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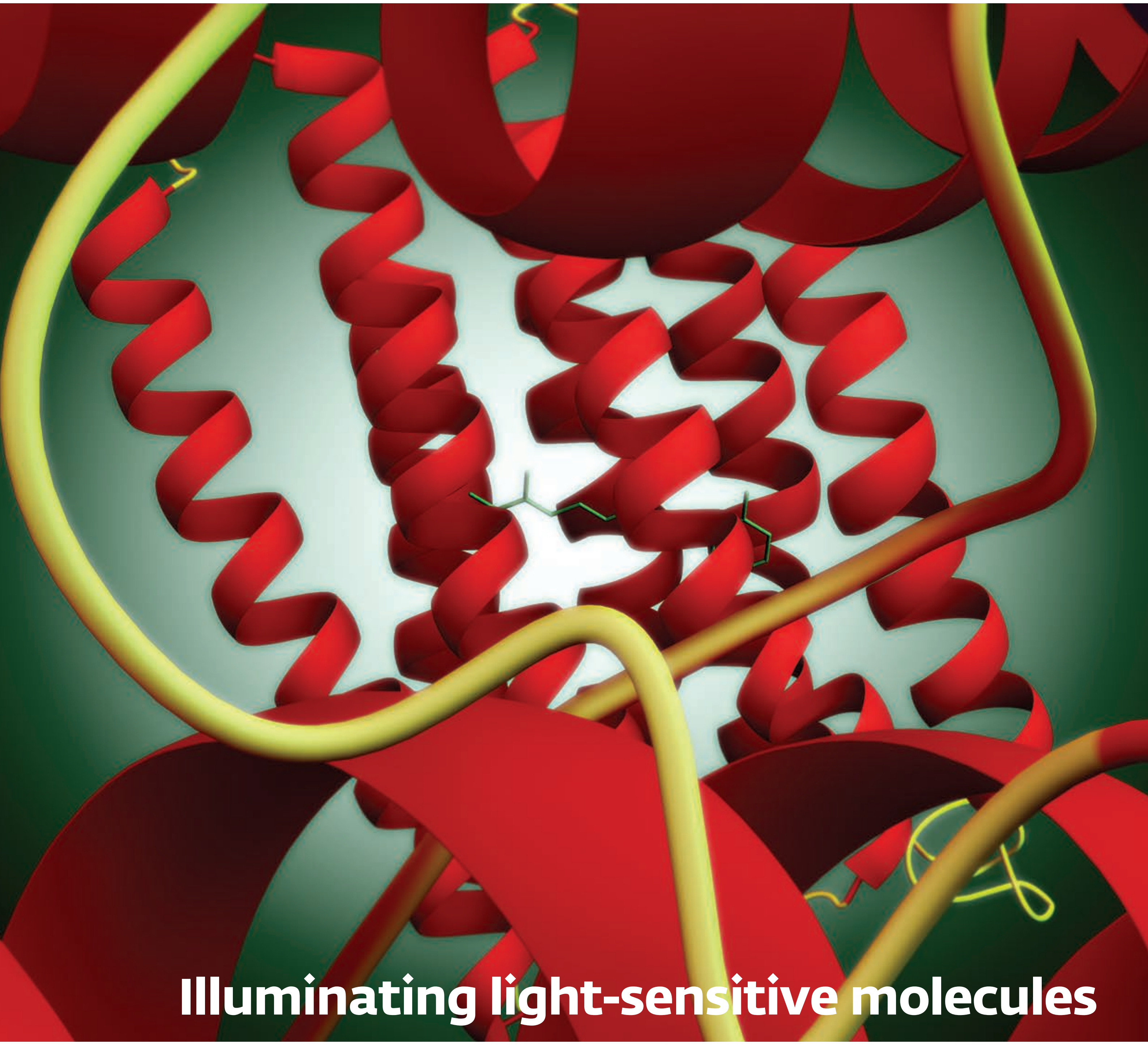

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Physics

Putting artificial atoms on the clock

Artificial atoms give insight into how real atoms interact with light in real time

Around the turn of the century, scientists began to understand that atoms have discrete energy levels. Within the field of quantum physics, this sparked the development of quantum optics in which light is used to drive atoms between these energy levels. The resulting ability to control the behavior of solid-state systems with free-space light—the former has discrete energy levels and the latter has continuously tunable energy—yielded new fundamental science as well as new technology. Some of the applications that emerged include lasers, atomic clocks and quantum information processing.

Despite these successes, however, quantum optics researchers were traditionally constrained by their reliance on the use of real, or natural, atoms. In previous work, Jaw-Shen Tsai and colleagues at the RIKEN Advanced Science Institute and NEC, Japan, circumvented this constraint by demonstrating that an engineered solid-state device can reproduce many of the characteristics of the quantum optics work done on real atoms, including fluorescence and absorption[1]. This suggested that the devices could be considered to be artificial atoms. Now, the researchers have reported in *Physical Review Letters* the first dynamic measurements of how their artificial atom interacts with light[2].

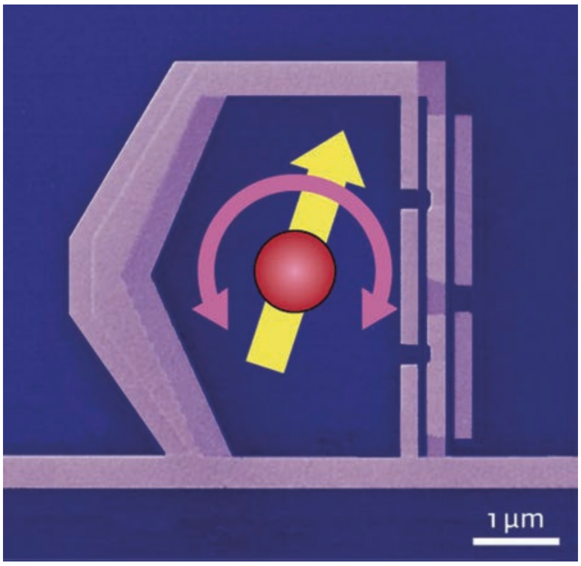

Figure 1: An electron micrograph of the artificial atom. A superconducting loop of metal is interrupted by non-superconducting Josephson junctions. The current can flow clockwise or counterclockwise around the loop, and are analogous to the electron spin of a real atom (yellow arrow). The horizontal wire along the bottom of the atom can be used to excite the atom, and to measure its emission.

Artificial enhancement

While real atoms are readily available and well understood, designing atoms from scratch gives experimentalists greater flexibility. It also lessens difficulties associated with trapping and integrating real atoms into complex systems. In addition, artificial atoms can be made to strongly interact with light, which makes possible highly integrated and scaled devices that exploit single-atom quantum optics. By comparison, it is difficult to achieve strong coupling between light in free space and a real atom; as a result, quantum optics work with real atoms requires many atoms, or highly concentrated light, making integration more difficult.

In place of real atoms, Tsai and his colleagues built a device that, on first glance, looks nothing like an atom: it consists of a loop of superconducting wire, about 16 micrometers in circumference, which is interrupted with four so-called 'Josephson junctions' that are not superconducting (Fig. 1). The relationship between the magnetic flux through the loop, and the current flowing around it, restricts the possible values of the current. Crucially, only certain amounts of current are allowed to flow around the device; so, like an atom, the energy levels of the device are discrete.

Rather than using free-space light to couple to their atom, the researchers built a thin wire along the bottom of their artificial atom. This wire, which

Figure 2: The properties of the wire along the bottom of the artificial atom are analogous to electrical transmission lines.

can be modeled as a transmission line (Fig. 2), supports electromagnetic waves, just as free space does. Unlike in free space, however, the researchers could carefully control the shape, energy and direction of the electromagnetic waves in the wire. Previously, Tsai and colleagues demonstrated that their artificial atom can scatter 94% of the power flowing down the wire, as a result of strong inductive coupling. This compares to, at most, a few percent scattering of a free-space photon by a real atom.

A real-time mimic

Going beyond showing that their artificial atom was able to mimic the behavior of real atoms under static conditions, Tsai and colleagues succeeded in demonstrating a precise measurement of how their artificial atom changes in time.

The researchers excited their artificial atom with a microwave field that was carried by the transmission line. Some of this driving field was absorbed by the atom and caused currents to flow around the superconducting loop. These currents could flow either clockwise or counterclockwise, with the two directions representing the two lowest-energy excited states of the atom. Because of the quantum nature of the atom, the actual current at any moment could be composed of a superposition of these counter-circulating currents: for example, a 20% counterclockwise rotation and an 80% clockwise rotation were possible. In a classic example of 'quantum weirdness', this was not the same as reducing the clockwise rotation by 20%—each current flowed independently and at the same time.

Tsai and colleagues could determine the degree of light absorbed by the device, and its characteristics, by monitoring the currents in the transmission line. In fact, by resolving different components of these currents, the researchers succeeded in building a complete picture of how the atom's excited state behaved: specifically, they could tell the amplitude of the two circulating currents, and the phase between them.

As good as real

Measuring the strengths and phases of the currents circulating through the artificial atom is similar to a much more difficult measurement on a real atom: the measurement of the direction and strength of the magnetic moment of its electrons—or electron spin. Measuring electron spin is a current focus of research because it is both an important quantum system and has a variety of proposed applications, ranging from computing to sensing. The team's measurement on their artificial atom was made easier by the strong coupling possible between the atom and the electromagnetic fields in the adjacent transmission line.

This new research thus serves as another demonstration of the versatility and control afforded by artificial atoms, and it extends the analogy between real and artificial atoms into the domain of time. As a likely next step, Tsai says, his group will work on applying their artificial atom to quantum computing applications, which require a quantum bit, or 'qubit', with two or more discrete energy levels that they can place into a superposition and allow to evolve in time. Tsai and his team have proven their artificial atom is capable of doing exactly that. ■

1. Astafiev, O., Zagoskin, A.M., Abdumalikov, A.A. Jr., Pashkin, Yu.A., Yamamoto, T., Inomata, K., Nakamura, Y. & Tsai, J.S. Resonance fluorescence of a single artificial atom. *Science* **327**, 840–843 (2010).
2. Abdumalikov, A.A. Jr., Astafiev, O.V., Pashkin, Yu. A., Nakamura, Y. & Tsai, J.S. Dynamics of coherent and incoherent emission from an artificial atom in a 1D space. *Physical Review Letters* **107**, 043604 (2011).

