

RIKEN RESEARCH

OCTOBER

2007 Volume 2 Number 10

Qubits switch on and off

HIGHLIGHT OF THE MONTH

Tuning into quantum computers

RESEARCH HIGHLIGHTS

Superconducting cement

Molecules switching position

Laser light switches molecular bonds

Halting the inflammation overload

A better way to make a muscle?

Observing single cells on the move

New scaffold supporting our molecular understanding of psychiatric disorders

Wrapping up a cell biology riddle

Enzymes lead the way

Surviving separation

FRONTLINE

Towards the creation of Astro Boy's brain

ROUNDUP

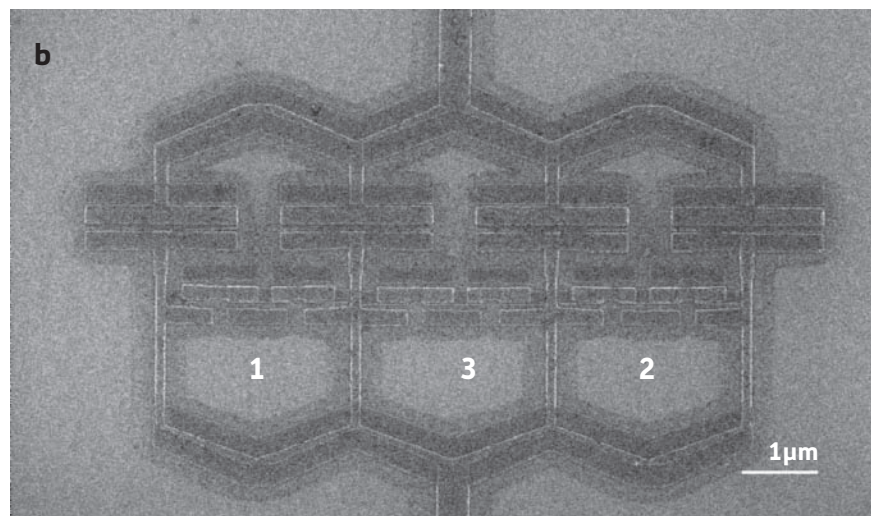
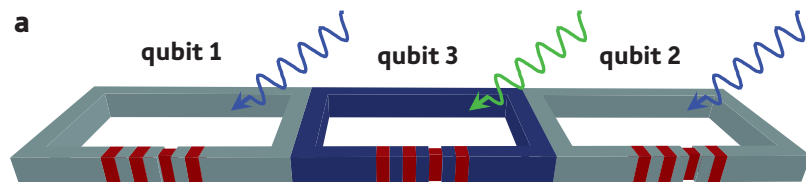
RIKEN leads project to build world's fastest supercomputer

HISTORY OF RIKEN

Opening to the outside world

Tuning into quantum computers

Improved device design enables the tunable interaction between the elements of a quantum computer



Science

For fast and efficient operation of quantum computers, control of the interaction between their components, the quantum bits (qubits), is necessary. Now, researchers from RIKEN's Frontier Research System, Wako, the Japan Science and Technology Institute, NEC Corporation and the US Massachusetts Institute of Technology have developed an architecture that allows tunable control over the qubits of a superconducting quantum computer. Their study represents a large step towards the realization of large-scale quantum computers with controllable qubit interactions.

Quantum computers are different

Compared with conventional computers, quantum computers hold great promise as a much faster alternative for solving certain mathematical problems, such as the simulation of quantum-mechanical systems. Another example is the factorization of integer numbers into the products of prime numbers—an operation that would require a huge effort by conventional computers and would take considerably longer to complete. The interaction between the qubits gives quantum computers their unique attributes, and it would take a significantly larger number of bits from conventional computers to even simulate the operation of a quantum computer.

There are a number of possible designs for quantum computers. One example uses atoms cooled to very low temperatures. For

this, the atoms are suspended in vacuum and lined up by complex electromagnetic fields. Although larger systems of qubits composed of atoms have been successfully demonstrated, such schemes remain relatively cumbersome. On the other hand, solid-state based systems offer desirable ease of fabrication—echoing the success of conventional silicon-based computing—and are therefore intensively pursued worldwide.

A representative type of qubit for solid-state based quantum computers is formed by loops of superconducting rings made from aluminum (Fig. 1). At certain points the rings are made insulating through oxidation of the aluminum, which creates so-called Josephson junctions. Tiny

magnetic fields within these rings then are able to generate electrical currents across these Josephson junctions.

When exposed to the right magnetic fields, a stable situation is reached that balances the current flowing clockwise and anti-clockwise through the rings. This renders the rings insensitive to small variations in the magnetic field and optimizes their use as qubits. Of importance to the performance of quantum-computing tasks is the quantum-mechanical coupling of neighboring rings.

Controlling coupling between qubits

While the interaction between the qubits of a quantum computer is important, good control over this coupling is essential.

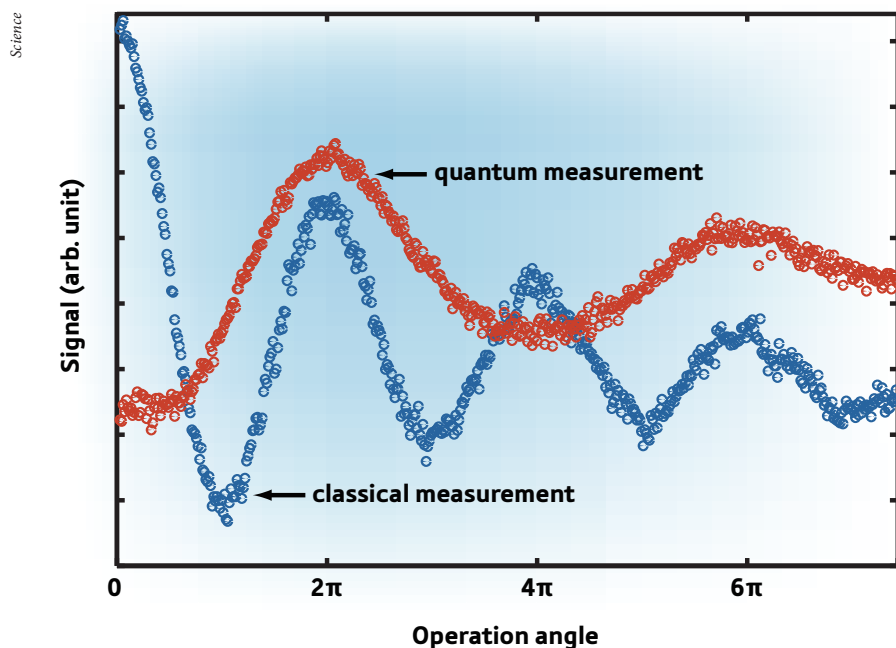


Figure 2: Example of the detection of a computer hacker. The modifications made by the hacker to the state of qubits cannot be detected classically but lead to an altered output in quantum circuits.

“Tunable coupling, in particular coupling which can be switched off completely, is highly desirable for implementing large-scale quantum computing,” comments Yasunobu Nakamura from the RIKEN team. Turning off the coupling prevents undesirable interaction between the qubits. Otherwise, as Nakamura points out, “the qubits would interact with each other all the time and even a simple decomposition of the signal would be difficult.” Cumbersome architectures would be required to compensate for such undesired side effects.

