of this channel and applied an electric field across the constriction, which provided further control over the effective channel width using electrostatic forces (Fig. 1).

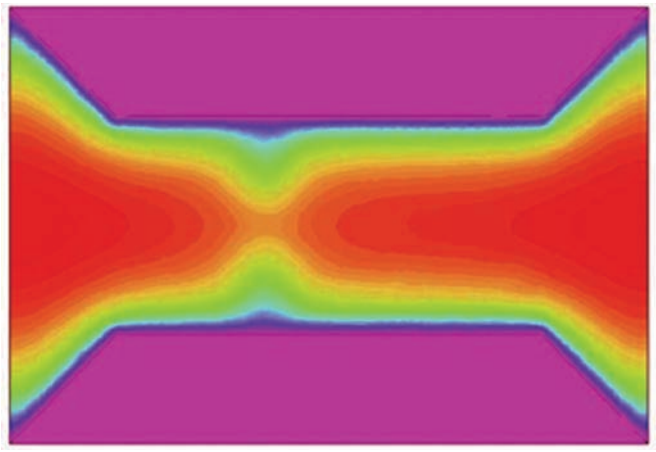


Figure 1: A graphical representation of the calculated electrostatic potential on the surface of liquid helium within a constricted passage on a silicon chip. Red colors indicate regions of lower energy.

When the channel width was sufficiently narrow, only one electron could pass through it at a time—the others were blocked by electrostatic repulsion. When the researchers slightly widened the channel by lowering the electric field across it, two electrons could pass through at the same time. Further widening would allow more electrons to pass through.

In addition to confirming the importance of electrostatic repulsions, these experiments open the door to further fundamental studies of electron behavior. If cooled to temperatures below one degree above absolute zero, the randomly floating electrons would arrange into a periodic and ordered array. This could provide the first opportunity to investigate the dynamics of a crystalline electron system, rather than a disordered liquid passing through a narrow constriction.

This model system of strongly interacting electrons may have other roles to play. According to Rees and team leader Kimitoshi Kono, if applied to other systems where the interactions between particles are strong, these findings could be used to understand the transport of particles such as ions in biological organisms. ■

1. Rees, D.G., Kuroda, I., Marrache-Kikuchi, C.A., Höfer, M., Leiderer, P. & Kono, K. Point-contact transport properties of strongly correlated electrons on liquid helium. *Physical Review Letters* **106**, 026803 (2011).

Putting the squeeze on rare earth metals

'Pincer' molecules trap reactive rare earth elements into previously unseen hydrogen-infused structures

Rare-earth metals are a series of elements that represent one of the final frontiers of chemical exploration. The vigorous reactivity of these substances, however, has made it difficult for researchers to transform them into stable materials with well-defined structures. But when they succeed, the payoff can be enormous—rare-earth compounds have important applications in areas ranging from catalysis to clean energy.

Now, Zhaomin Hou and colleagues from the RIKEN Advanced Science Institute in Wako have discovered a new way to isolate rare-earth metals as hydrogen-infused crystals by using wedge-shaped bis(phosphinophenyl) amido (PNP) ligands to 'pinch' them in place[1]. These ligands squeeze rare-earth yttrium atoms together tighter than any previous material, and can even stabilize highly volatile charged complexes.

Metallic compounds that incorporate multiple hydrogen atoms, or polyhydrides, into their frameworks are useful to chemists because they provide some of the purest understandings of bonding and reactivity available. Previously, Hou's team isolated an yttrium polyhydride containing a hydrogen ligand that simultaneously bonds to four metals[2]. This compound sparked remarkable chemical curiosity because of its structural novelty.

According to Hou, the trick to produce rare-earth polyhydrides is to surround them with large, cumbersome molecules that easily pack together to form crystals. The distinct structure of PNP ligands—two phosphorus atoms, linked together by a rigid aromatic–amino core that can bind to metals with a pincer-like grip—made this ligand a promising candidate for the researchers' investigation.

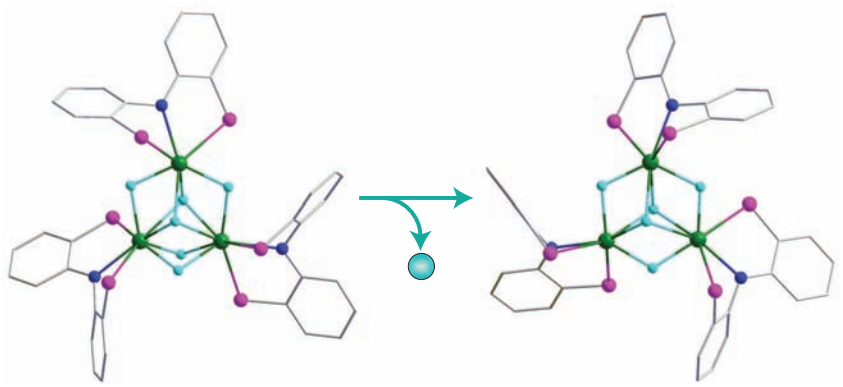


Figure 1: Bulky molecules known as PNP ligands help stabilize a novel rare earth polyhydride (left) as well as its cationic species (right) formed by removal of one hydrogen atom. Balls in green: yttrium; blue: nitrogen, pink: phosphorus, light-blue: hydrogen.

By first substituting extra methyl units onto the aromatic backbone of PNP to increase its bulkiness, and then mixing the ligand with an yttrium alkyl precursor and hydrogen gas, the team synthesized pale yellow crystals of a new yttrium polyhydride complex. X-ray structural analysis revealed that three yttrium atoms, held in place by PNP 'pincers', were interlinked by a set of double- and triple-bridged hydrogen ligands (Fig. 1). This intricate network of bonds produced the shortest yttrium–yttrium distance ever recorded—an extraordinary packing density that may be critical for future hydrogen-storage applications.

The researchers found that an ammonium proton could remove a hydride from the complex without disrupting crystallization, yielding the first-ever cationic tri- and di-yttrium polyhydrides. The charged nature of these materials should impart potent chemical activity, attributes which Hou and his team are currently investigating. "Our results clearly demonstrate the vital importance of ligand-tuning in the isolation and characterization of rare earth polyhydrides, and should encourage further explorations in this burgeoning area," he says. ■

1. Cheng, J., Shima, T. & Hou, Z. Rare-earth polyhydride complexes bearing bis (phosphinophenyl) amido pincer ligands. *Angewandte Chemie International Edition* **50**, 1857–1860 (2011).
2. Hou, Z., Nishiura, M. & Shima, T. Synthesis and reactions of polynuclear polyhydrido rare earth metal complexes containing "$(C_5Me_4SiMe_3)LnH_2$" units: A new frontier in rare earth metal hydride chemistry. *European Journal of Inorganic Chemistry* **18**, 2535–2545 (2007).

Mercury rising

Mercury-containing oxides offer a new perspective on the mechanism of superconductivity

To diversify the applications of superconductors that currently operate at chilly temperatures below 135 kelvin (K), scientists are searching for new classes of superconducting materials that will show this property at warmer temperatures. Now, a research team in Japan has synthesized a promising new class of superconductors[1], made of $Hg_{0.44}ReO_3$, where an unusual motion of the mercury (Hg) atoms enhances superconducting properties at temperatures up to 7.7 K.

The Dutch physicist Heike Kamerlingh Onnes discovered superconductivity one hundred years ago, when he noticed that the electrical resistance of mercury dropped to zero suddenly at 4.2 K. Superconducting materials are now used routinely in magnetic resonance imaging scanners.

In classical superconductors such as mercury, superconductivity arises through the combined vibrations of the atoms in the crystal. This makes the crystal structure a key factor for the superconducting properties of a material. In the case of Hg_xReO_3, the atomic structure consists of rhenium (Re) and oxygen (O) building blocks. In the empty spaces between them, the mercury atoms arrange in chains (Fig. 1). However, some of the available places along these chains lack mercury atoms, and the team's work suggests that this leads to an arrangement of paired mercury atoms.

"These pairs move within the channel in an oscillatory motion known as rattling", explains team-member Ayako Yamamoto from the RIKEN Advanced Science Institute in Wako. The rattling vibrations provide a strong feedback for the electrons, and therefore reinforce superconductivity in the material. In comparison to a similar structure lacking mercury pairs, the superconducting temperature of $Hg_{0.44}ReO_3$ at 7.7 K is almost twice as high. "Despite remaining below the present record of 135 K for a superconductor, there is potential for improving operation temperatures", says Yamamoto. "The application of pressure increases the superconducting temperature to 11.1 K, and this could mean that for the right crystal structure further enhancement is possible."