ABOUT THE RESEARCHER

Jaw-Shen Tsai was born in Taiwan in 1952. He graduated from the Department of Physics, University of California Berkeley, in 1975, and obtained his PhD in 1983 from the State University of New York at Stony Brook. Soon after graduation, he came to Japan as a research scientist at NEC Microelectronics Research Laboratories, where he started his career in superconductivity-related research. He was promoted to research manager in 1990, principal researcher in 1993, senior principal researcher in 1996, and fellow in 2001. He has concurrently worked as team leader of the RIKEN Macroscopic Quantum Coherence Lab since 2001. His research interests include quantum coherence in superconducting circuits, quantum bit and quantum information processing.

Nuclear spins get in line

Electrically controlling the magnetic polarization of nuclei offers a new way to store quantum information

Storing information in long-lasting quantum states is a prerequisite for building quantum computers. Intrinsic properties of nuclei known as magnetic spins are good storage candidates because they interact weakly with their environment; however, controlling them is difficult. Now, researchers in Japan have demonstrated an all-electrical method for preparing the magnetic states of nuclei that would be useful in storing quantum information[1]. Keiji Ono at the RIKEN Advanced Science Institute, Wako, led the work.

In an atomic nucleus, protons and neutrons pair up such that their magnetic spins align in opposite directions. However, in nuclei with an odd number of protons and neutrons, this pairing is incomplete; thus, they have a so-called 'magnetic moment' that points in no particular direction, hindering control.

Figure 1: Researchers can now use external voltage to better control the magnetic polarization of nuclei in their bid to store information in long-lasting quantum states.

Nuclear spins are difficult to align except at low temperatures and with large magnetic fields. But in devices called quantum dots, Ono and other researchers have shown they can manipulate the nuclear spins electrically. A quantum dot is made from a semiconductor material of just a few tens of nanometers in size. Using an external voltage (Fig. 1), the researchers could add electrons to a quantum dot one at time.

Similar to protons and neutrons, a single electron on a quantum dot possesses a spin that acts like an effective magnetic field on the surrounding nuclear spins. Physicists have used this interaction to control nuclear magnetic moments; but, they had only succeeded in significantly polarizing the nuclear moments in one direction. Ono's team, however, showed that it is possible to polarize the nuclear moments either up or down—a quantum version of the '1' and '0' on a digital bit.

Ono and his team demonstrated this behavior in a double quantum dot—two quantum dots in series—made from the semiconductor gallium-arsenide. They showed they can 'pump' the nuclear spins into a particular direction by using voltages to place one electron on each dot and then polarize their spins such that they are either both up, or both down. As the spins on the dot relaxed, they 'dragged' the nuclear spins, polarizing them in the process. The nuclei remained polarized for several milliseconds—significantly longer than the polarized states of electron spins in similar devices.

The work offers a new way of controlling nuclear spins, says Ono, who now plans to study the polarization reversal process of the nuclear spins in more detail. Nuclear spins could "become a ubiquitous resource for storing information in a semiconductor," he adds. ■

1. Takahashi, R., Kono, K., Tarucha, S. & Ono, K. Voltage-selective bidirectional polarization and coherent rotation of nuclear spins in quantum dots. *Physical Review Letters* **107**, 026602 (2011).

Capturing an elusive compound

Unprecedented formation of a boron–boron covalent bond, under laboratory conditions, opens a new corner of chemistry

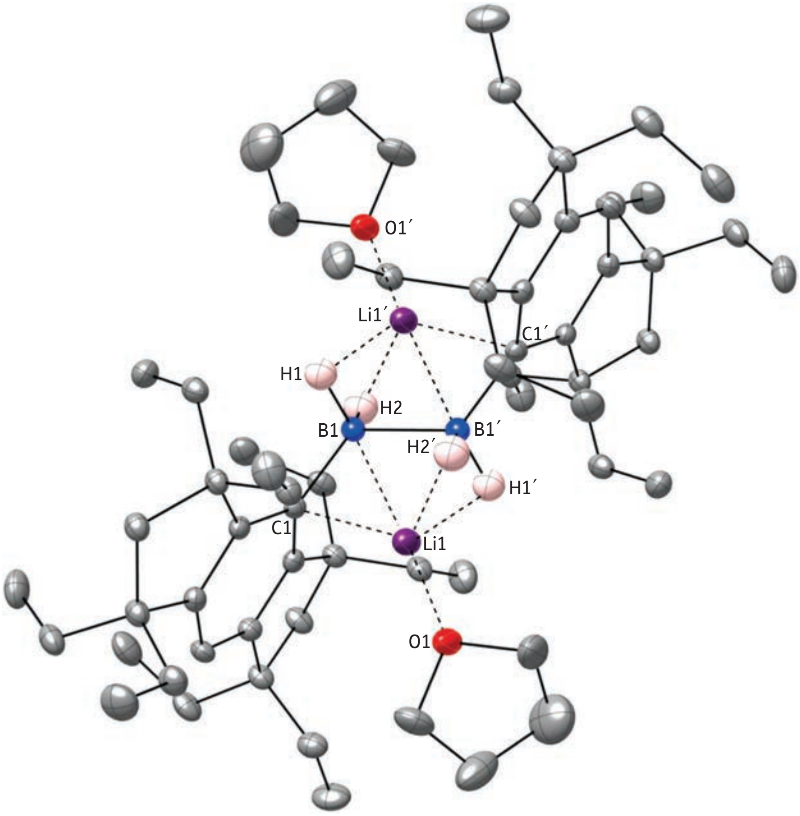

Figure 1: In the dilithimu diborane(6) dianion, bulky side-groups (grey) protect the delicate boron–boron bond (blue).

Boron-based chemical compounds rarely form simple structures. Boron is an electron-deficient element; and, as electrons are the glue that hold compounds together, this leads to some unusual bonding behavior. Using a new method developed in Japan to link two boron atoms together by a regular, single covalent bond, the element can be forced into more conventional behavior[1]. The method was developed by a team of researchers including Yoshiaki Shoji, Tsukasa Matsuo, and Kohei Tamao at the RIKEN Advanced Science Institute, Wako.

The compound that the researchers made features two boron atoms held together by a shared pair of electrons. For other elements—carbon, for example—that would be a typical bond, but electron-poor boron tends to prefer a more complex arrangement. In the boron compound diborane (B_2H_6), for example, two boron atoms are bridged by hydrogen atoms, with each boron–hydrogen–boron bond sharing a single pair of electrons across three atoms rather than the usual two.

Theory has long predicted that by pumping extra electrons into a compound such as diborane, the boron–hydrogen–boron structure should break down to form a boron–boron single bond. Until now, however, all such attempts to make and isolate such a structure had failed, instead generating clusters or single boron species.

Matsuo and Tamao's strategy for generating the boron–boron bond was to start with a borane precursor where each boron atom was fitted with a bulky side-group known as an Eind group. The researchers suspected that previous attempts probably succeeded in generating the boron–boron single bond but failed to protect that structure from quickly falling apart through over-reaction. Using the bulky side-groups, they were able to block these over-reaction processes, and successfully isolate the desired boron–boron single bond (Fig. 1).

Having discovered a new way to make the boron–boron bond, the next step will be to assess its chemistry and reactivity, and to explore related structures, says Shoji. The bond has already proved to be relatively stable: the team has shown that if protected from air and moisture, the boron–boron compound can be stored for months at ambient temperature. It can also be converted into a three-membered ring, in which a bridging hydrogen atom is the third member, forming a molecule with potentially useful properties. "We think that the hydrogen-bridged boron–boron bond has a double-bond character," says Matsuo. "We would like to explore the new reaction chemistry of multiply bonded boron species." ■

1. Shoji, Y., Matsuo, T., Hashizume, D, Gutmann, M.J. Fueno, H. Tanaka, K. & Tamao, K. Boron–boron σ-bond formation by two-electron reduction of a H-bridged dimer of monoborane. *Journal of the American Chemical Society* **133**, 11058–11061 (2011).

Making liquid crystals stand tall

Molecular 'handles' that allow on-demand growth of thick columnar films make enhanced liquid crystal devices viable

Most liquid-crystalline displays contain rod-like molecules that quickly switch from one orientation to another when subjected to electric fields. This movement creates a shutter effect that turns light on and off at high rates. But the conductivity of rod-like molecules pales in comparison to disc-shaped, or discotic, liquid crystals. Composed primarily of aromatic molecules surrounded by flexible side chains, discotic molecules can stack into extended columns that enable one-dimensional charge transport and semiconducting capabilities. However, these columns have such tight packing that no one has found a way to orient them reliably using electricity.

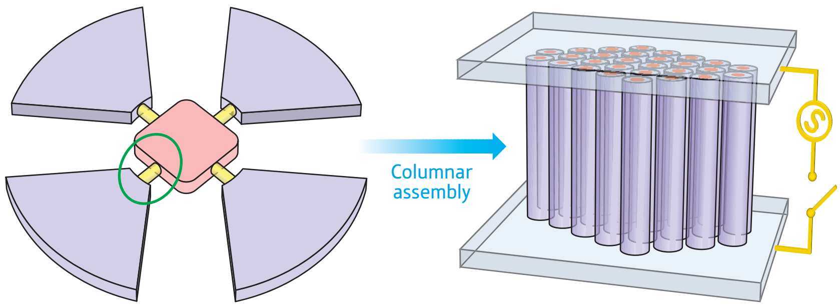

Figure 1: A new electric-field-responsive 'handle' (yellow bar, right) allows assembly of disc-shaped liquid crystals into thick columnar films suitable for practical devices.