Therefore, the team’s demonstration of tunable coupling between the qubits of such a superconducting quantum computer, as reported in the journal *Science*¹, represents an important step towards the realization of complex quantum computers.

In this approach, tunable coupling is based on two qubits that are linked via a third and passive qubit that mediates the interaction between the active qubits (Fig. 1a). Importantly, the internal energy scale of each of the three qubits is different. While the two active qubits have only marginally different energy spectra, the mediating passive qubit has a larger energy scale. Microwave radiation at selected energies then provides deliberate and controllable coupling between the energy states of the active qubits, whereas the energetic states of the passive qubit remain unaffected due to

the large energy difference. Therefore, the ‘coupler qubit’ merely mediates the coupling between the ‘active’ qubits. The microwave radiation is fed to the qubits via an on-chip transmission line, which is readily scalable to a higher number of qubits.

Detecting hackers

To experimentally apply the new design concept, the researchers implemented a simple quantum computing protocol to determine whether the system could detect a computer hacker attempting to modify the system. With a classical computer, such infiltrations are impossible to detect.

If the hacker altered the quantum state of the coupled qubits by using the same tunable interaction described above, it would lead to a periodic modulation of the quantum state with a periodicity of 4π inherent to such quantum-mechanical manipulation. However, classical measurements cannot detect the subtle change and results in observation of a 2π periodicity.

The test measurements performed by the researchers are shown in Figure 2. In an experiment simulating a classical computer, the 2π periodicity is seen (blue curve) and they could not distinguish whether the hacker had modified the state or not. However, the quantum measurement (red curve) clearly reflects the doubled 4π period, which clearly indicates the presence of the hacker.

Large-scale quantum computation

These experiments are an important demonstration of the principle, yet further improvements are needed. For example, longer lifetimes of the quantum states would allow for better and more complex quantum operations. These longer lifetimes can be achieved by improving the stability of the quantum states towards, for example, fluctuations in the external magnetic field.

This example of microelectronics technology by the team shows that large-scale integration requires precise control of each individual element. Indeed, Nakamura points out that the team “hopes to demonstrate that we can precisely control and characterize the quantum state of a large-scale artificial quantum system.” Eventually, such improvements could lead to the first large-scale quantum computer. ■

1. Niskanen, A. O., Harrabi, K., Yoshihara, F., Nakamura, Y., Lloyd, S. & Tsai, J. S. Quantum coherent tunable coupling of superconducting qubits. *Science* **316**, 723–726 (2007).

About the researcher

Yasunobu Nakamura was born in Osaka, Japan, in 1968. He graduated from the Faculty of Engineering, University of Tokyo, in 1990, and obtained an MSc in 1992 from the Superconductivity Research Course of the same university. Immediately after that, he joined NEC corporation, in Tsukuba, Japan, where he started his career in mesoscopic physics. Since the late 1990s he has been working on superconducting devices for quantum information processing. Nakamura also spent one year as a guest researcher at TU Delft in Delft, the Netherlands, from 2001 to 2002. Now he is a research fellow at the Nano Electronics Research Laboratories of NEC Corporation as well as a researcher at the RIKEN Frontier Research System.



Superconducting cement

Researchers find superconductivity in a material typically used as cement

The metal oxide known as $12\text{CaO}\cdot 7\text{Al}_2\text{O}_3$ (C12A7) is often used to make aluminous cements. Researchers from RIKEN's Discovery Research Institute in Wako and the Tokyo Institute of Technology have now found superconductivity in the metallic version of C12A7.

The crystal structure of C12A7 consists of a number of cages formed by calcium, aluminum and oxygen atoms (Fig. 1). Typically, such oxides are electrically insulating and of little interest to scientists. This changed recently, when researchers from the Tokyo Institute of Technology demonstrated that C12A7 can be made metallic by the chemical reduction that replaces negatively charged oxygen atoms with electrons. As a result, the conductivity of C12A7 changes by an impressive thirteen orders of magnitude. Such compounds, where electrons are used to achieve metallic conductivity, are called 'electrides'. Electrides are commonly used in batteries or fuel cells.

Owing to the open crystal structure of the C12A7 electride, the nature of the metallic state is quite different to normal metals. "The conduction of this material is supported by electrons trapped in the nano-scale cages," explains Kimitoshi Kono from the RIKEN team. Although the actual conductivity depends on the magnitude of this replacement, the absence of oxygen atoms allows the trapped electrons to extend and reach across the voids. The resultant overlap of electron distribution thereby enables the electrons to travel across the structure.

Superconductivity originates in the coupling of free electrons; so many metals are superconductive at low temperatures. The researchers therefore studied the

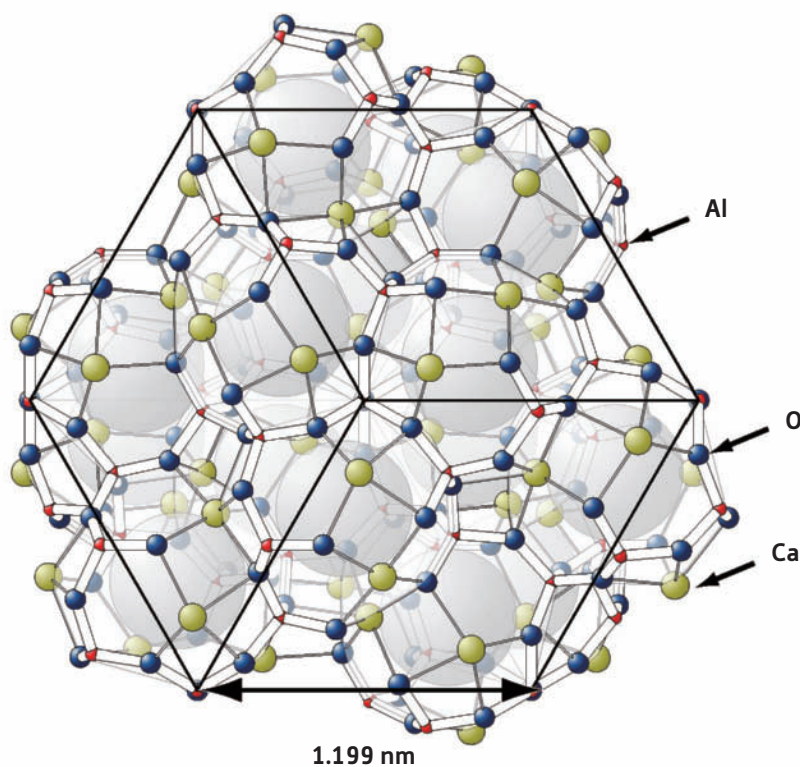


Figure 1: Atomic structure of C12A7. The compound consists of several empty cages formed by the arrangement of the aluminum (Al), calcium (Ca) and oxygen (O) atoms.

electronic properties of the C12A7 electride and observed superconductivity at about 0.4 K, which is less than $-272\text{ }^\circ\text{C}$. Their results have been published in the *Journal of the American Chemical Society*¹.