Yamamoto and her colleagues are now working to optimize the crystal structure further—for example, by replacing rhenium with other elements. A better understanding of the influence of the mercury atoms' rattling motion may also provide better insight into the mechanism of superconductivity in such structures. "Mercury seems to be a magic element in superconductivity, not only for its role in Kamerlingh Onnes' discovery, but also for the fact that mercury is part of the material with the highest known superconducting temperature, $HgBa_2Ca_2Cu_3O_x$," Yamamoto explains. "Once more, mercury is playing a key role for new superconductors," she says. ■

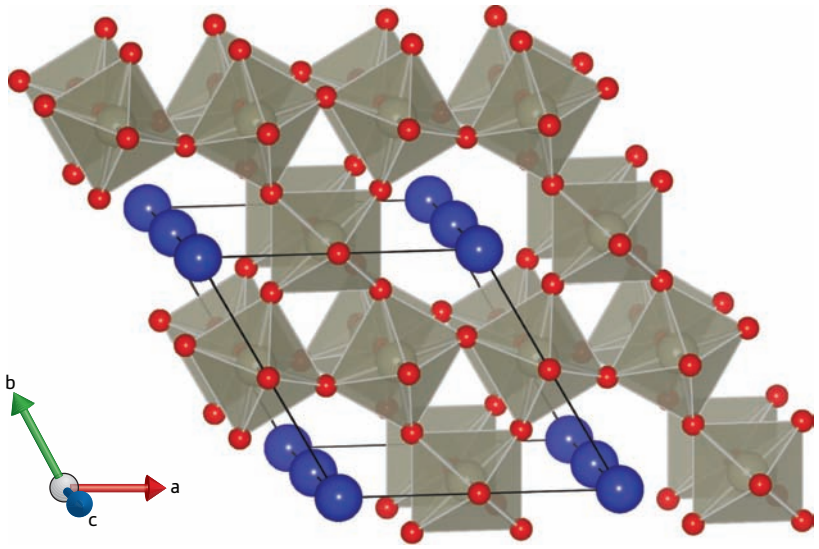


Figure 1: The crystal structure of Hg_xReO_3. The mercury (Hg) atoms are shown in blue, oxygen (O) in red and rhenium (Re) in brown.

1. Ohgushi, K., Yamamoto, A., Kiuchi, Y., Ganguli, C., Matsubayashi, K., Uwatoko, Y. & Takagi, H. Superconducting phase at 7.7 K in the Hg_xReO_3 compound with a hexagonal bronze structure. *Physical Review Letters* **106**, 017001 (2011).

Atomic-level crystal gazing

Revelation of the crystallization mechanism that enables fast writing of data to DVDs shows potential for quicker data storage in the future

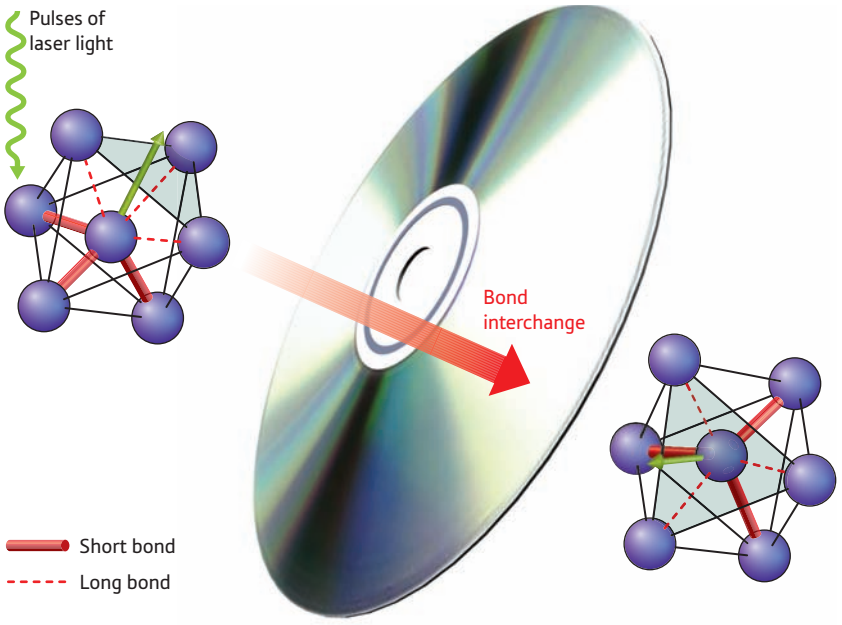


Figure 1: Pulses of light alter the atomic bonds (red) in the material AIST, enabling quick storage and deletion of data.

Some 300 exabytes (3×10^{20} bytes) of information were stored in electronic media—magnetic disks and tapes or optical disks—throughout the world by 2007. Yet, the demand for electronic storage grows daily, driving an ever-increasing need to pack data into smaller volumes in quicker time. By studying how laser pulses alter the atomic structure of data-storage materials, a research team in Japan has uncovered a fundamental mechanism that could aid in the design of even faster information storage in the future[1]. The finding was published by Masaki Takata from the RIKEN SPring-8 Center, Harima, Shinji Kohara from the Japan Synchrotron Radiation Research Institute/SPring-8, Noboru Yamada from Panasonic Corporation and a team of scientists from Japan, Germany and Finland.

Rewritable memory, such as the random-access memory found in computers or on DVDs, is based on a phase change in specific types of materials in which the atoms change from one stable arrangement to another. Pulses of laser light can induce a phase change, a process known as 'writing,' and the material's phase can be identified by 'reading' its signature optical properties.

To provide the first full understanding of the atomic structure of one such phase-change material, AgInSbTe (AIST)—often used in rewritable DVDs—Takata and his colleagues combined state-of-the-art materials-analysis techniques and theoretical modeling. A pulse of light can change AIST from an amorphous state, in which the atoms are disordered, into a crystalline phase in which the atoms are form an ordered-lattice structure. This process of crystallization happens in just a few tens of nanoseconds: the faster the crystallization, the faster data can be written and erased. No-one understood, however, why phase changes in AIST were so fast.

The team's analyses and modeling showed that AIST crystallizes in a different way to other commercially available phase-change materials. They found that crystallization of AIST is a simple process: the laser light excites the bonding electrons and causes them to move. A central atom of antimony (Sb) switches between one long (amorphous) and one short (crystalline) bond without any bond breaking (Fig. 1). "We hope to verify this bond-interchange model in the near future," says Takata. "Crystallization is the storage-rate-limiting process in all phase-change materials, and an atomistic understanding of it is essential."

The researchers also discovered that the absence of cavities within the crystal structure contributes to the faster writing speeds on AIST. This contrasts starkly with the alternative material germanium antimony telluride in which 10% of lattice sites in are empty. ■

1. Matsunaga, T., Akola, J., Kohara, S., Honma, T., Kobayashi, K., Ikenaga, E., Jones, R.O., Yamada, N., Takata, M. & Kojima, R. From local structure to nanosecond recrystallization dynamics in AgInSbTe phase-change materials. *Nature Materials* **10**, 129–134 (2011).

Mediating magnetism

Titanium oxide doped with cobalt produces magnetic properties at room temperature via a newly discovered mechanism

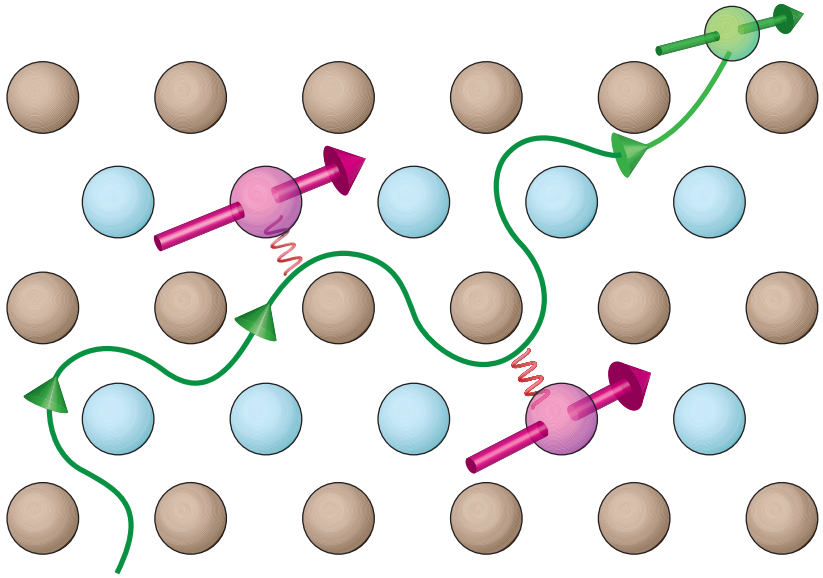


Figure 1: A representation of a thin film of Co:TiO_2 in which ferromagnetism arises because titanium 3*d* electrons (green) travel around the material aligning the spin of cobalt atoms (pink) so that they all point in the same direction. The blue and brown spheres correspond to titanium and oxygen atoms, respectively.