Now, researchers led by Takuzo Aida from the University of Tokyo, Hideo Takezoe from the Tokyo Institute of Technology and Masaki Takata from the RIKEN SPring-8 Center in Harima have discovered that aromatic amides with branched, paraffin-like side chains can act as molecular 'handles' for electric field alignment[1]. Furthermore, they succeeded in growing discotic films hundreds of times thicker than before, putting devices that incorporate this technology one step closer to production.

Aida and colleagues were investigating discotic liquid crystals consisting of molecules called corannulene derivatives when they made their finding. Corannulene has a core of five fused hydrocarbon rings surrounded by ten aromatic amides, giving it a bowl-like shape. Despite this compound's large size, the researchers found that electric fields could uniformly align the columns with hexagonal geometries over a range of temperatures (Fig. 1).

The researchers first postulated that the inner dipole of the curved corannulene core accounted for the field-induced orientations. But when they synthesized a similar discotic liquid crystal containing a flat, non-polar triphenylene core, they observed the same striking field alignment—key evidence that the amide side chains acted as responsive handles that interact with the applied electric field and guide the discotic molecules into place.

Armed with this knowledge, the researchers synthesized several discotic columnar liquid crystals with slightly tweaked handles to optimize this behavior. Nearly all of these entities showed columnar alignment that persisted even after extinguishing the electric field. The team could also break apart the columns and restore the molecules' random orientations using a simple heating procedure.

Because the column heights depended on applied field strength, the researchers produced millimeter-thick films in any desired orientation by sandwiching their compounds between two large-area electrodes. "Unless conducting discotic columns can be aligned to macroscopic length scales, they will remain impractical," says Aida. "Therefore, our achievement is quite important for organic electronic device applications." ■

1. Miyajima, D., Araoka, F., Takezoe, H., Kim, J., Kato, K., Takata, M. & Aida, T. Electric-field-responsive handle for large-area orientation of discotic liquid-crystalline molecules in millimeter-thick films. *Angewandte Chemie International Edition* **50**, 7865–7869 (2011).

Recognizing pathogenic invaders

Elucidation of the structure of receptors that detect invading pathogens in moths could aid the diagnosis of infectious fungal diseases

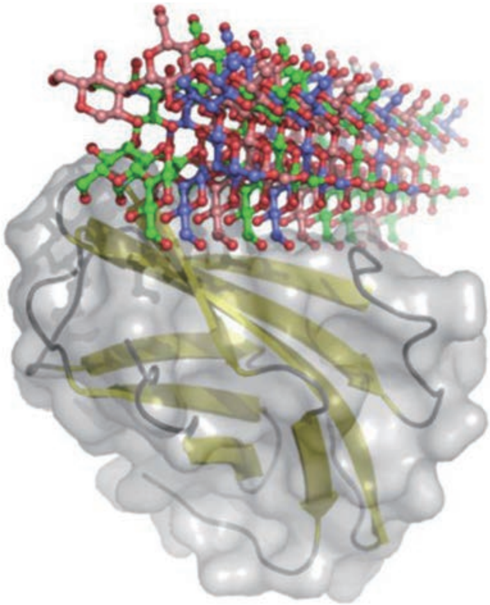

Figure 1: The β-glucan recognition protein (yellow) from *Plodia interpunctella* recognizes and binds to a triple helical β-glucan of invading pathogens.

Researchers in Japan have determined the structural basis of the molecular defense system that protects insects from pathogens[1], which provides clarity on the molecular binding that underpins this defense system.

Insects express pattern recognition receptors (PRRs) that provide an innate ability to detect fungi and plant pathogens. One of the PRRs, β-glucan recognition protein (βGRP), recognizes and binds to carbohydrate molecules called β-glucans that are synthesized by pathogens. Since little is known about how these molecules bind to each other, or about how the binding specificity is achieved, Yoshiki Yamaguchi of the RIKEN Advanced Science Institute and his colleagues used genetic engineering to produce the β-glucan-binding regions of βGRPs from two moth species, *Bombix mori* and *Plodia interpunctella*. They determined the structure of the receptors, both on their own and when bound to a β-glucan called laminarihexaose, using x-ray crystallography.

Analysis of the crystal structures revealed that the moth receptors recognize a complex of three laminarihexaoses bound to each other (Fig. 1), and that their conformation barely changes when they are bound to laminarihexaoses. The analysis also revealed that the proteins from both species bind to laminarihexaoses in an identical way, via a characteristic structural motif, suggesting that the entire βGRP family shares a common binding mechanism.

Yamaguchi and colleagues also revealed that the laminarihexaose molecules attach to each other with hydrogen bonds that form an ordered and highly stable helical structure. Six precisely arranged monosaccharide (sugar) residues, spread across three chains, interact with the receptor binding site simultaneously, and are essential for the interaction.

To verify their findings, the researchers introduced point mutations at specific locations in the binding region of the *Plodia interpunctella* receptor. Four of the mutations abolished binding of β-glucan altogether, and four others weakened the binding interaction.

Typically, interactions between carbohydrates and proteins are relatively weak because they involve just two or three monosaccharide residues. The finding that the interaction between the receptors and β-glucan involves six residues explains why this interaction is so strong; it also explains the high specificity of the receptors.

Mammals do not produce β-glucans, but they circulate in the bloodstream of patients with diseases such as invasive aspergillosis, a rapidly progressive and often fatal fungal infection.

"Our findings will be used for the development of diagnosis and monitoring tools with high specificity toward a variety of β-glucans," says Yamaguchi. "Detecting β-glucans in patients may be helpful for identifying infectious fungi, which could in turn be useful to tailor-make treatments for patients." ■

1. Kanagawa, M., Satoh, T., Ikeda, A., Adachi, Y., Ohno, N. & Yamaguchi, Y. Structural insights into recognition of triple-helical β-glucan by insect fungal receptor. *Journal of Biological Chemistry* **286**, 29158–29165 (2011).

Shaping up for cell division

Preparing chromosomes for cell division is a balancing act involving a tug-of-war between opposing molecular actions

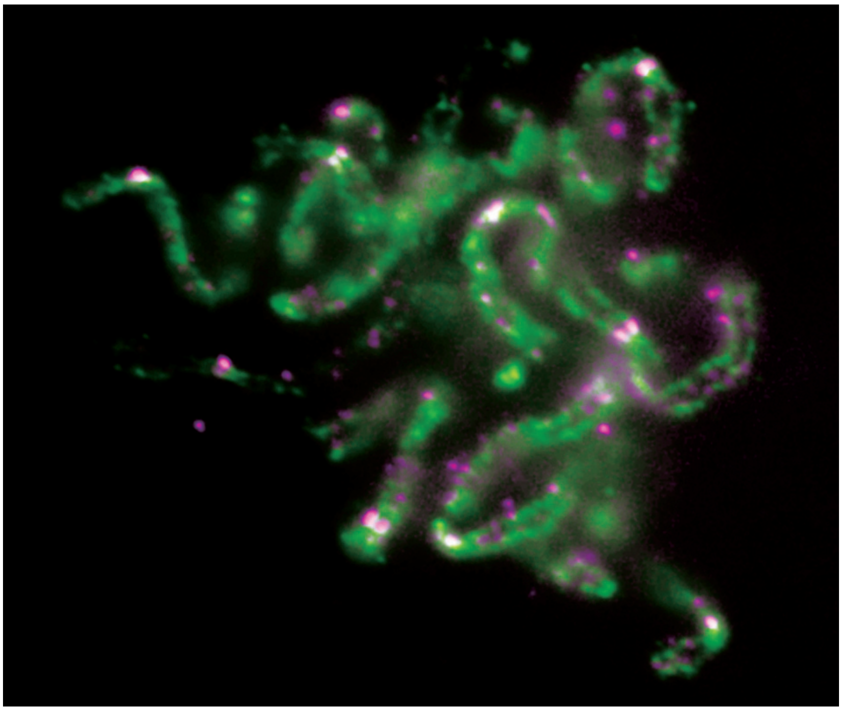

Figure 1: Mitotic chromosomes assembled in the *Xenopus* cell-free system. Condensin I (green) and II (magenta) display distinct localizations within the chromosomes.

The shape of chromosomes is determined by the relative levels of key protein complexes, research conducted by Keishi Shintomi and Tatsuya Hirano of the RIKEN Advanced Science Institute has shown[1].

As a cell prepares to divide via the process called mitosis, chromatin—the material in which DNA is packaged—condenses to form discrete rod-shaped structures called chromosomes. Each chromosome contains duplicated chromatids—sister chromatids—that are aligned in parallel. After 'mitotic chromosome condensation' is complete, the paired chromatids segregate such that each daughter cell receives one of each pair.

"For well over a century, biologists have noticed that the shape of condensed chromosomes is highly characteristic, but varies among different organisms or among different developmental stages in a single organism," explains Hirano. "We are interested in understanding how the shape of chromosomes is determined at a molecular level."

Hirano's group previously discovered that mitotic chromosome condensation requires the action of two protein complexes, known as condensins I and II. This group and others have shown that a third protein complex called cohesin is responsible for the pairing of sister chromatids within a chromosome.

To test exactly how condensins and cohesin may contribute to shaping of chromosomes, Shintomi and Hirano turned to a cell-free system based on extracts prepared from the eggs of the frog *Xenopus laevis*. "The *Xenopus* system perfectly suited our purposes because it enables us to recapitulate many chromosomal events, including chromosome condensation, in a test tube in a cell-cycle regulated manner (Fig. 1)," says Hirano.

To achieve their goal, the researchers then had to develop a series of sophisticated experimental protocols to precisely manipulate the levels of condensins I and II and cohesin present in the extracts.

Under the standard condition, chromosomes assembled in this cell-free system tended to be long and thin, which are general characteristics of chromosomes observed in early embryos. Strikingly, however, when the ratio of condensin I to II was reduced, they became shorter and thicker, being reminiscent of chromosomes observed in later stages of development. Further experiments revealed that cohesin works with condensin I and counteracts condensin II to properly place sister chromatids within a chromosome. Thus, their actions can be likened to a molecular 'tug-of-war'.