As the 'metallization' of the material was rather unexpected by scientists, the discovery of superconductivity in this mundane material is surprising to many. "Nobody else expected a cement to become superconductive," says Kono. Further investigations into the properties of these unusual superconductors are expected to follow from these pioneering findings. The design of the caged structure

of the C12A7 electride is also rather flexible, so many similar compounds exist or are theoretically possible. Kono says that "there is no reason why we should not expect that some of these materials might show superconductivity." Cement might hold further unexpected surprises for physicists and chemists. ■

1. Miyakawa, M., Kim, S. W., Hirano, M., Kohama, Y., Kawaji, H., Atake, T., Ikegami, H., Kono, K. & Hosono, H. Superconductivity in an inorganic electride $12\text{CaO}\cdot 7\text{Al}_2\text{O}_3:e^-$. *Journal of the American Chemical Society* **129**, 7270–7271 (2007).

Molecules switching position

Collective motion of molecules in a crystal could lead to new electronic devices

Researchers from the RIKEN Discovery Research Institute, Wako, and the Tokyo Institute of Technology have developed a new molecular switch that works by using the collective motion of molecules within a crystal.

Over recent years, many researchers from different backgrounds have focused their attention on developing molecular machines and devices. Molecular switches will play a crucial role in any such machines allowing the tiny devices to be turned on and off. The challenge is to develop a system that allows a reliable connection to be made between the switch and other devices to produce a system or circuit.

With this point in mind, the research group, led by Tatsuo Wada, decided on a new strategy to develop a switch from a supramolecular crystal. This strategy has been reported in *Angewandte Chemie*¹. The benefit of using a crystal is that connection to other devices is straightforward. The crystal is made up of supramolecules known as pseudorotaxanes, which consist of two parts: an axle and a wheel, that form a complex in which the axle is threaded through the wheel.

Using x-ray analysis, Wada and his colleagues could see that all the molecules were aligned in the crystal. Both parts of the molecule contained aromatic groups that were also perfectly aligned, face-to-face, throughout. Surprisingly, upon heating from 30 to 128 °C, all the aromatic groups on the axle rotated together through 45° changing their configuration. The groups then moved back to their original orientation on cooling. The molecules could be switched a number of

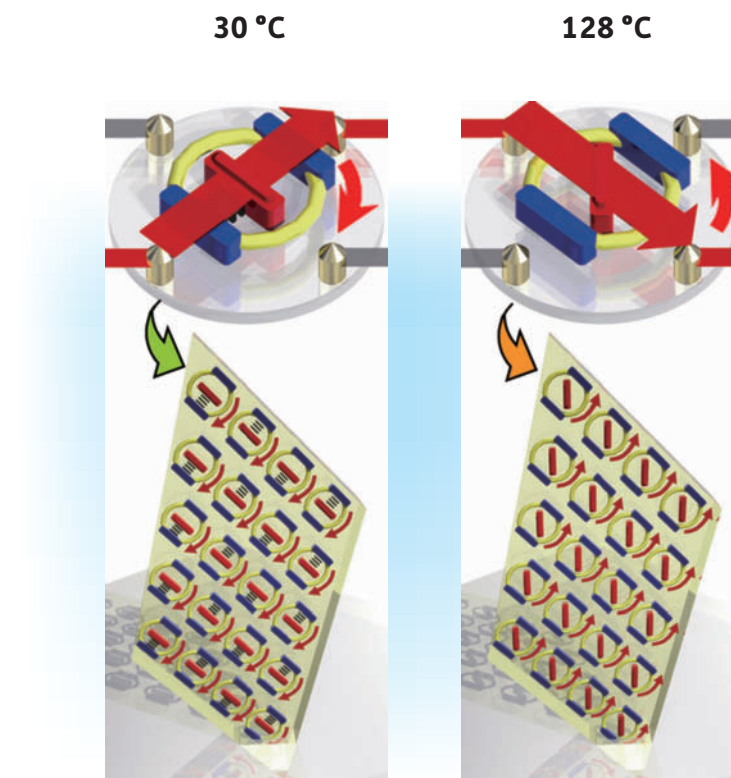


Figure 1: The collective motion of the pseudorotaxane, supramolecular switch occurs with changing temperature.

times between both orientations (Fig. 1).

This collective motion was also followed visually. Under polarized light the crystal appeared green then changed to orange when heated. The crystal reverted to green upon cooling. For such a clear color change to be seen, the motion of all the axle molecules must be in the same direction. Free movement of the axle is restricted as a consequence of the position of the wheel.

Masaki Horie, a member of the research group, points out that this project, and the results achieved in developing this thermo-optic switch, would not have been possible without the collaboration of experts from several different fields.

The researchers are now planning to extend this research and create new supramolecular systems that show a variety of controllable motions in the condensed state. They are constructing supramolecular systems that share molecular information and develop collective motion from random motion. ■

1. Horie, M., Sassa, T., Hashizume, D., Suzuki, Y., Osakada, K. & Wada, T. A crystalline supramolecular switch: Controlling the optical anisotropy through the collective dynamic motion of molecules. *Angewandte Chemie International Edition* **46**, 4983–4986 (2007).

Laser light switches molecular bonds

Laser irradiation switches the magnetic and structural properties of a molecular complex

Researchers from the RIKEN SPring-8 Center in Harima and from the universities of Tsukuba and Tokyo have demonstrated that laser light of a single wavelength can induce reversible transformations in the molecular bond, leading to changes in a material's magnetic properties.

Reversible magnetic transformation by laser light is a promising path towards optical telecommunications applications, as "this process can be used as a fast and efficient optical switching technique," explains Kenichi Kato from the RIKEN team. One candidate material for use in such applications is the $\text{Fe}(\text{phen})_2(\text{NCS})_2$ complex (Fig. 1). This compound shows no magnetism at low temperatures, but is magnetic above 176 K.

In their study, published in the journal *Applied Physics Letters*¹, the researchers demonstrate that illumination with laser light of the material in its low-temperature phase can induce an almost complete transformation from the non-magnetic to the magnetic state. As long as the laser light remains on, the magnetic phase is stable for more than eleven hours without any signs of deterioration. After the light is turned off, however, the relaxation speed is of the order of 10 seconds, which is several hours faster than previously observed at low temperatures. The team also found the magnitude of the switching can be controlled via the intensity of the laser light.