Spintronics—also known as magnetoelectronics—may replace electronics as the medium of choice for computer memory. The discovery of a mechanism that produces permanent magnets at room temperature, without any external influence, may soon improve the design of spintronic devices. Takumi Ohtsuki from the RIKEN SPring-8 Center, Harima and his colleagues in Japan, made the discovery in a class of material called a dilute ferromagnetic oxide[1].

Ferromagnetism is the mechanism responsible for making some materials magnetic without any external influence. In a ferromagnet, the axes about which a majority of the electrons spin are all parallel, but the underlying cause for this alignment is not always clear. A dilute ferromagnetic oxide is an oxide material doped with a small amount of a transition metal, which represents a marriage between magnetic materials and those used in electronics. Crucially, and unlike the ferromagnetic-semiconductors, dilute ferromagnetic oxides remain in a ferromagnetic state at room temperature.

Some materials have ferromagnetic constituents but exhibit no magnetism. However, some ferromagnets consist of substances that, on their own, are nonmagnetic. A full understanding of this enigma is vital for designing efficient spintronic devices and requires determining which electrons, or other type of charge carrier in a material, mediate the ferromagnetism. To resolve this question in dilute ferromagnetic oxides, Ohtsuki and his co-workers examined one commonly used example: cobalt-doped titanium dioxide (Co:TiO_2). "Several mechanisms have been suggested for the origin of ferromagnetism in Co:TiO_2, but no firm conclusion has been established," says Ohtsuki.

The researchers used a powerful material characterization technique known as x-ray photoemission spectroscopy. A beam of x-rays, in this case from the SPring-8 synchrotron radiation facility, excited electrons from the sample of Co:TiO_2. "The number of excited electrons versus their kinetic energies provided detailed information about the atomic composition and electronic state of the material," explains Ohtsuki.

Ohtsuki and his team established that ferromagnetism is mediated by the electrons in the third shell—so-called 3*d* electrons—of the titanium ions (Fig. 1), a mechanism that has never been considered as a possibility by scientists before. The titanium 3*d* electrons align the spin of the cobalt atoms as they travel through the material.

The team's discovery enhances the likelihood that dilute ferromagnetic oxides will be used as spintronic devices. "Our results have proven that magnetism and conductivity are correlated in Co:TiO_2 thin films," explains Ohtsuki. "This could make them applicable to magnetic random access memory (MRAM) or spin transistors." ■

1. Ohtsuki, T., Chainani, A., Eguchi, R., Matsunami, M., Takata, Y., Taguchi, M., Nishino, Y., Tamasaku, K., Yabashi, M., Ishikawa, T. *et al.* Role of Ti 3*d* carriers in mediating the ferromagnetism of Co:TiO_2 anatase thin films. *Physical Review Letters* **106**, 047602 (2011).

Distinguishing yourself from others

Social learning occurs in specific nerve cells in the cerebral cortex of the brain that become fully active only when observing others

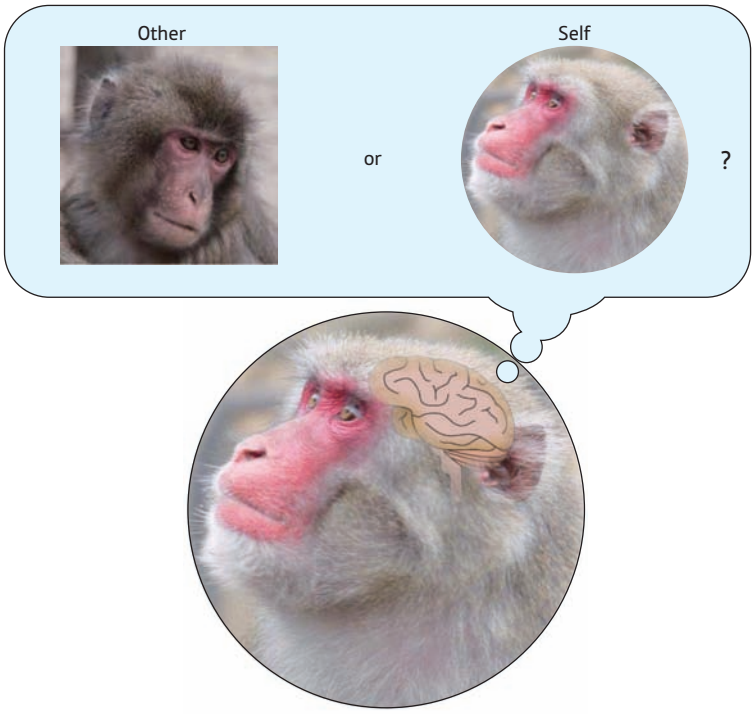


Figure 1: Groups of neurons in a specific part of the brain called the medial frontal cortex, which is associated with social learning, fire in ways that help individuals to distinguish between self and others.

Researchers in Japan have identified the specific nerve cells responsible for the ability to distinguish between the actions of self and others[1]. The discovery lays the foundations for studying social learning at the level of nerve cells using a new experimental technique. The work, led by Masaki Isoda from the Okinawa Institute of Science and Technology and Atsushi Iriki from the RIKEN Brain Science Institute, may lead to a better understanding of mental conditions where distinctions between self and others become confused.

Neuroscientists have long known that nerve cells called 'mirror neurons'—found mainly in the brain's cerebral cortex—fire when an individual performs an action or observes one performed by somebody else. The resulting information can be used as a basis for understanding others and for social interaction but, until now, a critical part of the puzzle was missing. If the same group of neurons fired when performing or observing an action, how could an individual distinguish self from other?

"Obviously, the brain needs a separate mechanism that enables one to make that distinction," says Isoda. The researchers recognized that to find that mechanism they needed to develop an interactive task involving both observation and action that could be used to measure associated differences in the activity of neurons.

The task they designed involved two monkeys sitting face to face and taking turns to make choices of pushing one of two different colored buttons for a reward. Both monkeys were rewarded for a right choice and neither received a reward for a wrong choice. Each monkey had two turns, and then control would pass to the other. For blocks of between 5 and 17 turns, the color associated with the reward remained the same, but then it would change. So, observing which color was rewarded was important to success.

The researchers found the monkeys were quite capable of observing and learning from another's action in planning their own response. Then, by monitoring the activity of 862 neurons in the medial frontal cortex (MFC) of the brain—which is associated with social cognition—they detected groups of neurons that were selectively activated only when a monkey's partner performed the action. The researchers observed these 'partner-fired' neurons in dominant and submissive monkeys, and found they were most prevalent in the dorsomedial convexity region of the MFC (Fig. 1).

"In future, we hope to be able to identify the entire neuronal network and precise neuronal operation involved in self/other distinction," Isoda says. ■

1. Yoshida, K., Saito, N., Iriki, A. & Isoda, M. Representation of others' action by neurons in monkey medial frontal cortex. *Current Biology* **21**, 249–253 (2011).

Following directions

A key regulator of nervous system development works by blocking a signaling protein with multiple roles in stem cell maturation

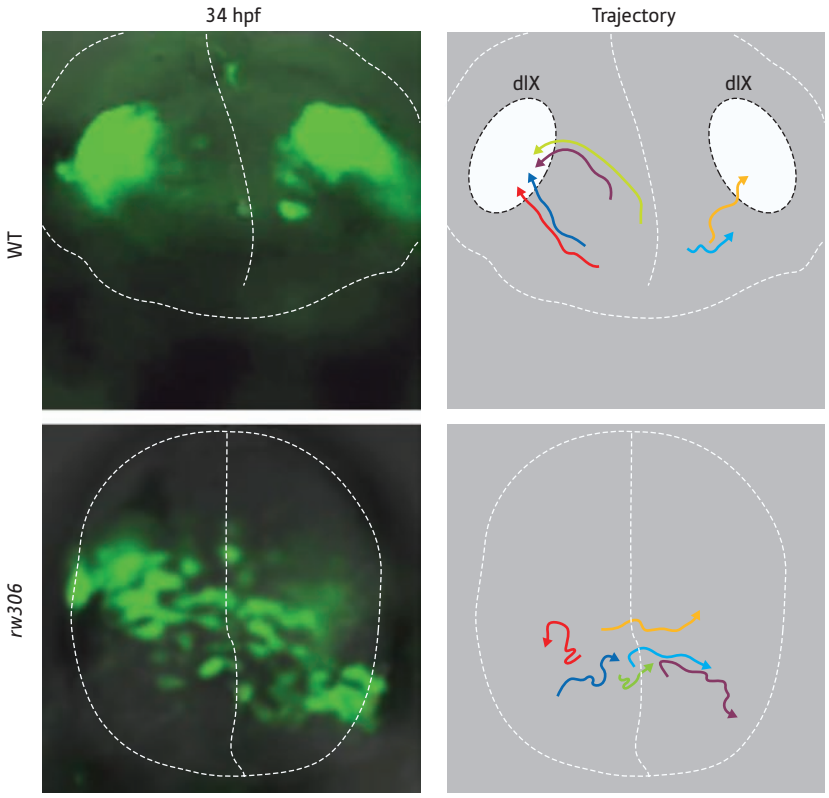


Figure 1: Thirty-four hours after fertilization, motor neuron precursors (green) in wild-type zebrafish embryos (top) show clear organization, relative to the disrupted migration apparent in the *moe*^{rw306} mutant fish (bottom). Right panels illustrate the trajectories of selected neuronal precursors over the course of development.