"Our findings demonstrated that chromosome shape is achieved by an exquisite balance between condensin I and II and cohesin," says Hirano. "Such a concept had been suspected for a long time, but has never been demonstrated so beautifully and convincingly until now." ■

1. Shintomi, K. & Hirano, T. The relative ratio of condensin I to II determines chromosome shapes. *Genes & Development* **25**, 1464–1469 (2011).

Inheriting stress

Flies can pass the effects of stress to their young in the form of chromosomal modifications that alter expression of selected genes

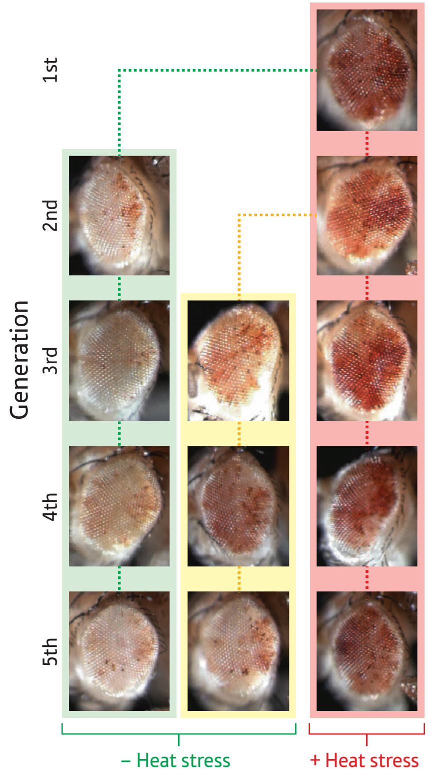

Figure 1: When w^{m4} flies are exposed to heat stress, they display increased *white* expression, resulting in red eye pigmentation (right column). Offspring of these flies retain this effect (green line); if these 2^{nd} generation flies are also heat-stressed (yellow line), the effects are still visible in their 5th generation offspring.

Most people don't realize the extent of the biochemical and physiological changes that stress causes; indeed, new research suggests that offspring might even be vulnerable to changes in gene expression wrought by chronic parental stress[1].

Different external traumas all appear to trigger a common response pathway, which is mediated in part by the activation transcription factor-2 (ATF-2) protein. "Environmental stress, psychological stresses, infection stress and nutrition stress can all activate ATF-2," explains Shunsuke Ishii, a scientist at the RIKEN Advanced Science Institute in Tsukuba, whose group first cloned ATF-2 nearly two decades ago.

Ishii was inspired by studies in yeast suggesting that ATF-2 triggers chemical changes to chromatin, the material formed when chromosomal DNA wraps around histone proteins. These changes can markedly affect gene expression, a mechanism known as 'epigenetic regulation'. In their recently published study, Ishii and his colleagues examined whether or not ATF-2 is associated with epigenetic regulation in the fruit fly *Drosophila melanogaster*.

The strain of D. melonogaster known as w^{m4} features a genomic rearrangement that results in epigenetic silencing of the *white* gene, a locus that controls eye color; and the researchers used this strain as their primary experimental model. They determined that ATF-2 normally binds to the chromatin and contributes to *white* silencing in these flies. However, when the flies were exposed to stress from heat or a high-salt diet, ATF-2 was released from the chromatin, which subsequently underwent chemical modifications that led to increased *white* expression.

Since epigenetic changes can be transmitted across generations, Ishii and colleagues performed a series of experiments in which heat-stressed flies were crossed with unstressed counterparts. Remarkably, offspring from these crosses maintained the increased *white* expression seen in the stressed parent. When these offspring were in turn subjected to heat stress and then crossed with unstressed flies, the effects were transmitted as far as the fifth generation (Fig. 1). "This shows that the effects of stress can be inherited without DNA sequence change," says Ishii.

All of these effects were dependent on ATF-2. The researchers also identified dozens of genes whose activity may be potentially modulated by this factor during stress response. Ishii hopes to further explore the biological significance of this finding in future studies. "We are planning to identify such target genes of ATF-2 and prove the inheritance of their stress-induced expression change," he says. "This could be correlated with various diseases." ■

1. Seong, K.-H., Dong, L., Shimizu, H., Nakamura, R. & Ishii, S. Inheritance of stress-induced, ATF-2-dependent epigenetic change. *Cell* **145**, 1049–1061 (2011).

On guard against drought

Revelation of the genetics underlying the response of plants to water shortage could lead to new drought-tolerant crop varieties

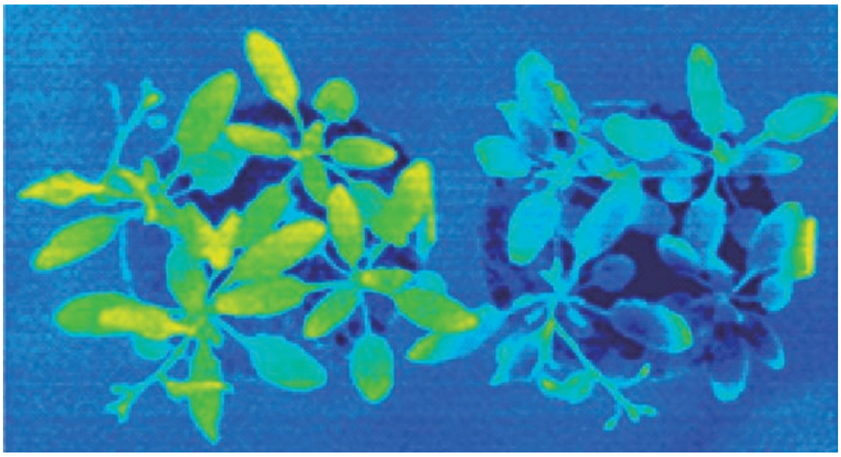

Figure 1: Thermal images of control plants (left) with normal leaf temperature, and *atabcg22* mutant plants (right), with lower leaf temperature and greater water loss, captured by an infrared thermography device.

Identification of a gene that helps plants to conserve water under drought conditions will bring biologists closer to understanding how plants tolerate drought. Researchers, led by Takashi Kuromori at Japan's RIKEN Plant Science Center, Yokohama, report this discovery in *The Plant Journal*[1].

In order to grow, green plants must take up carbon dioxide via gas exchange from the atmosphere for photosynthesis, which occurs through tiny pores called stomata on the surface of leaves and other aerial organs. However, plants also lose water during this opening through a separate process called transpiration.

During drought, plants protect themselves from excessive water loss by closely regulating stomatal opening and closing. Each stomatal pore is flanked by a pair of kidney-shaped guard cells. When the plant becomes desiccated, the plant hormone abscisic acid (ABA) mediates the drought response by facilitating stomatal closure through its action on the specialized guard cells. Only when sufficient water is available do the guard cells change back to their original shape, opening the pore and allowing transpiration to resume.

"We wish to understand the molecular mechanisms that trigger guard cell responses to environmental and hormonal stimuli," explains Kuromori.

Working with the plant *Arabidopsis thaliana*, Kuromori and colleagues previously identified a gene called *AtABCG25*, which is expressed in vascular tissues and is involved in ABA transport and responses[2]. In their latest work, they identified a related gene called *AtABCG22*, which is expressed predominantly in guard cells and regulates stomata in *Arabidopsis*. Both genes encode 'ATP-binding cassette' (ABC) transporter proteins, which use chemical energy stored in the biological molecule ATP to ferry other molecules across cell membranes.

Evaporative cooling during transpiration reduces leaf temperature. Thermal imaging methods can therefore be used to monitor transpirational water loss (Fig. 1). Using such methods, the researchers showed that mutant plants lacking functional AtABCG22 protein had lower leaf temperature and increased water loss compared to normal, wild-type plants. They also found that the mutant plants were more susceptible to drought stress than were wild-type plants. "These findings imply that AtABCG22 plays a role in stomatal regulation and in protecting plants against drought stress," says Kuromori.

Further experiments, in which the researchers crossed various mutant plants, revealed that *AtABCG22* interacts genetically with other genes already known to be involved in ABA biosynthesis, transport or signaling.

"Our next task will be to identify the exact target molecule, or molecules of AtABCG22," says Kuromori. "We hope that our work will eventually lead to the breeding of drought-tolerant crop varieties." ■

1. Kuromori, T., Sugimoto, E. & Shinozaki, K. *Arabidopsis* mutants of *AtABCG22*, an ABC transporter gene, increase water transpiration and drought susceptibility. *The Plant Journal* **67**, 885–894 (2011).
2. Kuromori, T., Miyaji, T., Yabuuchi, H., Shimizu, H., Sugimoto, E., Kamiya, A., Moriyama, Y. & Shinozaki, K. ABC transporter AtABCG25 is involved in abscisic acid transport and responses. *Proceedings of the National Academy of Sciences USA* **107**, 2361–2366 (2010).

Shedding light on a photosensitive protein

Special techniques for handling membrane proteins provide insight into the structure and function of an algal light-sensing molecule

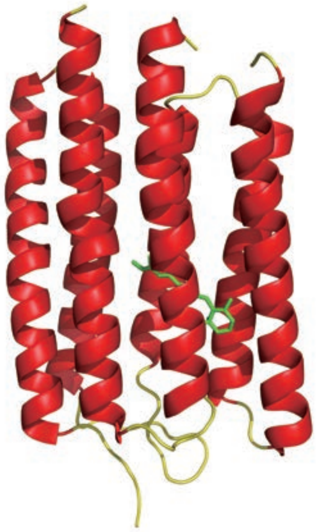

Figure 1: Crystal structure of ARII, a light-activated proton pump from the algae *Acetabularia acetabulum*.

Even without eyes, many single-celled organisms can perceive and react to light. This is achieved via rhodopsins, proteins at the cell surface that trigger responses to specific wavelengths of light by directing the flow of ions into or out of the cell.