To elucidate the origin of the switching process, the researchers studied the material's crystal structure at the SPring-8 synchrotron x-ray light source. They showed that the molecular bonds between the iron and nitrogen atoms

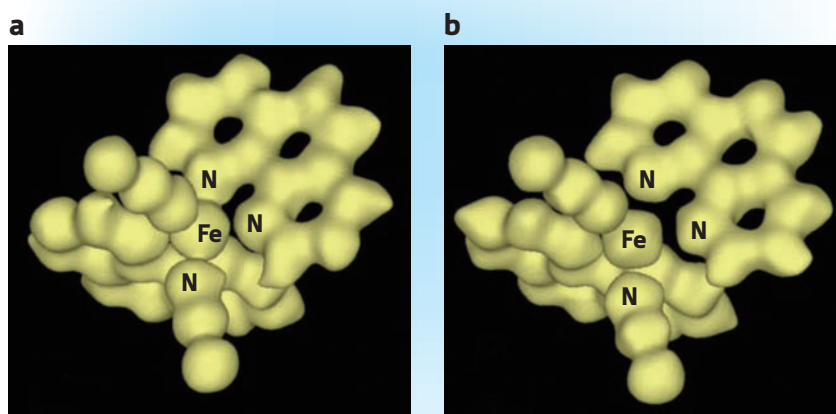


Figure 1: Transformation of $\text{Fe}(\text{phen})_2(\text{NCS})_2$ (phen=1,10-phenanthroline). (a) Low-temperature ground state. (b) The slightly modified molecular bonds between iron and nitrogen under optical illumination.

are important for the magnetism of the compound. In the crystal structure, the iron atom is surrounded by six nitrogen atoms, which form an octahedron—a structure formed by two pyramids attached to each other at their respective bases. The experiments show that the iron–nitrogen bonds in the octahedra are modified in the 'on' state under laser illumination. This peculiar change is the origin of the reversible magnetic properties of the complex.

To improve the switching properties of the molecules, the details and dynamics of this re-arrangement need to be understood. "Our next target is to see the switching process as moving

pictures of the electron distribution using the high-time resolution possible with SPring-8," says Kato. When complete, these experiments could lead to the design of improved molecules for even faster switching and for operation temperatures closer to room temperature. ■

1. Kato, K., Takata, M., Moritomo, Y., Nakamoto, A. & Kojima, N. On-off optical switching of the magnetic and structural properties in a spin-crossover complex. *Applied Physics Letters* **90**, 201902 (2007).

Halting the inflammation overload

Researchers discover a key molecule involved in regulating our immune response

Our immune system protects us against microbial pathogens that invade our cells and cause illness. When receptors on the cell surface detect microbes, a cascade of signals and activities within the cell is triggered, resulting in inflammation, which is part of our early defense against pathogens.

Immunologists from the RIKEN Research Center for Allergy and Immunology, Yokohama, and the Harvard School of Public Health, US, recently published a study on the regulation of this system¹. Without regulation, an unstoppable immune reaction leads to excessive inflammation, which causes conditions such as asthma and arthritis.

The researchers studied a molecule called NF- κ B that contains two different subunits known as p65 and p50 and normally resides in the cytoplasm of cells. When this molecule receives the appropriate signal, it enters the cell nucleus and switches on immunoregulatory genes that encode pro-inflammatory molecules. If the process is not stopped, the immune reaction continues. To terminate this reaction promptly, it is important that the p65 molecule that starts this sequence of events is degraded once it has done its job.

RIKEN's Tsuneyasu Kaisho and his team have identified a pathway that leads to the degradation of p65. Their work shows that the process involves the specific attachment of the protein molecule ubiquitin to p65 followed by transportation of the 'ubiquitinated' p65 to distinct sub-nuclear domains, called nuclear bodies, where it is ultimately degraded by the proteins found there (Fig. 1).

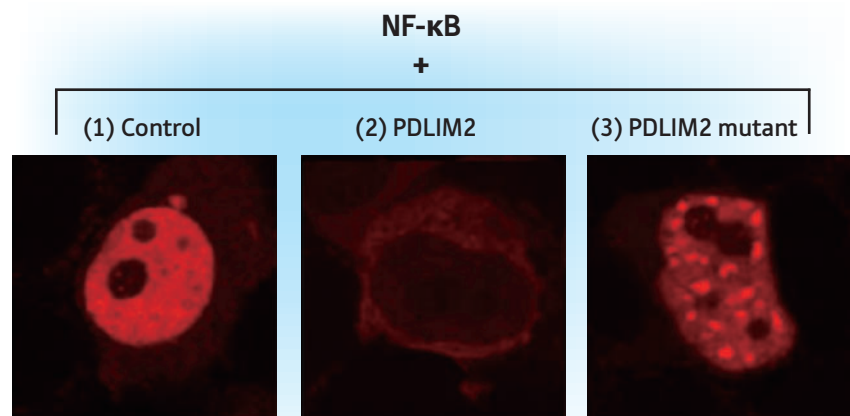


Figure 1: PDLIM2 has two major activities, polyubiquitination of p65 for subsequent degradation and intranuclear targeting of p65 into nuclear bodies. The control (left) shows expression of p65 (stained in red) in the nucleus. The central image demonstrates the absence of nuclear p65, suggesting that p65 is degraded when PDLIM2 is present. The image on the right shows that PDLIM2 transports p65 into nuclear bodies. In this image, the red spotty staining represents the nuclear bodies where p65 has accumulated, since this PDLIM2 mutant has impaired ubiquitin binding activity and intact intranuclear trafficking activity.

Critically, the researchers have described a factor called PDLIM2 that has two highly important roles in the regulation of the immune response. It helps ubiquitin to bind to p65 and then targets this complex to the appropriate nuclear bodies for degradation.

The team showed that PDLIM2-deficient mouse cells had uncontrolled immune responses due to the constant activity of NF- κ B and augmented production of molecules that cause inflammation. *In vivo* studies showed mice lacking PDLIM2 were more sensitive to stimulation of the immune response than mice with normal levels of the molecule.

Developing treatments for inflammatory and autoimmune diseases by modifying the PDLIM2-mediated

pathways to terminate NF- κ B p65 activation is the future aim of the team. According to team member, Takashi Tanaka, the next step towards this goal is to clarify how PDLIM2 activity itself is regulated. This is very important for developing a way to modify its activity in living cells, he says. ■

1. Tanaka, T., Grusby, M.J. & Kaisho, T. PDLIM2-mediated termination of transcription factor NF- κ B activation by intranuclear sequestration and degradation of the p65 subunit. *Nature Immunology* **8**, 584–591 (2007).

A better way to make a muscle?

New revelations about how muscle tissue forms could help scientists develop more effective strategies for therapeutic tissue replacement

Even the mightiest individuals are vulnerable to muscle loss, whether from severe injury, old age, or as a byproduct of disease, and many scientists see the engineering of replacement muscle as a promising solution. Current methods involve the culture of progenitor stem cells, known as myoblasts, for transplantation. These cells in turn fuse and differentiate to form myofibers—mature muscle fibers capable of contraction.

Myoblasts show promise for muscle replacement, but cultured myofibers may be superior for clinical use, and could reduce the risk of tumor formation—a potential hazard with undifferentiated myoblasts. Unfortunately, current strategies for myofiber production have proven inadequate, and myofibers produced from cultured myoblasts tend to be poorly differentiated. “Myoblast transplantation is far ahead of myofiber transplantation,” explains Nobuhiro Morishima, of the RIKEN Discovery Research Institute in Wako. “And one of the reasons for the slow progress of cultured myofiber transplantation is the inefficiency of myofiber formation in culture.”

Previous work by Morishima’s team revealed that differentiation of myoblasts appears to correlate with functional disruption of the endoplasmic reticulum (ER), the cellular organelle responsible for protein folding and processing¹. Now the team has used chemicals that directly trigger this condition, known as ‘ER stress’, in cultured myoblasts to better understand the role of this process in muscle development².