Neuroepithelial stem cells, the early progenitors for much of the nervous system, need to maintain a keen sense of direction in order to properly manage replication, migration and maturation. These cells are highly polarized, and exclusively initiate cell division at their apical (top) end rather than at their basal (bottom) end, although it has remained a mystery how they determine which way is up.

By studying a zebrafish mutant with defective migration in a subset of motor neurons (Fig. 1), a team led by Shinya Ohata and Hitoshi Okamoto at the RIKEN Brain Science Institute in Wako has now uncovered valuable details about how polarity is managed[1]. The linchpin in this process is Notch, a membrane-spanning signaling factor; when activated, Notch sheds its intracellular portion, which enters the nucleus and switches on genes that prevent neuroepithelial cells from differentiating into neurons. The researchers determined that their mutant fish contained an alteration in the gene encoding the Mosaic eyes (Moe) protein, which stimulates Notch signaling by blocking one of its inhibitors, the Crumbs (Crb) protein, and thereby maintains cells in an undifferentiated state.

Moe also proved to be an important regulator of cell migration and apico–basal polarity, although Ohata and Okamoto were surprised to learn that these effects are mediated by a poorly characterized secondary Notch-mediated signaling mechanism. In this 'non-canonical' pathway, the intracellular domain of Notch does not need to enter the nucleus to achieve an effect, but instead transmits instructions via another protein, R-Ras. The data suggest that these effects are further promoted by a positive feedback loop in which R-Ras activation stimulates Moe activity.

By acting as a high-level regulator for these various pathways, Moe serves a crucial role in ensuring that neuroepithelial cells preserve proper directionality during division and maintain their stem cell state until they arrive at the appropriate position within the embryo. "Immature status and apico–basal polarity of neuroepithelial cells, which are critical for apically restricted cell division, are both maintained by a single signaling pathway: the Crb/Moe complex-Notch pathway," says Ohata. "This could be a key link in understanding the fundamental properties of neuroepithelial cells."

The researchers are now examining their favored model for Moe function, in which this protein inhibits Crb by physically sequestering it from the Notch receptor. "We are testing this hypothesis by investigating the dynamics of Crb, Moe and Notch using *in vivo* time-lapse imaging, which is a great advantage of doing experiments in zebrafish," says Ohata. ■

1. Ohata, S., Aoki, R., Kinoshita, S., Yamaguchi, M., Tsuruoka-Kinoshita, S., Tanaka, H., Wada, H., Watabe, S., Tsuboi, T., Masai, I. & Okamoto, H. Dual roles of Notch in regulation of apically restricted mitosis and apicobasal polarity of neuroepithelial cells. *Neuron* **69**, 215–230 (2011).

Maintaining a proper distance

A protein-devouring enzyme complex uses two different mechanisms to determine which targets to destroy

The proteasome is the garbage-disposal system of the cell, enzymatically clearing away unwanted proteins. Since this requires the recognition of individual targets within the crowded cellular environment, it is critically important that molecules 'marked for death' are appropriately flagged.

This signal, known as the degron, is composed of two components: an unstructured 'initiation region' within the target protein and a proteasome recognition tag. This tag typically consists of a chain of ubiquitin molecules, but some proteins get steered to the proteasome with the help of ubiquitin-binding 'adaptor' proteins. "These two pathways work in parallel with and independently from each other, and converge at the initiation step," explains Tomonao Inobe of the RIKEN Brain Science Institute in Wako.

By analyzing the efficiency with which different synthetic protein constructs get degraded by the proteasome, Inobe and colleagues in Andreas Matouschek's laboratory at Northwestern University in Illinois, USA, have uncovered important structural details of the recognition mechanisms used by the proteasome to manage these distinct pathways[1].

The team's initial experiments showed that the minimum length for the initiation region is shorter in proteins tagged with ubiquitin alone (Ub_4) than those tagged with an adaptor-derived ubiquitin-like (UbL) domain. Similarly, they found that Ub_4–mediated degradation was most efficient when these sites were close together, and was impaired by the insertion of rigid 'spacer' protein segments between the two degron components. With UbL-tagged constructs, however, degradation was maximized when these components were moderately separated.

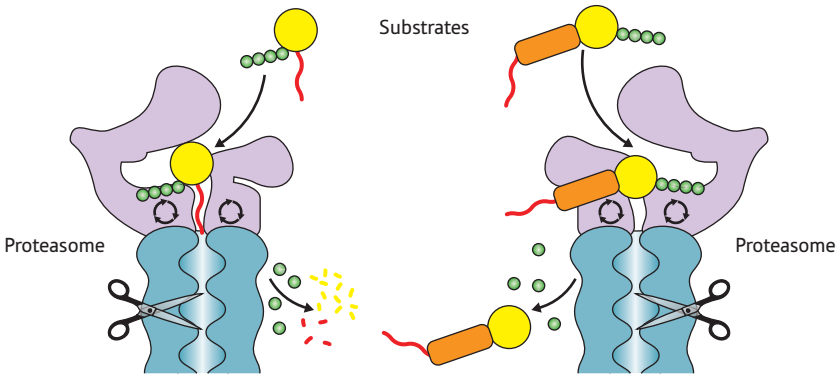


Figure 1: For intracellular proteins (yellow) tagged with ubiquitin chains (green), the tag and initiator region (red) must be close together for the tagged protein to be broken down (left). When the separation between these elements (orange) is too great, degradation becomes highly inefficient (right).

Based on their data, the researchers concluded that these physical constraints arise because Ub_4- and UbL-tagged proteins bind to completely different sites on the proteasome; ubiquitin binds very near to the digestion machinery, requiring the initiation region to be close by (Fig. 1), while the UbL-binding site is considerably farther away, and thus accommodates greater separation. Inobe compares this to how an electrical plug must match its outlet. "The proteasome can recognize different plugs," he says, "but each one has to have the correct specific arrangement of prongs."

Inobe hopes to better characterize the functional role of this distance restriction in the future, but suggests that this mechanism may enable this protein complex to achieve both direct destruction of individual proteins and the targeted degradation of specific molecules nestled within larger complexes. "The spacing rules fit well with the way these tags are used physiologically and help explain how substrates are selected for degradation or manage to escape the process," says Inobe. ■

1. Inobe, T., Fishbain, S., Prakash, S. & Matouschek, A. Defining the geometry of the two-component proteasome degron. *Nature Chemical Biology* **7**, 161–167 (2011).

Supporting the troops

In the absence of vitamin A, the body loses immune cells that put the brakes on the earliest stages of infection

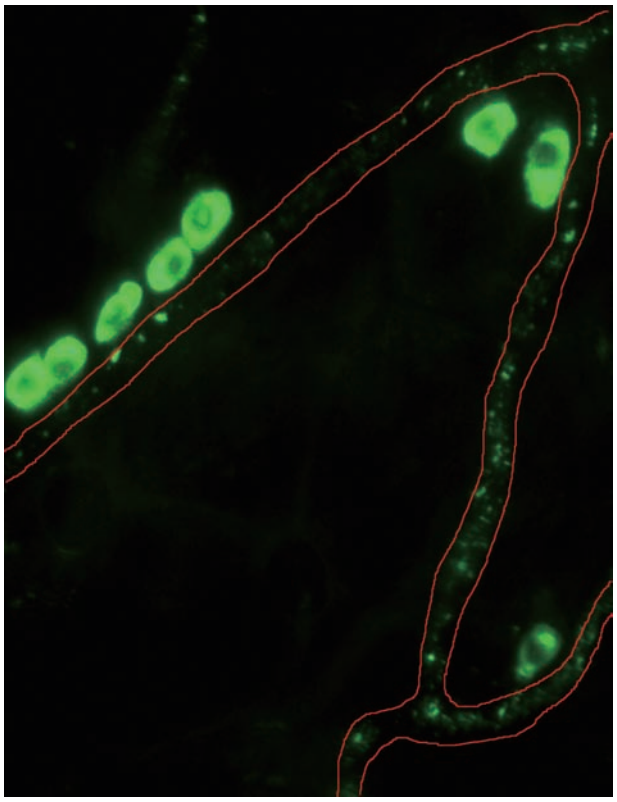


Figure 1: Once activated by the presence of pathogens, B1 cells develop into IgM-secreting cells (green) which travel along the blood vessels (outlined in red) from the peritoneal cavity into the effector sites such as spleen.