Naoki Kamo's group at Matsuyama University in Ehime recently began working with *ARII*, a gene encoding a rhodopsin from the algae *Acetabularia acetabulum*. The encoded ARII protein proved extremely difficult to characterize and its function was initially ambiguous. However, Kamo's team found success by joining forces with Shigeyuki Yokoyama's group at the RIKEN Systems and Structural Biology Center in Yokohama[1].

To reveal a protein's structure and function, scientists typically generate highly ordered crystals of that protein and then analyze the diffraction pattern that results when the crystals are bombarded with x-rays. Membrane proteins will fold only under very specific conditions, but Yokoyama's team devised a 'cell-free' system that provides tight control over protein manufacture[2]. By mixing the cellular protein synthesis machinery with lipids and detergents, they were able to achieve an environment highly hospitable to ARII production.

"This tough target could be expressed very efficiently using our cell-free protein synthesis system, even to the same degree as easy, soluble proteins," says Yokoyama. He was subsequently able to rapidly purify the resulting protein and obtained a high-resolution structure for ARII by crystallizing it in the presence of lipid molecules (Fig. 1).

ARII proved to be relatively similar to bacteriorhodopsin (BR), a proton pump from the archaeal species *Halobacterium salinarum*. Preliminary analysis of ARII suggested that this protein likewise acts to transport protons from the cytoplasm to the exterior of the cell in response to illumination.

By analyzing the ARII structure, the researchers were able to identify a network of amino acids that directly participate in the uptake and release of individual protons. There are some notable differences in the kinetics of proton transport between BR and ARII. Kamo and Yokoyama also noted subtle structural disparities that might explain why ARII releases its protons 'late' relative to the rapid release observed with BR.

Having demonstrated the effectiveness of this membrane protein synthesis approach, the researchers are now delving deeper into the structure and function of ARII and ARI, another rhodopsin expressed by *A. acetabulum*. "We will produce various mutants with this efficient cell-free system and use many biophysical methods to understand the detailed proton transport mechanism and physiological roles of ARI and ARII," says Yokoyama. ■

1. Wada, T., Shimono, K., Kikukawa, T., Hato, M., Shinya, N., Kim, S.Y., Kimura-Someya, T., Shiroruzu, M., Tamogami, J., Miyauchi, S. *et al.* Crystal structure of the eukaryotic light-driven proton-pumping rhodopsin, *Acetabularia* rhodopsin II, from marine alga. *Journal of Molecular Biology* **411**, 986–998 (2011).
2. Shimono, K., Goto, M., Kikukawa, T., Miyauchi, S., Shirouzu, M., Kamo, N. & Yokoyama, S. Production of functional bacteriorhodopsin by an *Eschericihia coli* cell-free protein synthesis system supplemented with steroid detergent and lipid. *Protein Science* **18**, 2160–2171 (2009).

Crystalizing the foundations of better antihistamines

Minor differences in receptor structures account for variation in the selectivity and side effects of antihistamine drugs

Researchers in Japan have solved the structure of a complex between the antihistamine drug doxepin and its target receptor histamine H_1 receptor (H_1R)[1]. Led by So Iwata of Kyoto University and the RIKEN Systems and Structural Biology Center in Yokohama, the team's findings should aid the development of better treatments for allergies and inflammation.

Histamine, which is released by mast cells of the immune system, is an important mediator of allergic and inflammatory reactions. It exerts its effects by activating cell-surface receptors, thereby triggering cell signaling events. Of the four known human histamine receptor types, H_1R is expressed by various tissues, including airways, the vasculature, and the brain.

Pharmacologists have developed various antihistamine drugs that interfere with histamine–receptor interactions. "Many of us will have taken antihistamines to alleviate the symptoms of hay fever, for example, or to stop the swelling and itchiness caused by insect bites," Iwata says.

Iwata and his collaborators solved the structure of H_1R with bound doxepin using x-ray crystallography. Like all proteins, H_1R is composed of amino-acid building blocks. The amino acid tryptophan is found at a particular position in H_1R and is known to be important for receptor activation. The researchers revealed that doxepin sits deep within a binding pocket in the receptor, where it interacts directly with this key amino acid (Fig. 1), helping to explain its pharmacological activity.

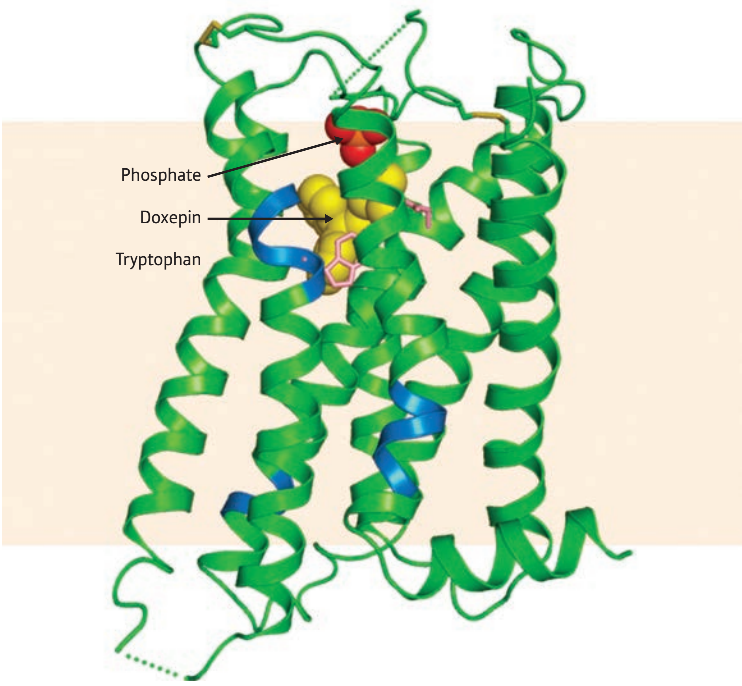

Figure 1: The crystal structure of H_1R with bound doxepin, showing the position of tryptophan and phosphate.

Doxepin was one of the first antihistamines that effectively blocks histamine receptor activation. Unfortunately, however, these drugs also bind other related receptors. "This low selectivity along with their ability to enter the brain means that these first-generation drugs have considerable side effects such as sedation, mouth dryness, and heart arrhythmias," explains Iwata.

The researchers' structural findings suggested that the low selectivity of doxepin is due to the hydrophobic ('water hating') nature of the binding pocket, a characteristic found in other receptors to which the drug binds. However, they found that the binding pocket of H_1R has a distinctive region occupied by the negatively charged ion phosphate. Through molecular modeling, they demonstrated that the second-generation drugs such as olopatadine would interact with this region, which is not conserved in other related receptors. This explains why these drugs are more selective and have fewer side effects compared with doxepin.

"Our findings demonstrate how minor differences in receptors affect drug selectivity and will be useful in the development of the next generation of antihistamines," says Iwata. ■

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Knowing when to tighten the belt

By relocating a protein that causes cellular constriction, a factor tentatively linked to growth also helps cells retain their natural shape

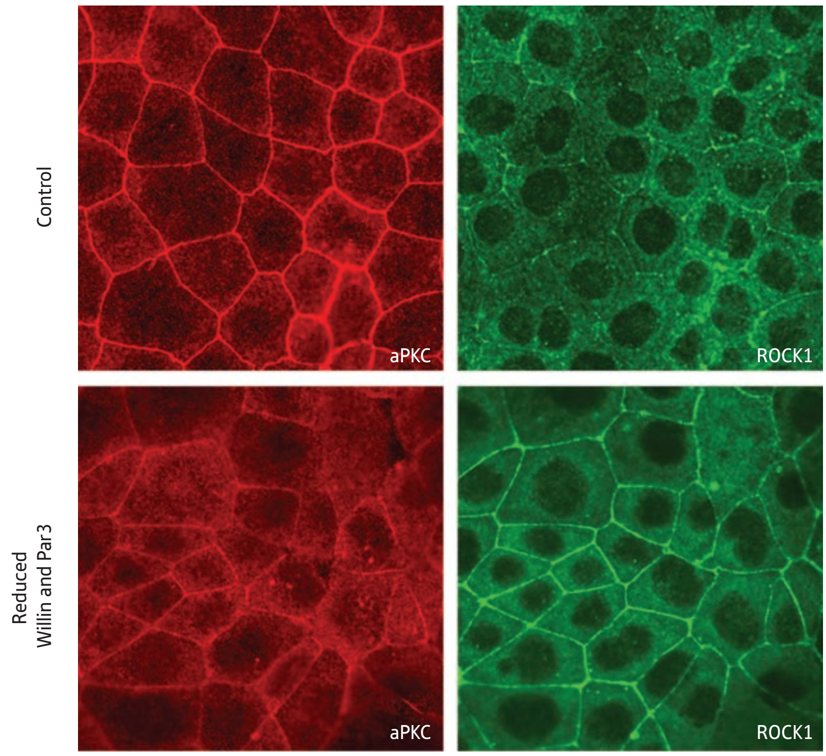


Figure 1: When both Willin and Par3 are active (top), aPKC (red; left) localizes to the AJCs and introduces modifications to ROCK1 (green; right) that cause this protein to remain in the cytoplasm. When Willin and Par3 levels are artificially reduced (bottom), far less aPKC reaches the AJCs, and ROCK1 redistributes to the AJCs.

The epithelial cells that line the surface of tissues form a tightly sealed barrier, with individual cells joined together by structures called apical junctional complexes (AJCs). However, embryonic epithelium undergoes multiple physical rearrangements over development. For example, early in the formation of the brain and spinal cord, a subset of epithelial cells fold inward to form a groove that ultimately develops into a 'neural tube'.

Such changes are achieved through the physical constriction of the apical (upper) domains of selected epithelial cells, a process driven by a ring-shaped network of cables composed of actin and myosin protein that are anchored at the AJCs. Now, work from Masatoshi Takeichi and postdoctoral fellow Takashi Ishiuchi of the RIKEN Center for Developmental Biology in Kobe has revealed an unexpected role for a protein named Willin in regulating this constriction[1].