Surprisingly, treated cells responded in different ways; nearly half the treated cells died, via a process known

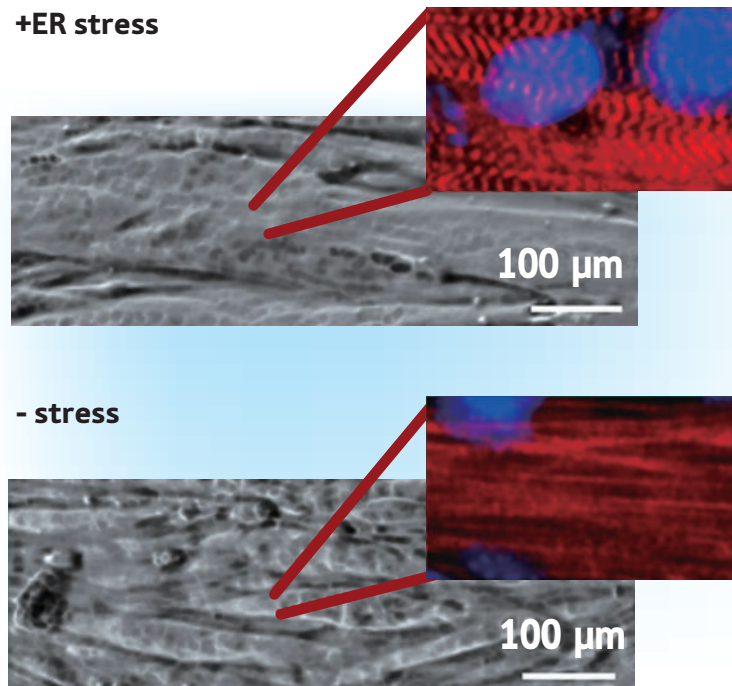


Figure 1: ER stress (top) enhances the formation of myofibers from myoblasts compared with the ‘stressor-free’ control (bottom). The inset image (top) depicts the formation of fully differentiated myofibers with functional muscle contractile units (sarcomeres) following exposure to ER stress.

as apoptosis, while the other cells survived and differentiated to form fully functional myofibers (Fig. 1). Closer examination revealed that the ‘survivors’ were expressing higher levels of Bcl-xL, a protein known to block apoptosis. Morishima suggests that this process of stress-mediated death may be a means for preventing ‘weak’ cells from forming myofibers, as muscle tissue is routinely exposed to stressful physiological conditions. What remains unclear is how otherwise identical cells end up choosing between two different pathways during differentiation, and Morishima hopes to examine this further in the future.

For now, however, his team is encouraged by the high yield of functioning myofibers that can be generated through this culture method, and they are now attempting to better

understand the differentiation process and how to exploit it for biomedical applications. “We would like to answer the question of how the myoblast-differentiating ER stress conditions naturally occur in the body,” he says, “and hopefully we will be able to show the merit of ER stress for myofiber formation *in vivo* for the advancement of both basic biology and clinical research.” ■

1. Nakanishi, K., Sudo, T. & Morishima, N. Endoplasmic reticulum stress signaling transmitted by ATF6 mediates apoptosis during muscle development. *Journal of Cell Biology* **169**, 555–560 (2005).
2. Nakanishi, K., Dohmae, N. & Morishima, N. Endoplasmic reticulum stress increases myofiber formation *in vitro*. *FASEB Journal*, **21**, 2994–3003 (2007).

Observing single cells on the move

Researchers hold a key to studying cancer, wound healing and development

A team of researchers from RIKEN and other Japanese research institutions has developed a flexible technique for studying migration behavior of single cells. It relies on guiding cell movement by creating adhesive pathways through a non-adhesive environment using a light-driven reaction.

With their technique, the researchers are able to study details of the mechanics of how individual cells move. Already, for example, the team has been able to determine that cells which move by extending a broad front known as a lamellipodium travel faster than cells which can only use the much narrower filopodium.

The study is significant as migration of cells is fundamental to important medical processes such as growth and development, wound healing and the spread of cancer. In addition, the new technique allows researchers to guide individual cells into position, thus engineering nerve networks, for instance.

In the past, migration has been

investigated using methods involving monolayers of cells. But cells within layers are unavoidably squeezed into different shapes and orientations and contact variable numbers of other cells, all of which affect movement. So the research team from RIKEN's Discovery Research Institute in Wako, the Japan Science and Technology Agency, and Waseda and Kanagawa universities set about developing a way of studying the motion of individual cells in isolation, free from these influences.

In a recent paper, the researchers describe coating a glass coverslip with a compound to which cells cannot stick¹. The chemical nature of this surface can be changed into one to which cells can adhere by exposure to ultraviolet light. And this can be done with great precision.

The team then prepared coverslips with adhesive patches just big enough for a single fibroblast cell (Fig.1). Leading from those cells they created pathways of adhesive surface in two forms—a broad form, the same width as the patch, which could accommodate lamellipodia, and a

narrow pathway, one fifth the width, only fit for filopodia.

Movement of the cells could be followed under a conventional fluorescent microscope. When presented with a broad pathway, less than 10% of the cells extended filopodia. And those cells which used filopodia for movement traveled only about 80% as fast as those employing lamellipodia.

“We now want to combine this technique with advanced fluorescent microscope technologies to observe the molecular events in migrating cells,” says one of the project leaders, Jun Nakanishi. “We are also hoping to engineer neuronal networks by applying our technique to control the movement of single cells.” ■

1. Nakanishi, J., Kikuchi, Y., Inoue, S., Yamaguchi, K., Takarada, T. & Maeda, M. Spatiotemporal control of migration of single cells on a photoactivatable cell microarray. *Journal of the American Chemical Society* **129**, 6694–6695 (2007).

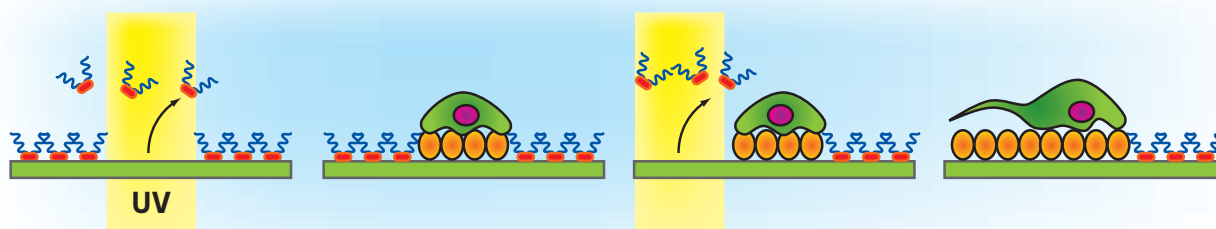


Figure 1: Using UV light to generate an adhesive patch for a single cell on a coverslip (left panels), then initiating its migration by creating a pathway (right panels).

New scaffold supporting our molecular understanding of psychiatric disorders

Researchers establish a causative link between mutations in a single gene and the pathology of psychiatric illnesses

New work in mice indicates that defective function of the molecular ‘scaffold’ protein *Disc1* results in behaviors resembling human schizophrenia and depression. Current treatments for these devastating diseases are palliative but not curative.