Scientists have recognized the immune-boosting capabilities of vitamin A for the better part of a century, even without fully understanding how it helps the body fight off bacteria and viruses. "Soon after its discovery, vitamin A was termed 'the anti-infective vitamin' and was widely used to enhance recovery; but with the introduction of antibiotics, the therapeutic use of vitamin A diminished," says Sidonia Fagarasan of the RIKEN Research Center for Allergy and Immunology in Yokohama.

Fagarasan and her colleagues have now revealed how vitamin A deficiency can critically undermine the body's initial defense against infection[1]. B1 cells within the peritoneal cavity (PEC), the space surrounding the intestines and other organs, are important 'first responders' to the presence of pathogens (Fig. 1). Upon activation, B1 cells mature into cells that produce immunoglobulin M (IgM) and A (IgA) antibodies that target bacteria and viruses in the bloodstream and gut, respectively. "These cells usually act at the early time window after infection, thus preventing the expansion of microorganisms," explains Fagarasan.

Mikako Maruya, a young researcher with her team, observed dramatic depletion of PEC B1 cells in mice fed a vitamin A-free diet, which grew more severe with age. Accordingly, these vitamin A-deficient (VAD) animals also produced lower levels of both IgA and IgM, and failed to marshal an effective antibody response following injection with pneumonia vaccine. B1 cells transplanted from healthy donors to VAD animals showed impaired proliferation, and considerably dwindled in number over the course of a week. Importantly, bone marrow-derived stem cells from VAD mice retained the capacity to give rise to B1 cells, although they failed to do so in the absence of vitamin A.

The key turned out to be nuclear factor of activated T cells 1 (NFATc1), a transcription factor protein that regulates expression of numerous important genes in B1 cells. The researchers observed reduced NFATc1 levels in VAD B1 cells, but found that expression could be largely restored if these mice were injected with ATRA, a product of cellular vitamin A metabolism. This also led to rapid B1 cell proliferation, which increased in number by more than four-fold increase within 10 days of injection.

Motivated by these findings, Fagarasan is now exploring how levels of vitamin A affect other components of the immune response to infection. "We were very excited to discover something that we had never thought about, that active products of vitamin A contribute to the induction of some very important transcription factors," she says. ■

1. Maruya, M., Suzuki, K., Fujimoto, H., Miyajima, M., Kanagawa, O., Wakayama, T. & Fagarasan, S. Vitamin A-dependent transcriptional activation of the nuclear factor of activated T cells c1 (NFATc1) is critical for the development and survival of B1 cells. *Proceedings of the National Academy of Sciences USA* **108**, 722–727 (2011).

Giving tumor vaccines a proper introduction

Therapies that target specialized cells residing within the lymph nodes may help to rally tumor-killing immune responses

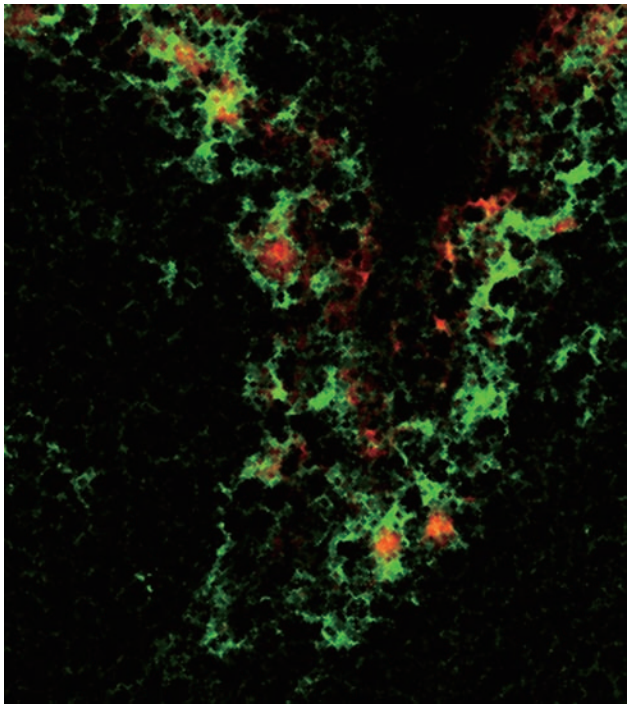


Figure 1: CD169-positive macrophages (green) residing within the lymph sinuses rapidly consume the dead tumor cells (red) that make their way through the lymphatic system following subcutaneous injection.

Given how effectively the immune system can eliminate foreign threats such bacteria and viruses, hopes are high for the development of strategies that might turn these same defense mechanisms against cancerous targets. However, attempts to train the immune system to recognize malignancies via the intravenous injection of vaccines that present tumor-derived antigens have fallen short.

According to Kenichi Asano, a researcher with Masato Tanaka's group at the RIKEN Research Center for Allergy and Immunology in Yokohama, this is the result of 'tolerance' mechanisms that protect against autoimmune disease. "Billions of cells die every day, and cell corpses must be removed swiftly from our body in order not to induce detrimental effects," he says. In this scenario, macrophage cells in the spleen clean house by devouring such debris in a process known as phagocytosis, thereby preventing dead cells from triggering an inflammatory response.

Tumor cells delivered into the lymphatic system via subcutaneous injection, however, can successfully elicit a strong immune response, and new research from Asano and colleagues explains why this is the case[1]. In order to rouse an effective reaction, phagocytic cells must present recognizable chunks of those dead cells to tumor-killing cytotoxic T lymphocytes (CTLs). The researchers identified a very specific subset of macrophages within the lymph nodes that perform this task.

Intriguingly, these cells, which are distinguishable by their expression of the cell-surface protein CD169, are non-migratory and reside stably within the sinuses of the lymph node, awaiting their prey like spiders in a web. Dead cancer cells delivered to these sinuses via the lymphatic system are rapidly digested by the macrophages (Fig. 1), which in turn cross-present the resulting antigens to CTLs. By selectively killing off these macrophages with diphtheria toxin, the researchers were able to essentially disable the immune response. "Without CD169 macrophages, tumor-directed T cells were no longer activated—that means these cells dominate anti-tumor immunity after tumor cell death," says Asano.

These findings help explain why the dead cells that slough off of tumors into the lymphatic system during radiation or chemotherapy are sometimes sufficient to provoke an immune response, and could provide the foundation for far more effective cancer immunotherapy strategies. "I believe it is very promising to mount anti-tumor immunity in patients with solid tumors by delivering tumor antigens specifically to CD169 macrophages," says Asano. "It's my dream to invent artificial materials that possess the characteristics of dead cells and are safe for administration to patients." ■

1. Asano, K., Nabeyama, A., Miyake, Y., Qiu, C.-H., Kurita, A., Tomura, M., Kanagawa, O., Fujii, S.-I. & Tanaka, M. CD169-positive macrophages dominate antitumor immunity by crosspresenting dead cell-associated antigens. *Immunity* **34**, 85–95 (2011).

New imaging techniques reveal the workings of supramolecular nanomachines

Koji Yonekura

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Supramolecules comprising many kinds of proteins and nucleic acids are present in all living organisms. Often with precise structures and a variety of parts, these supramolecules exhibit complex movements and exhaustive functions, essentially behaving like nanomachines. "How do these tiny supramolecular nanomachines work in the bodies of living organisms? I want to know the mechanism behind their actions," says Koji Yonekura, associate chief scientist of the Biostructural Mechanism Laboratory in the Photon Science Research Division of the RIKEN SPring-8 Center. Because function is closely related to form, the action mechanism cannot be understood without clarifying the conformations of the components of supramolecules. Yonekura is working to develop new techniques such as cryo-electron microscopy to elucidate the action mechanism behind these supramolecular nanomachines.

The wonder of the flagellum

Escherichia coli and *Salmonella enterica* exhibit active movements, including moving towards places where nutrients are available and moving away from places of low temperature. The flagellum, an appendage that protrudes from bacterial surfaces, produces the driving force for these movements. The bacterial flagellum has a supramolecular structure of about 30 different proteins, comprising a basal body that works as a rotary motor, a flagellar filament that revolves like a propeller, and a hook that joins the two (Fig. 1).