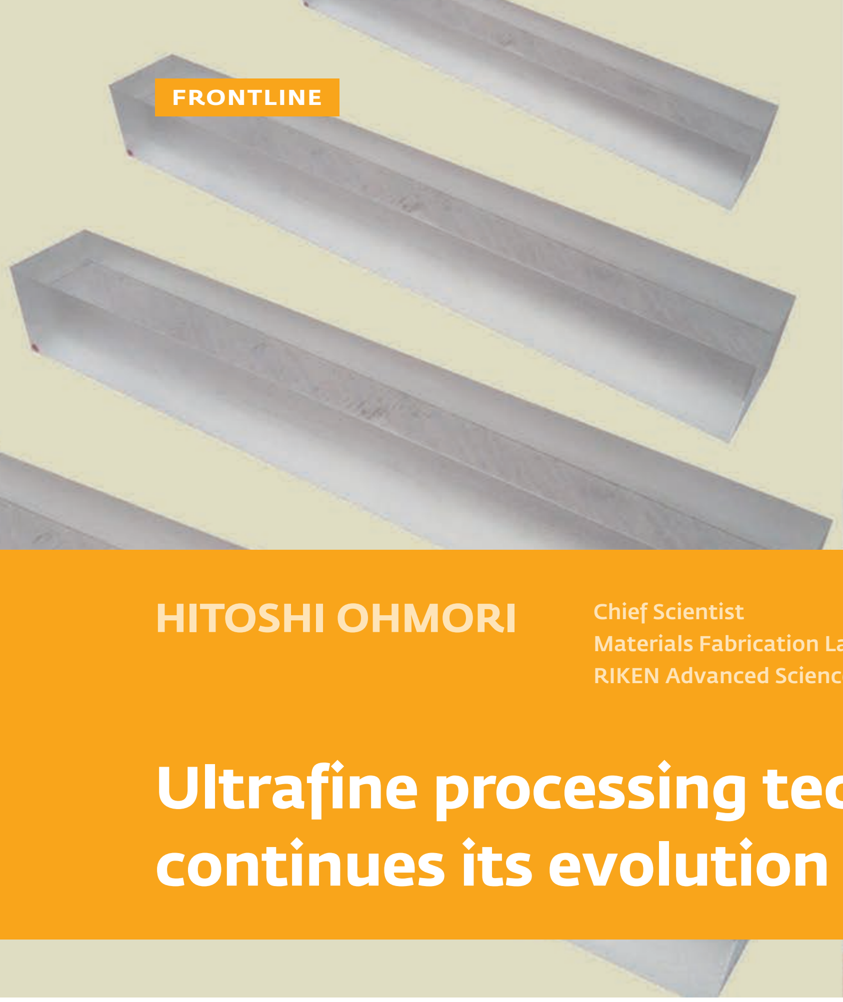
Willin was previously assumed to act primarily as the mammalian equivalent of Expanded, a fruit fly protein that regulates growth. "It turned out that Willin localizes along cell junctions," says Takeichi, "and we got interested in what it was doing there."

They determined that Willin associates with a pair of proteins—Par3 and atypical protein kinase C (aPKC)— that help epithelial cells maintain their polarity, with clearly defined apical (top) and basal (bottom) segments. Willin and Par3 both seem to execute highly similar functions: they bind to and shepherd aPKC to AJCs, where aPKC acts to inhibit actomyosin-mediated constriction.

Since aPKC is an enzyme that regulates the function of other proteins by tagging them with chemical modifications, Takeichi and Ishiuchi searched for potential targets. Proteins known as Rho-associated kinases (ROCKs) localize to AJCs and modulate the function of actomyosin fibers, and the researchers confirmed that the ROCKs are direct targets of aPKC. The presence of unmodified ROCK at AJCs appears to promote apical constriction; however, after delivery of aPKC to the AJC, it inhibits constriction by modifying ROCK and triggering its release into the cytoplasm (Fig. 1). "This was really an unexpected discovery," says Takeichi.

These results show that Willin is an important regulator of epithelial cell shape, but Takeichi is not ready to discard the possibility that it may still perform functions that echo those of its cousin, Expanded. "Growth control and junctional contraction might be physiologically linked," suggests Takeichi. "A future goal would be to clarify whether vertebrate Willin is involved in growth control and, if so, how this relates to its ability to induce epithelial apical constriction." ■

1. Ishiuchi, T. & Takeichi, M. Willin and Par3 cooperatively regulate epithelial apical constriction through aPKC-mediated ROCK phosphorylation. *Nature Cell Biology* **13**, 860–866 (2011).



HITOSHI OHMORI

Chief Scientist
Materials Fabrication Laboratory
RIKEN Advanced Science Institute

Ultrafine processing technology continues its evolution

The performance of optical and electronic components such as lenses and semiconductors is strongly influenced by the precision of surface grinding, which involves shaping the surface, and polishing, and provides the product with a mirror finish. Electrolytic in-process dressing (ELID), a technological innovation developed more than 20 years ago by Hitoshi Ohmori, chief scientist of the Materials Fabrication Laboratory at the RIKEN Advanced Science Institute, revolutionized these processes by providing nanometer-level precision in surface finishing. Ohmori's laboratory frequently plays host to researchers and industry engineers interested in new methods, and his group continues to make steady improvements to the ELID grinding technology. Now, the laboratory has its sights set on a new target—what Ohmori calls "broadband fabrication."

A work in progress

In 1987, almost a quarter of a century ago, Ohmori published a paper on the electrolytic in-process dressing (ELID) grinding method. At that time, mirror finishing required two separate processes: grinding and polishing. ELID made it possible to perform the two simultaneously.

"An ELID grinding wheel is a uniform mixture of electrically conductive materials including metals and abrasive particles such as pieces of diamond," says Ohmori. "A conventional grinding wheel rotates to grind the workpiece with a relatively high degree of precision, but frequently becomes clogged or glazed after a short period in use, meaning that the grinding work must be stopped to 'dress' or sharpen the grinding wheel in order to make abrasive grains protrude from the wheel surface. In contrast, ELID enables grinding with in-process dressing because electrically conductive (mainly metallic) bonding materials on the grinding wheel are selectively removed by electrolytic action while the surface of the workpiece is being ground with extreme precision. As the degree of dressing can be controlled electrically, ELID allows very fine abrasive grains to be used, making it possible to reduce the size of grinding traces and making precision mirror-quality finishing a reality."

ELID attracted broad interest in industry because of its innovativeness. Later, with demands for higher work surface precision increasing day-by-day and a growing range of soft work materials in use, such as special metals or composite materials, further development of the ELID method became paramount. For some time, smaller abrasive grains were used to process these pieces. However, using abrasive grains smaller than 1 micrometer with such rigid bonding materials as metals led inevitably to vibration problems, placing limitations on the ground surface precision due to a lack of grinding wheel rotational precision. This made technological innovation essential.

In 1993, Ohmori started working on ELID using an 'elastic' grinding wheel and successfully developed a system capable of creating a mirror-finish surface with an average roughness of just 0.3 nanometers. "Despite what the word 'elastic' might suggest, metal accounts for 60–70% of the grinding wheel, with the rest made up of synthetic resin or plastic. The ratio is just right. Today, elastic grinding wheel-based ELID has become the mainstream, and is commonly used for finishing optical components such as mirrors."

Ohmori subsequently started working on machining three-dimensional shapes. He combined ELID with machine tools capable of positioning the grinding wheel and workpiece with a resolution of 1 nanometer or less, successfully developing a computerized, superfine, multi-degree-of-freedom machining system to mirror-finish aspheric lenses.

Today, there is a growing need for microfabrication, which allows more efficient machining and production of fine components with a higher degree of accuracy than previous machines. Figure 1 shows a desktop ELID grinding system that can produce a working tip diameter of 1 micrometer or less. The tip functions as a tool, sensor and electrode. Out of a conviction that small grinding machines could be developed for small workpieces, in 2004 Ohmori created a desktop ELID grinding machine with electrodes built into the nozzle that sprays grinding fluid. The grinding machine can process workpieces like the long tapered microtool shown in Fig. 1 without breakage and to nanometer-surface precision. To make the system even more compact, a smaller electrolytic power-generating unit for the desktop ELID grinding machine was developed in 2010.

Desktop ELID grinding machines can now be found in many companies, research institutes, and universities. "The machine allows precision machining of small workpieces of 1 micrometer to 10 centimeters in size. It also has a small footprint and runs on commercial AC 100V power. It is generally used to process small numbers of workpieces. We envision that mass-produced items will be manufactured in large-scale factories to reduce production costs, while the desktop ELID system is suitable for on-demand fabrication and precision machining in relatively small quantities," says Ohmori.

The major users of ELID are manufacturers requiring precision machining. They manufacture a wide range of items ranging from optical components, semiconductors, dies and molds and automobiles to medical components. Some manufacturers have customized the ELID grinding machine and introduced it onto their mass-production lines. In 2006, Ohmori developed the ELID honing method in partnership with Fuji Heavy Industries by applying ELID to the honing process for finishing the cylinder inner walls in automobile engines, successfully reducing the processing time by half.

Rubber and carbon grinding wheels

ELID continues to evolve. One of the current research themes Ohmori and his laboratory members are working on is the development of a new grinding wheel that is even more elastic than previous models. One of the candidate materials is rubber. Pure rubber, however, cannot be electrolyzed because it does not conduct electricity. "We are planning to develop a grinding wheel made of a mixture of rubber and electrically conductive materials or metals," says Ohmori. Carbon is one of the candidates.