Prior work hints at a link between *Disc1* and psychiatric illness. Some mood disorders in humans are ameliorated by drugs suppressing the function of PDE4B: a protein that binds to molecular scaffolds including *Disc1* and metabolizes cAMP, a compound essential for transmission of cellular signals. From studies in humans, scientists are also aware of associations between *Disc1* mutations and the incidence of psychiatric illnesses. However, whether these mutations altered *Disc1* function, and thus whether *Disc1* dysfunction actually contributed to brain pathology, was not determined.

An international group led by Yoichi Gondo, a scientist at RIKEN Genomic Sciences Center in Yokohama, used a mouse model to forge a causative link between alterations in *Disc1* function and the pathology of psychiatric disorders. This work was published in a recent issue of *Neuron*¹.

The researchers used a chemical mutagen to scatter random infrequent mutations throughout the genome of laboratory mice, and extensive DNA sequencing to identify two mice that each contained a distinct mutation predicted to change the sequence of the PDE4B-binding region of *Disc1*.

Like brains of some patients with mood disorders, brains in mice expressing mutated versions of *Disc1* were of small volume (Fig. 1). However, although

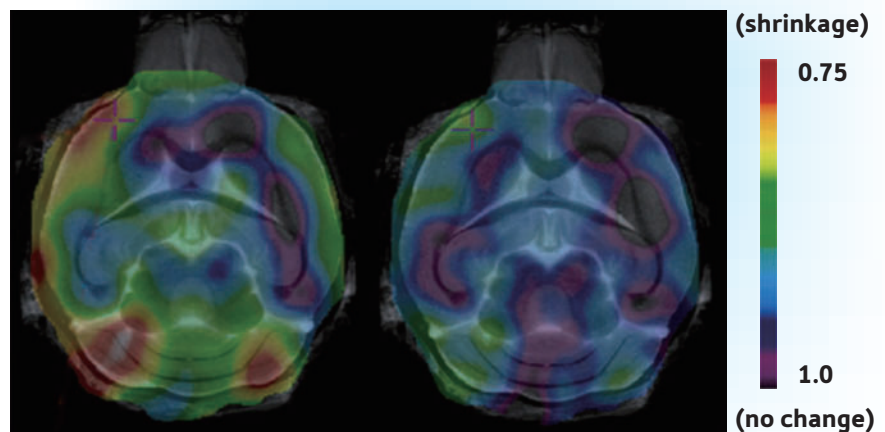


Figure 1: Brains of both *Disc1* mutants were smaller than those of unmutated mice. Left and right panels depict the average shrinkage patterns of several brains from schizophrenia-like and depression-like mutants with overall reduction of total brain volume to be 13% and 6%, respectively.

both mutated *Disc1* proteins exhibited impaired binding to PDE4B, only one *Disc1* mutant reduced PDE4B activity.

Mice expressing this *Disc1* mutant exhibited behaviour characteristic of depression; these mice displayed reduced sociability and disinterest in pleasurable activities. In contrast, mice expressing the *Disc1* mutant that left PDE4B function intact failed to process and respond to distracting stimuli; this behaviour is more reminiscent of humans with schizophrenia. PDE4B inhibitors ameliorated the behaviour only of mice expressing the latter mutant.

Whether mutations having similar consequences on *Disc1* function arise naturally in humans is unknown. Nevertheless, these findings reveal a complex role of *Disc1* in brain function, and suggest that psychiatric disorders

caused by distinct lesions of *Disc1* may require different treatments.

“Studies in mouse models should lead to precise molecular diagnostics for psychiatric illness and allow us to develop preventive and therapeutic medicines. The RIKEN mutant mouse library (<http://www.gsc.riken.jp/PQG/genedrivern.htm>), from where these *Disc1* mutant mice were obtained, provides mouse models for the study of many human diseases,” says Gondo. ■

1. Clapcote, S.J., Lipina, T.V., Millar, J.K., Mackie, S., Christie, S., Ogawa, F., Lerch, J.P., Trimble, K., Uchiyama, M., Sakuraba, Y., Gondo, Y. *et al.* Behavioral phenotypes of *Disc1* missense mutations in mice. *Neuron* **54**, 387–402 (2007).

Wrapping up a cell biology riddle

New research has revealed how protein filaments drive a key cellular process by physically wrapping around and constricting bits of cell membrane

The process of endocytosis, by which a cell internalizes molecules bound to outward-facing receptors, is essential for a wide variety of cellular functions. During the first steps of endocytosis, the cell membrane invaginates, puckering inward to form a pocket that is ultimately pinched off to become a bubble-like vesicle, which can act as a vehicle for delivering encapsulated molecules to various locations within the cell.

This invagination requires the assembly of various proteins into complexes that associate with the membrane and induce deformation and the subsequent formation of membrane ‘tubules’. Tadaomi Takenawa’s group at the Kobe University Graduate School of Medicine has focused much of their work on these proteins, and recently identified a protein domain known as EFC/F-BAR that plays a direct role in membrane tubulation¹. At the same time, Shigeyuki Yokoyama’s research team at the RIKEN Genomic Sciences Center in Yokohama was studying the Cdc42-interacting protein (CIP4), which happens to contain a functional EFC domain. Yokoyama and Takenawa decided to collaborate on an in-depth structural analysis of EFC in an effort to clarify its function.

They found that EFC domains pair off to form crescent-shaped dimers—much like BAR, another known membrane-binding domain, although the curve is far subtler for EFC domains². “This explains why the EFC domain generates tubular membranes with diameters that are several times larger than those induced by the BAR domain,” says Yokoyama. Surprisingly, the structural

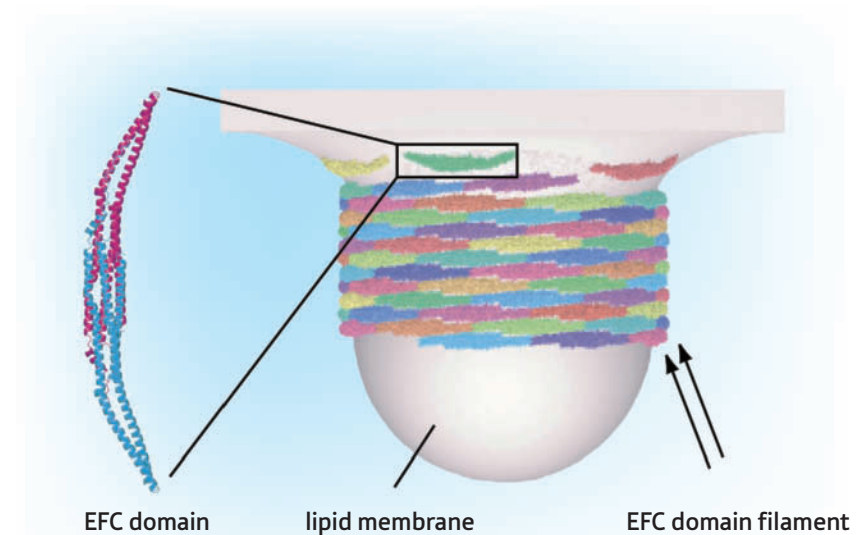


Figure 1: A model for membrane tubulation by the EFC domain—EFC dimers join end-to-end to form filaments that wrap around the tubular membrane, increasing the invagination.

data also suggested that these EFC dimers can further assemble into lengthy filaments, which can tightly wrap around—and thereby extend—tubulations in the cell membrane (Fig. 1). Subsequent microscopic analysis of EFC-induced tubular membranes would demonstrate that this model was accurate. “The physiological function of the EFC filament was predicted by the structure-function analysis of the EFC domain,” says Yokoyama.