"As the ions flow into the flagellar cell, the rotor in the basal body revolves at up to 300 revolutions per second, so that the flagellar filament revolves like a propeller and causes the bacterium to move forward. The flagellum is like a well-designed nanomachine. I want to know how complex biological nanomachines like these work in living organisms," says Yonekura. After learning the structural analysis of biomolecules by electron microscopy from Chikashi Toyoshima at the Tokyo Institute of Technology (currently at the Institute of Molecular and Cellular Biosciences, The University of Tokyo) in 1997, Yonekura joined the Namba Protonic Nanomachine Project (directed by Keiichi Namba, Graduate School of Frontier Biosciences, Osaka University) in an Exploratory Research for Advanced Technology (ERATO) program sponsored by the Japan Science and Technology Agency. Since then, he has been engaged in elucidating the mechanism behind the actions of the flagellum.

The flagellar filament is more than 10 μm in length, much longer than the main cell body of the bacterium, which measures just 1–2 μm. Each flagellar filament consists of a tubular bundle of 11 thin, long filaments known as protofilaments.

"If the flagellar filament were linear, no propelling force would be generated even when it revolves at an extremely high speed. The reason why the bacterium can move its body forward is because the flagellar filament has a superhelical structure with a slight curvature. However, the very fact that the flagellar filament assumes this form is wonderful."

The flagellar filament is made up of a stack of flagellin, a protein produced in the cell body. When a form of protein of the same size and shape is stacked, only a linear structure is produced. Flagellin, however, occurs in structurally distinct left- and right-handed (L- and R-) types. As the L- and R-type protofilaments coexist in combination at different ratios, the flagellar filament can be transformed between the L and R structures (Fig. 2). However, this is not the total mechanism behind bacterial movement by flagellar revolution. The bacterium repeats a motor pattern in which it goes forward for 2–3s, then tumbles and changes direction to propel itself forward again.

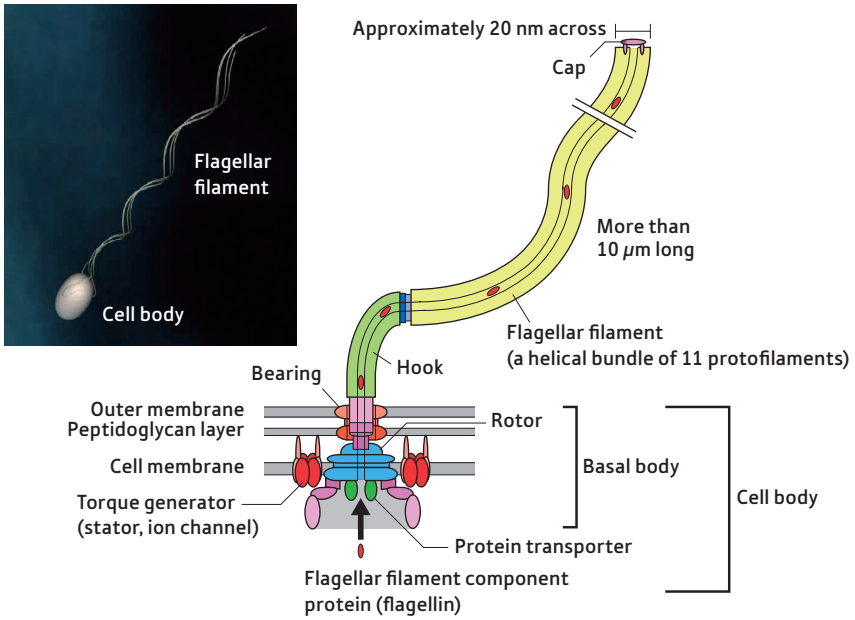


Figure 1: Schematic diagram of a bacterium.
Bacteria swim by rotating their flagella at up to 300 times per second. The flagellum is more than 10 μm long, about 10 times as long as the main cell body of the bacterium. It comprises a basal body, which acts as a rotary motor, a flagellar filament that revolves like a propeller, and a hook linking the two components.

What mechanism does the bacterium use to change its swimming direction?

It is known that when the bacterium changes direction, the counterclockwise rotor revolves in the reverse direction for 1 ms. With this motor reversal, a torsional force is exerted on the flagellar filament, causing some of the L-protofilaments to turn right-handed, and at this time the bacterium changes direction with the imbalance. This is the conjectured mechanism behind the directional switching in the bacterium. "The mechanical details of the directional change cannot be understood without clarifying the conformation of flagellin," says Yonekura. However, this is a difficult task.

Cryo-electron microscopy and a new technique for helical reconstitution

A representative method for examining protein conformations is X-ray crystallography, in which a prepared protein crystal is exposed to an X-ray beam. Colliding with the crystal, X-rays are scattered by the electrons around the atomic nuclei, interfering with each other to produce a diffraction image. The distribution of electrons in the sample material is determined from the position and intensity of the diffraction to show how the atoms are arranged. A crystal is used because the orderly atomic arrangement ensures clear, regular diffraction images, which allow the investigator to examine the conformation at high resolution.

"However, X-ray crystallography cannot be applied to the flagellar filament because it is quite difficult to create a crystal of fibrous protein. Hence, we decided to use an electron microscope. In electron microscopy, the sample is exposed to an electron beam. The use of an electron microscope offers the advantage that a real image of the sample can be seen. However, the energy of electron beams is so intense that the sample is destroyed if it is treated as it is."

To solve this problem, Yonekura used cryo-electron microscopy. "The sample is frozen rapidly and enclosed in ice. By keeping the sample under cooling conditions at –269 °C, the damage it experiences due to electron irradiation during observation is reduced dramatically. Additionally, because the procedure takes place while the sample is in ice, another advantage is the ability to obtain observations in nearly the same state as in a living organism in aqueous solution."

However, cryo-electron microscopy alone does not enable conformational data to be obtained at high resolution because a high-intensity electron beam must be applied to obtain the desired level of resolution. "Even though protein damage is reduced markedly, it is still severe, so the exposure to the electron beam must be minimized. The images taken under these conditions contain a great deal of noise, and almost nothing is visible. To extract useful information from the noisy image at high resolution, a special technique is required for image analysis."

Because of this, Yonekura has developed a technique for image analysis to reconstitute conformations using helical symmetry. "To obtain information at high resolution from noisy images, a common approach is to take and average

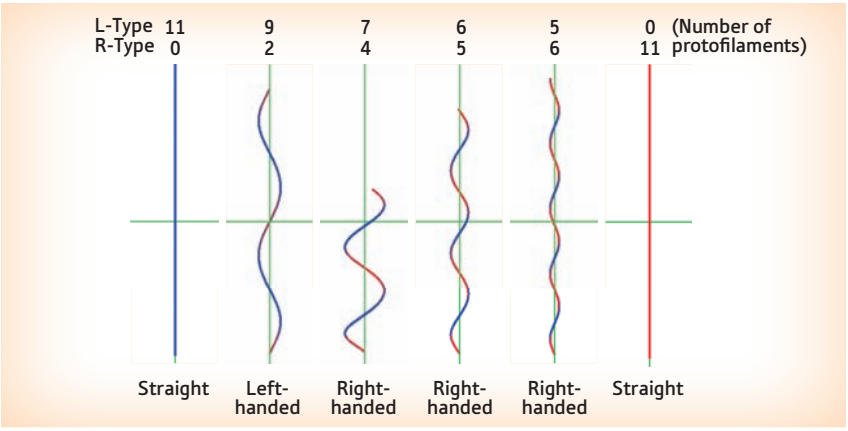


Figure 2: Flagellar filament forming various helical structures.
The flagellar filament consists of a bundle of 11 protofilaments comprising a stack of the protein flagellin. Flagellin occurs in left- and right-handed (L- and R-) conformational types. Protofilaments comprising a stack of R-flagellin (red) and those comprising a stack of L-flagellin (blue) coexist at particular ratios to produce various helical structures.