One application for ELID using a carbon-containing elastic grinding wheel is in the machining of the backside surfaces of memory substrates. With ELID, the silicon substrates can be made thinner and subsurface damage by grinding can be minimized. The ELID method,

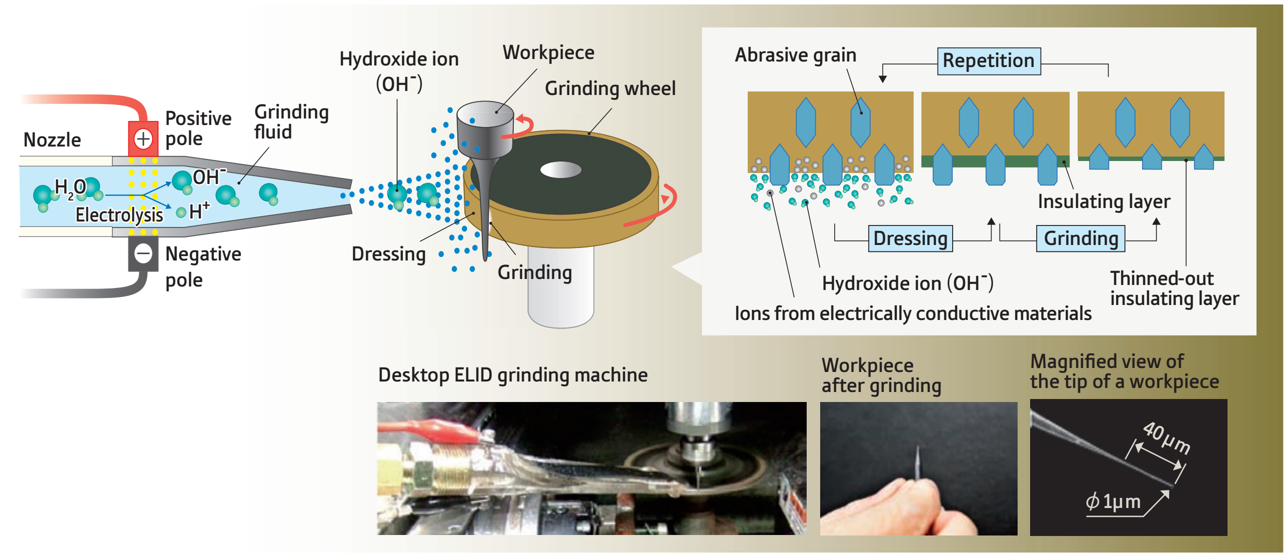


Figure 1: Microfabrication using the desktop ELID grinding machine

When hydroxide ions (OH^-) produced by the electrolysis of water within the nozzle fall on the grinding wheel, they react with the electrically conductive materials on the grinding wheel surface and form an insulating layer. This causes abrasive grains to appear on the surface of the grinding wheel, effectively 'dressing' the wheel. In this state, the workpiece is ready for grinding. As grinding proceeds, the wear on the abrasive grains increases, leading to flaking of the insulating layer. However, hydroxide ions continue to fall on the grinding wheel, dissolving the electrically conductive materials and redressing the wheel. This cycle enables machining to proceed without interruption.

however, leads to the production of metal ions from the grinding wheel through electrolysis. "In most cases, this was not a major problem. However, manufacturers asked us to develop an ELID grinding wheel without any metals, so we came up with the idea of using carbon. We used carbon because it is not a metal, but still conducts electricity and does not affect semiconductors when ionized."

The laboratory is planning to produce the carbon material for the grinding wheels itself. "We will use untapped natural resources such as rice bran or waterweeds such as reeds. When waterweeds are burned they leave behind fibrous carbon. We are still at the basic research stage, but our carbon grinding wheel may exhibit unique characteristics." In the future, they may be able to put environmentally friendly grinding wheels with carbon produced from rice bran or waterweeds into practical use.

Changing surface properties

The second research subject of the Materials Fabrication Laboratory is surface modification. When ELID first appeared, users sometimes noted that a surface finished using ELID became rust-resistant. "We were surprised at this unexpected feedback. We examined the mechanism and found that the key was hydroxide ions (OH^-). Electrolysis causes the grinding fluid to produce OH^- while it is flowing from the electrodes to the grinding wheel. The hydroxide ions falling onto the surface of the grinding wheel dress the wheel, and they also fall on the surface of the workpiece, forming a thin oxidized layer that serves as a protective, rust-resistant film. ELID is therefore very suitable for machining rust-susceptible mold materials and various medical products such as dental implants and artificial joints.

Ohmori is now looking at ways to use the surface modification characteristics more actively. Intentional modification of the components of the abrasive grains or grinding fluid can lead to the generation of a variety of surface modification characteristics. "For example, changing diamond-based abrasive grains to aluminum- or chromium oxide-based grains can contribute to changes in the wettability of the surface. When the surface of a workpiece is machined with a grinding wheel containing abrasive grains made up of a mixture of diamond and silica, it exhibits good adhesion with a coating layer applied later. We also found that the workpiece became stronger."

The surface modification functionality of ELID is also what makes it possible to machine long tapered micro-tools such as that shown in Fig. 1 without breakage. "Investigation showed that many oxygen ions penetrated the inside of the workpiece during machining, strengthening its metal structural bonding forces."

Overall, the ELID grinding method has three distinct advantages over other machining techniques: it is suitable for processing complex shapes such as combined curved surfaces, it can be used to machine a smooth mirror finish to a surface precision of 1 nanometer, and it adds functionality to the surface of the workpiece. "Recently, our research has been shifting towards adding functionality."

From finishing to broadband fabrication

"The ELID grinding method has seen major improvements, from a rigid grinding wheel to an elastic grinding wheel. The next target is liquid tool machining instead of solid tool machining," says Ohmori.

In 2008, in collaboration with Kazuto Yamauchi of Osaka University, Ohmori developed a light-collecting mirror (Fig. 2) for X-ray light produced by the SPring-8 Angstrom Compact Free Electron Laser (SACLA) at the RIKEN Harima Institute, which was completed in March 2011. The light-collecting mirror has a complex aspheric surface. Surface precision at the atomic level was required for the mirror finish. "Even ELID was insufficient for finishing the surface to that level of precision. We attempted to combine ELID grinding with elastic emission machining (EEM), which has been studied by the research group headed by Prof. Yamauchi. EEM uses a chemical reaction and provides mirror-finish machining at the single atom level. We first used ELID to produce the shape with the specific surface precision of the mirror, and then used EEM to finish the mirror to the single-atom level. Nobody else has developed the technology for completing long aspheric surfaces to that level of precision."

The light-collecting mirror was developed by Ohmori and Yamauchi by combining their two machining methods. At present, Ohmori is studying a new finishing method that will make a foray into uncharted territory. "Liquid-tool machining allows mirror finishing to single-atom precision, but it takes an enormous amount of time to finish workpieces with large, uneven surfaces. So we are working on finding a way to shorten the machining time and improve the machining precision by using more viscous liquids or viscoelastic bodies." Candidate viscoelastic bodies include fluids that increase in viscosity when a magnetic field is applied and return to free liquid form when the magnetic field is removed. Changing the strength of the magnetic field can be used to control the viscosity. "To begin with, the surface of the workpiece is planarized with the solid-tool machining principle. Then magnetic viscous fluids (acting as a semi-liquid-tool) are applied to the surface to smooth any unevenness remaining on the pre-machined surface. Finally, liquid-tool machining is applied to finish the surface to the single-atom level of precision."

"We are studying how to apply gas polishing (gas-tool machining), which is a process to remove processing strain and/or subsurface damages by applying gas plasma to the surface of the pre-finished workpiece. We are planning to develop a prototype product later this year," says Ohmori. With this technique, ionized gas particles are applied to the surface of the workpiece in the same way as plasma etching in a vacuum.

Figure 2: Light-collecting mirror prepared for the SPring-8 Angstrom Compact Free Electron Laser (SACLA) at the RIKEN Harima Institute

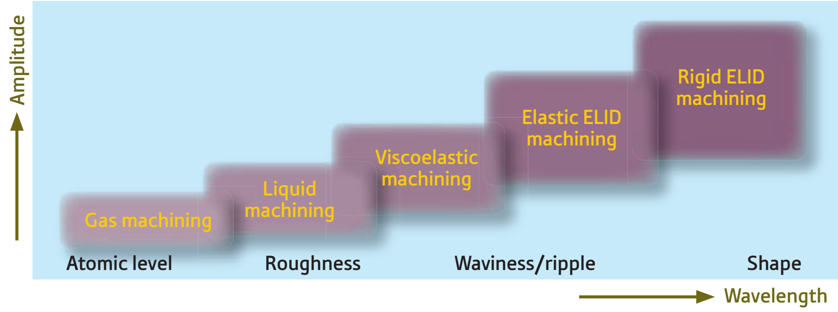


Figure 3: Schematic diagram of broadband fabrication

When a cross-sectional view of a workpiece is magnified in steps, the relationship between overall shape, waviness/ripple and roughness can be expressed as a combination of overlapping and nested 'waves'. Broadband fabrication technology provides the best combination of machining principles and methods for the wavelengths and amplitudes of these waves.

Ohmori has devised and developed new methods one after another. "Our goal, however, is to make broadband fabrication technology a reality," he says. "When the cross-section of a workpiece is regarded as a wave, we can see that the overall shape, large curves, and rough irregularities are nested like a waveform. Depending upon the wavelength and amplitude of the surface, rigid, elastic, viscoelastic, liquid and gas-tool machining each have their own area of proficiency. In order to finish a workpiece in a finite period of time to within a prescribed precision irrespective of the type of target workpiece, it is best if all adjacent machining regions overlap to produce a 'broadband' machining region. We will face many research challenges in these overlapping regions, such as clarification of the machining mechanisms and development of controlling and tuning technology. However, we hope to establish a new methodology and a new field: broadband fabrication. When we have transformed machining principles to include broadband, we will be able to get a clear view of the most suitable machining principle and method, or the best combination of machining principles and methods, for any required size and precision.

Supporting cutting-edge science and technology

Recently, researchers have been making an increasing number of requests not only for ELID and microfabrication, but also for 'ultrafabrication', which deals with large target workpieces. "Machining large objects requires significant time. The objects expand or contract with changes in temperature, causing tool wear or misalignment of the machining position. No precision measuring instruments have been developed to work on large pieces. We also need specific programs to ensure stable machining precision. Thus, ultrafabrication has to be applied on an individual product basis."