Based on these findings, Yokoyama, Takenawa and colleagues were able to develop a more sophisticated model for endocytosis, where EFC proteins like CIP4 drive early stages of invagination through filament formation, then gradually recruit additional proteins like dynamin, which further constrict the tubules before pinching them off to form mature vesicles.

Yokoyama doesn’t think this is the end of the story, however, and his

group is continuing to investigate EFC proteins with Takenawa’s team. “We would like to investigate the function of the full-length protein and its interaction partners,” he says, “because we believe that yet unknown, interesting regulatory mechanisms are hidden in this molecule.” ■

1. Tsujita, K., Suetsugu, S., Sasaki, N., Furutani, M., Oikawa, T. & Takenawa, T. Coordination between actin cytoskeleton and membrane deformation by a novel membrane tubulation domain of PCH proteins is involved in endocytosis. *Journal of Cell Biology* **172**, 269–279 (2006).
2. Shimada, A., Niwa, H., Tsujita, K., Suetsugu, S., Nitta, K., Hanawa-Suetsugu, K., Akasaka, R., Nishino, Y., Toyama, M., Chen, L. *et al.* Curved EFC/F-BAR-domain dimers are joined end to end into a filament for membrane invagination in endocytosis. *Cell* **129**, 761–772 (2007).

Enzymes lead the way

A protease enzyme called MIG-17 points cells in the right direction during the development of organs

During the growth and development of organs, proteins act from outside the organs to direct the movements of cells. Researchers at the RIKEN Centre for Developmental Biology in Kobe have identified one such protein that is essential for the development of gonads in the nematode roundworm *Caenorhabditis elegans*¹.

In *C. elegans*, the gonads grow along the body wall and then turn through 180°, making two U-shaped gonad arms. The movement is directed by two specialized leader cells called 'distal tip cells' (DTCs). The researchers found that when they inhibited the activity of a proteolytic enzyme called MIG-17, the DTCs failed to function properly, resulting in misshapen gonads.

"We mutagenized wild-type worms with [a] chemical mutagen and isolated many mutant worms with misshapen gonads," says group leader Kiyoji Nishiwaki. "The MIG-17 mutant is one of these isolates and was found to encode a protein of the ADAMTS protease family."

The MIG-17 enzyme is secreted from muscle cells, and is initially folded over to hide an active zinc ion (Fig. 1). The researchers discovered that actions in part of the MIG-17 molecule called the prodomain are essential for moving the molecule to the gonad. However, the prodomain must first be modified by another protein, MIG-23, in a process called glycosylation.

Previous studies had indicated a role for the prodomain in protein folding and secretion, but this is the first time it has been shown to be crucial for targeting the whole MIG-17 molecule to the gonad. "It is possible that prodomain targeting

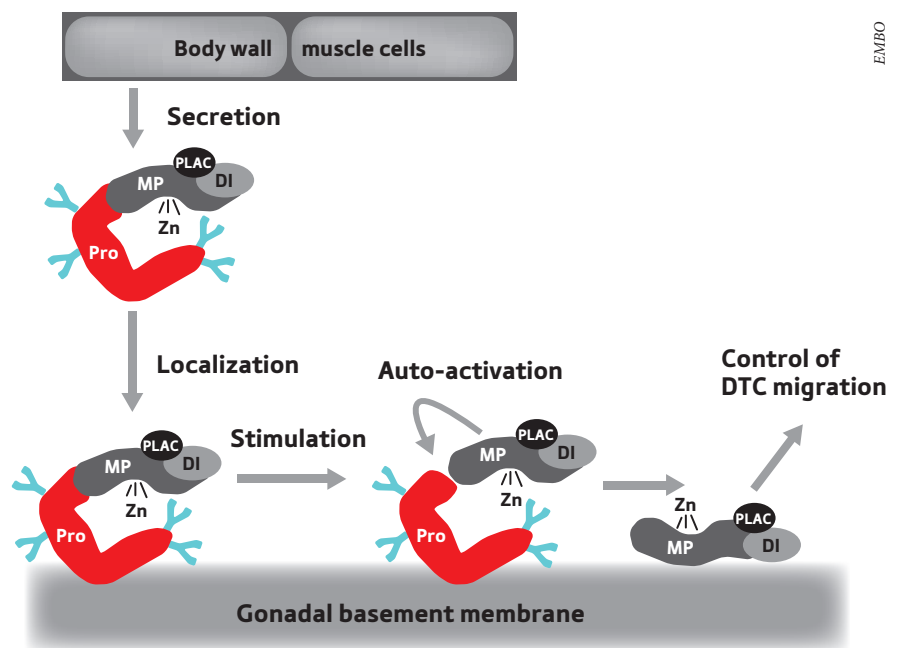


Figure 1: MIG-17 is secreted from muscle cells and relocates to the gonad, dependent on action of the prodomain (Pro). An unknown stimulus then causes cleavage of the molecule, leaving the metalloprotease (MP) domain exposed with an active zinc (Zn) ion that controls migration of the distal tip cells (DTCs) during growth of the gonad.

is one of the key strategies employed by ADAMTS proteins to localize to specific tissues," says Nishiwaki.

Once the MIG-17 molecule reaches the gonadal membrane, an unknown stimulus initiates autocatalytic cleavage of the molecule. The prodomain falls off, leaving the active zinc ion exposed (Fig. 1). "The zinc ion probably degrades a specific substrate in the gonadal membrane and thereby acts in directing DTCs," explains Nishiwaki.

In humans, mutations in ADAMTS proteins cause various hereditary diseases related to disorders in connective tissues. MIG-17 is most similar to an enzyme called ADAMTS-10 that may have a role

in organ development in humans.

"ADAMTS-10 is a causative gene for Weill–Marchesani syndrome [in humans], characterized by short stature, shortness of fingers and toes and eye abnormalities," says Nishiwaki. "Abnormalities of internal organs may also occur, although this is not examined yet."

1. Ihara, S. & Nishiwaki, K. Prodomain-dependent tissue targeting of an ADAMTS protease controls cell migration in *Caenorhabditis elegans*. *The EMBO Journal* **26**, 2607–2620 (2007).

Surviving separation

ROCK-blocked human embryonic stem cells survive dissociation to grow in culture

Japanese researchers may have found a simple solution to the problem of keeping human embryonic stem (hES) cells alive after dissociation of the embryo into individual cells. Inhibition of the enzyme rho-associated coiled-coil kinase (ROCK), which is believed to play a role in the initiation of apoptosis or programmed cell death, results in a marked reduction in dissociation-induced apoptosis, and an increase in cloning efficiency.

Human embryonic stem cells hold much potential for the treatment of many diseases, but the cells have proven far more difficult to grow in culture than murine embryonic stem (mES) cells. The poor survival of dissociated cells in culture has hindered efforts to isolate or subclone specific populations of cells after the induction of differentiation or gene transfer.