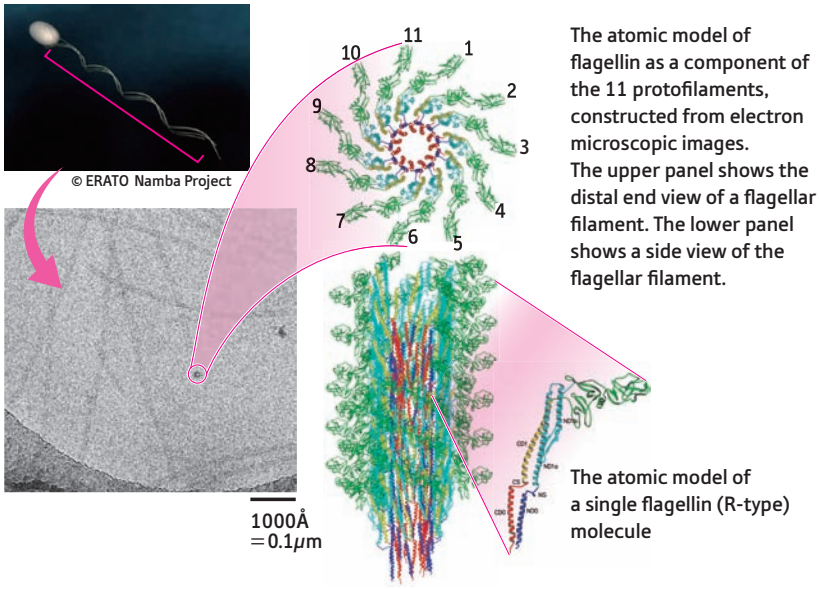


Figure 3: A cryo-electron microscopic image of flagellar filaments embedded in amorphous ice. Each flagellar filament consists of a bundle of 11 protofilaments, each comprising a stack of the protein flagellin (L- or R-types). Seen in this photomicrograph are flagellar filaments lying in various directions, one of which appears with 11 protrusions and a center hole.

out a large number of images. However, since it was thought that an astronomical number of images would be required to obtain data at sufficient resolution, the conventional approach was impractical. Using the new technique of helical reconstitution we have developed, the conformation of a sample can be visualized at a workable resolution by totaling about 100 micrographs, provided that the sample has a helical structure like the flagellar filament. When we analyze a sample that has a helical structure, molecules aligned in various directions are visualized in one photograph. We utilize them efficiently."

The mechanism of flagellar actions now revealed

In 2003, Yonekura succeeded in analyzing the conformation of R-flagellin as a component of the flagellar filament using a combination of cryo-electron microscopy and the new technique of helical reconstitution (Fig. 3). The resolution they achieved was close to 4 Å, or just 0.4 nm. Although that was a groundbreaking achievement that allowed the analyst to clarify the atomic arrangement in the amino acids that constitute flagellin, Yonekura and his colleagues continued to conduct their challenging work. "Analyzing the conformation of R-flagellin only allows us to know one state of the flagellar filament. The mechanism behind the morphological transition cannot be known without analyzing the conformation of the L-type."

Then in 2008, Yonekura established his Biostructural Mechanism Laboratory at the RIKEN SPring-8 Center. At last, in March 2010, the laboratory succeeded in analyzing the conformation of the L-flagellin filament. The analysis took much time to develop because L-flagellin is unstable, but finally the molecular mechanism of the directional change in bacterial swimming was revealed. "By comparing the conformations of the L- and R-types, we find little change in the inner portion of the flagellar filament. On the other hand, the outer portion was found to change very flexibly (Fig. 4). On motor reversal, part of the flagellin transits from the L-type to the R-type, switching the direction of the flagellar filament helix. As a result, the bacterium changes its swimming direction."

The flagellar filament meets two contradictory requirements. One is the toughness needed to endure high-speed rotation, and the other is the flexibility required for the transition between the L- and R-types. "The conformation of flagellin really reconciles this toughness and flexibility. In fact, when we succeeded in analyzing the conformation, I was very impressed by the fact that the conformation is finely fabricated," says Yonekura. "Actually, the conformation we determined proved to be rather different from the predicted structure. I realized again the importance of actually seeing what happens.

"In recent years, there has been a trend for research achievements to be influenced by the researchers' ability to purchase expensive and sophisticated equipment. This is not very enjoyable. To make extensive efforts to allow myself to do what has not been done so far-that's interesting. I would like to stick to this approach because a strong point of research is developing an 'only-one' technology."

Three-dimensional crystallography of very fine crystals by electron microscopy

"I want to clarify the conformations of proteins at the highest possible resolution," emphasizes Yonekura. He has devoted himself to developing a broad range of analytical techniques.

"A big feature of electron microscopy resides in dispensing with the need for sample crystallization. Despite this, crystals with a regular atomic arrangement are still attractive for those who want to examine the conformations of substances at high resolution. Even proteins that are usually unlikely to crystallize happen to form very fine crystals. We considered analyzing them by electron microscopy, but no suitable techniques were available. So we are developing a new technique in cooperation with Prof. Toyoshima at The University of Tokyo, Hitachi High-Technologies Corporation and Hitachi High-Tech Fielding Corporation."

Electrons are 100,000 times more energetic than X-rays in terms of their potential for interactions with substances. This makes it possible to obtain information on atomic arrangement even in extremely small crystals. Recently, analytical techniques for very fine crystals using X-rays have been developed, and it is becoming possible

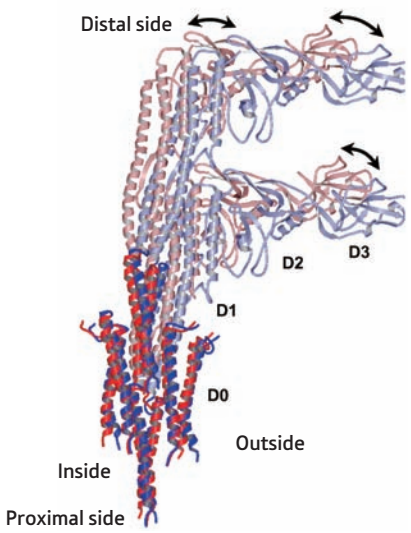


Figure 4: Structural change in flagellin. In the inner portion of the flagellar filament (dark area), the difference between the R- (red) and L- (blue) types is small. The outer portion (light area), however, changes structure significantly in the direction indicated by the arrows.

to analyze crystals several micrometers long at SPring-8, the synchrotron radiation facility at the RIKEN Harima Institute. "Electron microscopy makes it possible to analyze even smaller crystals less than 1 μm in length. In membrane proteins and supramolecular complexes, which mediate a wide variety of biological activities and serve as drug discovery targets, only very fine crystals are formed in some cases, so this technique will be an important analytical tool."

Crystallography using electron microscopy offers another major advantage. "While X-rays are scattered by electrons, electrons are influenced by electrical charge. As such, electron beams allow us to know not only how atoms are arranged in crystals, but also which portions of a protein are positively charged and which portions are negatively charged. When a protein is in action, the distribution of charge is very important."

Yonekura targets the flagellar ion channel in his crystallographic work using electron microscopy (Fig. 1). The ion channel is present in the basal body, through which ions enter the cell from outside. The ionic flow drives the rotor in the basal body to allow the flagellar filament to rotate. "Because ions are charged particles, it is possible to track their pathways. So far, no one in the world has been successful in three-dimensional crystallography of very fine crystals using electron microscopy. I hope that we will achieve this in a few years time."

Another target of his is the telomere, a structure at the end of the chromosome. The telomere is said to shorten upon each cell division and control cell longevity. Conversely, the telomere elongates in cancer cells. "The telomere is a large, complex supramolecule comprising DNA and proteins. I want to unveil the mechanism that controls the length of the telomere by determining its conformation."

Making the best use of all technical resources

In 2009, Yonekura and Saori Maki-Yonekura, a researcher in the Protein Crystallography Research Group at the RIKEN SPring-8 Center, were awarded the 2009 Ernst Ruska Award for their work entitled 'Contribution toward elucidating the mechanisms of biological macromolecular machines by cryo-electron microscopy'. The award was established in 1980 by the German Society for Electron Microscopy in commemoration of Ernst Ruska, 1986 winner of the Nobel Prize in Physics and the inventor of electron microscopy. "I hear that the award is bestowed for achievements that involve a technical innovation, as well as a groundbreaking application of electron microscopy to visualize something previously invisible. This is what I have been aiming at, and I am very proud to have received the award."

Yonekura is looking forward to utilizing the X-ray Free Electron Laser (XFEL) facility under construction at the RIKEN Harima Institute, which is scheduled to be completed in fiscal 2011. "The XFEL is expected to enable us to perform conformational analyses on whole cells and organelles as they are. We are now developing a new technique for analyzing biological samples by a combination of the XFEL and cryo-electron microscopy, jointly with Prof. Masayoshi Nakasako in the Department of Physics of the Faculty of Science and Technology at Keio University, as well as Director Masaki Yamamoto of the Research Infrastructure Group in the Advanced Photon Technology Division of the RIKEN SPring-8 Center and others. I am aiming at elucidating the mechanism behind the actions of nanomachines in living organisms. To this end, I am not fixed only on electron microscopy. Here at the RIKEN Harima Institute, a radiation facility with the world's highest performance is in operation, and the associated equipment is available in a comprehensive link-up. I want to clarify the mechanism behind the actions of nanomachines by making the best use of the technical resources that have been compiled here over a long period. Many people are working to develop a broad range of equipment, and I believe that I can create a new technique by listening to their valuable advice and combining it with my own knowledge. I am now enjoying my research a lot." ■

Koji Yonekura

Koji Yonekura was born in Tokyo, Japan, in 1969. He graduated from the Graduate School of Biosciences of the Tokyo Institute of Technology in 1997, and obtained his PhD from the same university. He subsequently jointed a JST ERATO project to study the structures of biological macromolecules. He was appointed group leader of this project in 2000, and has acted jointly as assistant professor of the Graduate School of Frontier Biosciences of Osaka University since 2002. In 2004, he was elected a Keck fellow of the Department of Biochemistry & Biophysics of the University of California, San Francisco, USA, where he led his own laboratory. In 2008, he returned to Japan and started the Biostructural Mechanism Laboratory at the RIKEN SPring-8 Center as an associate chief scientist. His research interests are focused on the structural mechanisms of biological macromolecular complexes. In 2009, he was awarded the Ernst-Ruska prize for 'Contribution toward elucidating the mechanisms of biological macromolecular machines by cryo-electron microscopy'.