One example of an ultrafabrication-based product is the lens for the JEM-EUSO telescope that will be installed in the Japanese Experimental Module (JEM) 'Kibo' laboratory in the International Space Station (ISS). The acrylic lens is 1.5 meters in diameter. Fresnel processing was required to cut shallow and sharp grooves on both sides as well as thinning to produce a lightweight diffractive lens. Machining the large sunlight collection lenses is an example of ultimate ultrafabrication. A two-meter lens has already been requested for research and development purposes to explore new applications that include laser beam and energy generation using solar energy collectors.

Other requests include lenses for astronomical observation equipment and cutting-edge research in optical science. "The requirements for cutting-edge optical devices will continue to increase in the future. To meet these requirements, we need to make broadband fabrication technology a reality."

When a new requirement becomes apparent, Ohmori makes it a rule to set the machining guidelines from three perspectives. The first is the size of the workpiece, where ultrafabrication and microfabrication are the two extremes. The second is quantity, which extends from single-product machining to mass-production. "The key is to have a viewpoint of on-demand fabrication that enables flexible and quick production in response to various needs," says Ohmori. The third perspective is precision, with the guideline that machining should aim for precision of one nanometer.

"Looking back over the last 20 years since the publication of my paper on the ELID grinding method, I regret that I seem to have responded on a case-by-case basis. I think I could have made more progress if I had seen the individual improvements as being technically linked to each other and if I had worked on them at the same time. In the future, I will continue to systematize the various techniques we have built up, including newly developed techniques such as broadband fabrication technology, so that we can deal rationally with various external requirements by analyzing them from these three viewpoints or by selecting suitable tools and approaches accurately and promptly."

Ohmori is now searching for a way to help Japan's skilled manufacturing survive in an increasingly competitive global economy. He is also working on innovative technologies that support cutting-edge science and technology. "Our dream is to use our technology to help researchers win the Nobel Prize." ■

ABOUT THE RESEARCHER

Hitoshi Ohmori was born in Ibaraki, Japan, in 1962. He obtained his Doctor Degree in Engineering from the Precision Engineering Doctoral Course of the University of Tokyo in 1991, and subsequently joined RIKEN as a research scientist. He was promoted to vice chief scientist in 1998 and chief scientist in 2001. Since then, he has acted as director of his own research group. His research focuses on the development of revolutionary and new material processing technologies in grinding, lapping, polishing, cutting, molding and forming for an extensive range of materials through the electrolytic in-process dressing method.

RIKEN PEOPLE

Kayo Takahashi

Research Scientist
Molecular Probe Dynamics Laboratory
RIKEN Center for Molecular Imaging Science

Imaging new pathways in the human brain

What do you do at RIKEN?

I work as a researcher in the Molecular Probe Dynamics Laboratory, which is a part of the RIKEN Center for Molecular Imaging Science (CMIS).

How and when did you join RIKEN?

In November 2006, I was studying at the graduate school of Uppsala University in Sweden when I heard that the RIKEN facility for the Molecular Imaging Research Program (MIRP) was starting up. Center for Molecular Imaging Science director, Yasuyoshi Watanabe, invited me to the institute and I was delighted to have the opportunity to join the program as one of the original members.

What attracted you to RIKEN?

I had a very favorable impression of RIKEN as being one of the leading research centers in Japan, providing an environment where researchers can dedicate themselves to their research. This is the main reason why I looked forward to being involved with the newly established MIRP.

How was the transition to life at RIKEN?

As I was starting a new research project, some aspects did not progress as smoothly as expected at the beginning. However, I greatly enjoyed this challenge, and it has been an invaluable experience to observe how my research and that of my colleagues has gradually produced results over time.

Please tell us about your research or other work at RIKEN.

I am currently investigating how the distribution of an enzyme in the brain called aromatase, which plays a vital role in controlling both male and female hormones, affects an individual's temperament. Until now, I have been researching aromatase expression in the brains of rats and monkeys. However, through the use of positron emission tomography (PET) technology, I am now able to carry out molecular imaging *in vivo*, and hence conduct clinical research of the human brain. I have enlisted the help of healthy volunteers, and eventually aim to carry out PET trials to investigate aromatase expression in those who have a tendency towards aggressive behavior. People who suffer from abnormally high levels of aggressiveness may have issues with lack of self-control that influence their social adjustment. I hope that my research will provide insight into improving the quality of life of those who suffer from behavioral problems.

What have been the highlights of your time at RIKEN so far?

I have been very fortunate to be supported by people who have so generously given much of their time and expertise in helping me. Their assistance has enabled me to take on one of the greatest challenges that I have faced—starting clinical trials. Also, since people have normally heard of RIKEN, they are interested in my research and it's relatively easy for them to understand what I do, which motivates me to try even harder to make a contribution to society.

What is the best thing about working at RIKEN?

RIKEN enables me to carry out the research that I want to focus on, and I work in a stimulating environment where I am surrounded by highly knowledgeable and motivated individuals. Currently at RIKEN I am able to see novel research taking place around me that nobody had thought of several years ago.

What would you say to other people considering joining RIKEN?

I would encourage people to cherish their identity and originality but also recognize that cooperation is often the key to success.

CONTACT INFORMATION

For details about working at RIKEN, please contact the RIKEN Global Relations Office:
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RIKEN President visits Malaysia and Singapore

RIKEN President Ryoji Noyori visited Malaysia and Singapore from 19 to 23 September 2011 to promote research cooperation among Asian countries. On his visit to Malaysia, Noyori was awarded an honorary doctorate of science from the Universiti Sains Malaysia (USM), presented by His Highness the Raja of Perlis, D. Y. M. M. Tuanku Syed Sirajuddin Ibni Al-Marhum Tuanku Syed Putra Jamalullail, the chancellor of the USM. In his address to an audience of graduates, Noyori noted that Asian scientists had made contributions to the progress of science and technology with ideas forged through a long history and unique cultures. "In the twenty-first century," he added, "it is clear that the role you are expected to play will be more important than ever."

RIKEN President Noyori (second from left) and his wife (left), His Highness the Raja of Perlis, D. Y. M. M. Tuanku Syed Sirajuddin Ibni Al-Marhum Tuanku Syed Putra Jamalullail and USM chancellor (center), accompanied by Her Royal Highness Tuanku Raja Perempuan Perlis (second from right), and vice-chancellor Dzulkifli Abdul Razak (far right)

Noyori's visit to Universiti Sains Malaysia also coincided with the opening on 22 September of the RIKEN–USM Joint Laboratory for Bioprobe Discovery at the USM's Institute of Research in Molecular Medicine. This landmark collaboration between RIKEN and the USM aims to isolate novel biological active compounds from tropical plants found in Southeast Asia, particularly in Malaysia. Attended by Noyori and ASI Director Kohei Tamao, the ceremony was followed by the signing of a Memorandum of Understanding (MOU) on the joint laboratory.

His Highness the Raja of Perlis, D. Y. M. M. Tuanku Syed Sirajuddin Ibni Al-Marhum Tuanku Syed Putra Jamalullail, the USM chancellor, at the USM graduation ceremony

RIKEN also signed another MOU with the University of Malaya to promote further collaboration and exchange of students and researchers between Malaysia and Japan.

In Singapore, Noyori met with university officials from Nanyang Technological University (NTU), where he signed an MOU to enable RIKEN and NTU to embark on further joint projects. Scientists from RIKEN are already carrying out joint research with NTU researchers in addition to acceptance programs for students. These activities have been very fruitful for RIKEN, and the recently signed MOU will further strengthen this important partnership, which is a lasting asset for both institutions.

Noyori separately visited A*STAR Chairman Lim Chuan Poh, the National Research Foundation's former Permanent Secretary Teo Ming Kian, and National University of Singapore President Tan Chorh Chuan, and discussed various science and technology policy issues and future collaboration possibilities with RIKEN. ■

Delegates from the Chinese Academy of Sciences visit RIKEN to promote women in research

On 14 September 2011, the RIKEN Yokohama Institute hosted a delegation of female scientists from the Chinese Academy of Sciences (CAS) as part of the group's visit to Japan to promote the role of women in research among Japanese research institutes and universities. The delegation to Japan was led by Fang Xin, a member of the CAS Presidium, and included researchers, institute directors, deputy directors and other prominent women of the CAS.

The delegates visited the RIKEN Research Center for Allergy and Immunology (RCAI), the RIKEN Plant Science Center (PSC) and the Yokohama Institute's nuclear magnetic resonance (NMR) facility, where they were introduced to RIKEN's various research activities and achievements.

During their visit, the CAS delegates met and exchanged views with researchers at RIKEN on various topics, including the organization of research, researcher evaluation systems, and management issues such as research budget allocation. The meeting was a valuable experience for all participants and lays the foundations for future collaboration and the sharing of views on science in China and Japan. ■

RIKEN Executive Director visits the UK and France

RIKEN Executive Director Kenji Oeda visited various universities and research institutes in the UK and France from 12 to 22 September 2011 to celebrate a key collaboration with the University of Liverpool (UoL) and to further discussions on research organization and management.

Oeda's visit to Europe coincided with the second RIKEN–UoL symposium in Liverpool, UK. Held over three days, the symposium marked the ongoing collaboration between RIKEN and the UoL, and drew speakers from a wide range of research fields, including neuroscience and engineering. The closing session was attended by Sir Howard Newby, vice-chancellor and executive director of the UoL, who pledged the continuation of UoL's successful partnership with RIKEN in the future.

After the symposium, Oeda visited several institutes and universities in London, Strasbourg and Paris, including the Royal Society, the University of Cambridge, University College London, the University of Strasbourg, the Pasteur Institute and the French National Center of Scientific Research (CNRS). There Oeda engaged with university executives and researchers on issues such as international and research strategies, and the internationalization of institutes. Oeda's visit promotes further research cooperation with RIKEN's European collaborators and the advancement of key partnerships in the UK and France. ■

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