RIKEN Wako Institute Open Day

On April 23, RIKEN Wako Institute held its annual Open Day to promote public understanding of RIKEN's work at the cutting edge of science and technology. Many laboratories and facilities opened their doors to the public, and a number of lectures and events were held. Over 5,500 visitors came to the campus despite the after effects of the Tohoku earthquake.

The event featured a special lecture on radiation by Yoshitomo Uwamino, director of the Safety Management Group, RIKEN Nishina Center for Accelerator-Based Science. He provided the audience with fundamental knowledge of radiation, such as its fundamental properties and effects on health. As a result of the accident at the Fukushima I Nuclear Power Plant, many radioactive substances were released, residents near the power plant were evacuated, and parents are especially concerned about their children's health. RIKEN Wako Institute monitors radiation levels and posts data from the readings on RIKEN's website every day. The lecture was heavily attended, showing that many visitors have a strong interest in the issue.

Another event that attracted interest was a tour of the supercomputer of the Advanced Center for Computing and Communications (ACCC). Known as the RIKEN Integrated Cluster of Clusters (RICC), it is the seventh-fastest supercomputer in Japan, and is used for a wide range of research areas. Visitors were excited by the virtual baseball stadium simulated by supercomputers in the 4D theater.

People were also interested in the power saving efforts at the RICC. In the initial period following the earthquake, its operations during the day were limited to file access and other minimal functions, but from April 18, full-time and full-node operations were restarted. Only short jobs are being permitted to make it possible to quickly change the mode of operation when an emergency request for power saving arises.

Outside of the Wako Institute, Open Day events were held at the RIKEN Harima Institute on April 30. The RIKEN Kobe Institute will open its doors to the public on November 5, and other institutes and facilities will hold their own events.

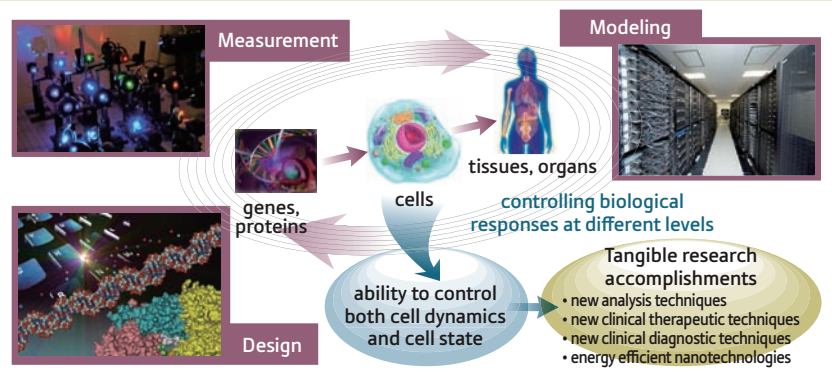
Yoshitomo Uwamino explains the fundamental facts about radiation

Establishment of the RIKEN Quantitative Biology Center (QBiC)

A new research group, the RIKEN Quantitative Biology Center (QBiC), was established in April 2011 based on the idea that life should be seen as "dynamic biological systems" made up of elements which interact in complex spatiotemporal relationships, and that these systems need to be understood in order to gain a true understanding of life. QBiC belongs to the Kobe campus, along with other centers focusing on various areas of biology and drug design. It is headed by Toshio Yanagida, and is composed of three cores (15PIs) dealing with different aspects of quantitative biology: cell dynamics, computational biology and cell design.

The new center was set up with the aim to contribute to systems science on cells, using "whole cell modeling" as its principal method. Scientists will work on the crucial task of trying to understand how cells, with their extraordinary number of interrelated components that could easily fall into a state of combinatorial explosion, are able to respond to external stimulus in such a tightly controlled way using minimal energy. The aim of QBiC is to develop innovative measuring, analysis, and modeling technologies and techniques to recreate the dynamics of this hyper-complex biological system —the cell—and to approach the dynamism of cell systems through a fusion of these techniques.

The development of whole cell modeling will bring us closer to the ability to predict various cellular phenomena and to freely manipulate cells and the groups they form. Cell system manipulation has the potential to become a significant technology of the 21st century, similar in importance to genetic manipulation, which drove the development of life sciences in the 20th century. This technology is expected to make major contributions to innovations in areas such as regenerative medicine and patient diagnostics.



Depiction of the strategy of the RIKEN Quantitative Biology Center (QBiC)

RIKEN's response to the Tohoku Pacific offshore earthquake

The Tohoku earthquake of March 11, the largest in Japan's recorded history, left enormous devastation and large numbers of casualties in its wake. The only significant impairment RIKEN suffered was at the Sendai facility, where there was some damage to the building and to research instruments and equipment. Repairs will be required, but there were no injuries to RIKEN staff and other personnel.

For the moment, the most serious impact on research activities has come from the power shortages. To conserve electricity, RIKEN has kept office lights and air conditioning turned off to the greatest extent possible without hindering the safety of daily operations. RIKEN has also limited the use of the accelerator at the Wako campus and the RIKEN Integrated Cluster of Clusters supercomputer.

Though RIKEN itself was largely untouched, the earthquake and subsequent tsunami caused major damage to universities and research institutions in the Tohoku area and parts of the Kanto region, with significant ramifications for scientific research throughout Japan. In response, RIKEN has launched support activities for graduate students and young scientists in the Japanese scientific community.

To provide up-to-date information on RIKEN's response to the Tohoku earthquake for non-Japanese researchers, a blog (http://www.lifeatriken.com/blog.html) and twitter feed (http://twitter.com/#!/lifeatriken) have been launched as part of the "Life at RIKEN" website.

RIKEN will continue to do all it can as a public institution to serve Japan in this time of great need.

Jaw-Shen Tsai
Laboratory Head
Macroscopic Quantum Coherence Laboratory
RIKEN Advanced Science Institute

Dear Dr Tsai,

How are you? It's freezing in Beijing now, how about Tsukuba?

How time flies! It has now been over five years since I joined your group. In 2003, I became a doctoral student at Tsinghua University in China and started working in the field of quantum computation and quantum information. The first paper my supervisor asked me to read was the one published in *Nature* by your group. I learned quite a lot from all of your publications, and it was a dream that one day I could join your world-class laboratory. Thanks to RIKEN's internship students program, that dream came true. I was so excited when I got the great news.

My visit to RIKEN started in November 2005. I can still remember that morning when I first came to the lab, everyone welcome me warmly, and I met all the lab members, whose names were already familiar to me. I was amazed by the research environment at the RIKEN/NEC Tsukuba lab, it is the best I have ever seen anywhere. And you are a great supervisor and team leader. During my stay I was lucky to study with Dr Yuri Pashkin, who taught me much about microelectronic fabrication technology and low-temperature experimental techniques. I am now transferring this knowledge to my students here, and I hope one day we can contribute more to this field.

My time in Japan was colorful and happy. I enjoyed not only the academic research, but also many other activities. The one I liked most was soccer. I didn't expect that so many of my colleagues would be playing soccer together everyday at lunchtime. I even joined the NEC soccer team to play in the Tsukuba league! Many of my teammates became my friends, and on my farewell party they gave me a football with their signatures as a souvenir, which even now sits on my bookshelf. Whenever I see it, all the happy times with my teammates are revived.

The culture is pretty similar between China and Japan, so living in Japan was not difficult for me. I like the Japanese food very much, and even got addicted to *sushi* and *natto*. Fortunately there is a very good *sushi* restaurant close to my campus here in Beijing. I believe it's genuine — please come and judge it for yourself next time you visit Beijing.

I am really grateful for the experience of working in your group. I am now an assistant professor in Tsinghua, and my experience in Japan was very helpful in securing the position. I sincerely appreciate my time with you and all of the group members, and am looking forward to visiting your lab again.

All the best,

Tiefu Li
Institute of Microelectronics,
Tsinghua University, Beijing, China

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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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