The researchers, at the RIKEN Center for Developmental Biology, Kobe, Japan's National Center for Geriatrics

and Gerontology and Kyoto University, have recently published their findings in *Nature Biotechnology*¹. They showed that the cloning efficiency of cells treated with the compound Y-27632, which selectively inhibits ROCK, increased from around 1% in untreated cells to 27% in the treated cells (Fig. 1).

The cells treated with Y-27632 could also be grown in a serum-free suspension culture and induced to differentiate into precursor cells that resemble the cells of the embryonic brain and neural system.

Team leader Yoshiki Sasai says while it isn't well understood why hES cells are so prone to apoptosis after dissociation, a better understanding of the role of ROCK in triggering apoptotic cell death may provide some answers.

"This is one of the most interesting questions for future study: why hES cells, but not mouse ones, are so prone to go apoptotic upon dissociation," he says. "We have no answer for it, and are currently

comparing these two systems both upstream and downstream of ROCK."

In the meantime, the use of Y-27632 to improve cell survival and cloning efficiency will enable researchers to manipulate hES cells with greater ease, allowing large-scale dissociation culture, and easier isolation of genetically modified cells after gene transfer as well as the ability to establish cell lines of hES cells from a single cell.

Ultimately, Sasai says, the use of hES cells may lead to new therapies for degenerative diseases and intractable conditions including Lou Gehrig's disease (amyotrophic lateral sclerosis (ALS)) and other neurological diseases. ■

1. Watanabe, K., Ueno, M., Kamiya, D., Nishiyama, A., Matsumura, M., Wataya, T., Takahashi, J.B., Nishikawa, S., Nishikawa, S., Muguruma, K. & Sasai, Y. A ROCK inhibitor permits survival of dissociated human embryonic stem cells. *Nature Biotechnology* **25**, 681–686 (2007).

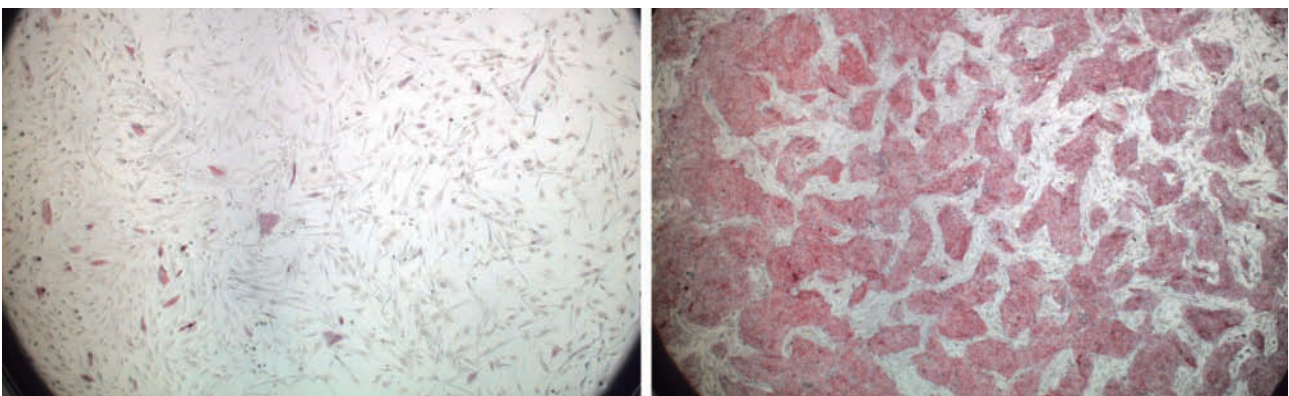


Figure 1: Increased survival of hES cells in dissociation culture (red) after treatment with ROCK inhibitor Y-27632 (right); compared with untreated hES cells (left).

Towards the creation of Astro Boy's brain

Shiro Usui

Director, Neuroinformatics Japan Center,
and Laboratory Head, Laboratory for
Neuroinformatics
Advanced Technology Development Group
Brain Science Institute

Recently, remarkable advances have been made in brain science, and an enormous amount of knowledge is being produced on a daily basis. If the development of brain science continues at this speed, can we expect the day to come when we can say that we have perfectly understood the human brain? "What's happening now is that, because current brain science is becoming more specialized and segmentalized, it is hard to integrate this knowledge, and so we cannot get a complete picture of the brain," says Shiro Usui, director of Neuroinformatics Japan Center. To cope with this difficulty, researchers around the world have started exploring neuroinformatics, in which information and communication technologies are used to commoditize and integrate knowledge. The dream of Usui and his laboratory members is to get closer to Astro Boy's brain.



Worldwide collaborative efforts to understand the brain

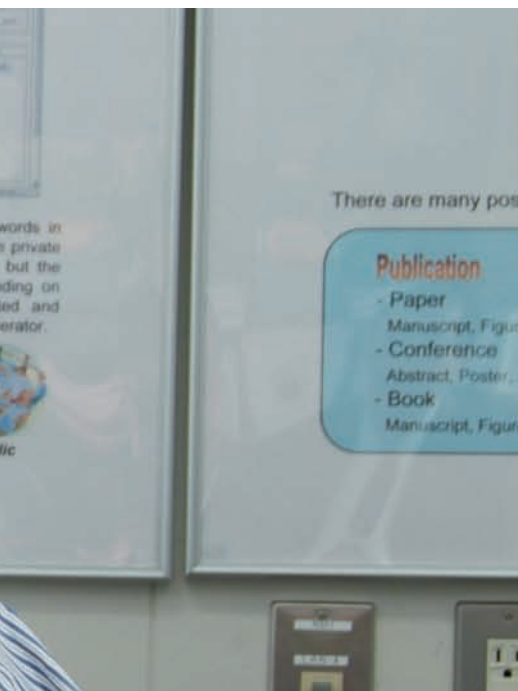
"When I was a child," Usui reminisces, "I used to read the manga magazine 'Astro Boy'. Astro Boy was born on April 7, 2003, so he will soon be four years old." In the real world, however, we do not yet have humanoid robots with human will. Why is this? "This is because a large part of the brain still remains unknown," says Usui.

Usui points to one of the important problems in current brain science. "Each researcher conducts studies mostly focused on a small part of the brain," he explains. "For example, I have been conducting research on the visual system, but it is difficult for me to follow in detail research in other areas, such as the auditory system." He adds that today, research in many fields has been advancing at a dizzying speed. However, the researchers belong to different academic societies, submit their papers to different journals, and use different technical terms. "Thus, it is impossible for a single researcher to elucidate the function of the brain as a whole."

In the human brain, as many as 100 billion neurons form a complex network, which functions as a system that interacts with the external world. Then, how can we integrate knowledge on the human brain in order to understand the whole brain system? "I believe that neuroinformatics is the only means that will allow us to truly understand the human brain," says Usui.

Neuroinformatics is a method that allows us to understand the mechanisms of the brain; all knowledge of the human brain available in the world is commoditized and integrated by making use of information technology and information science, such as the Internet and computer simulations. "I call neuroinformatics the brain science of the IT age," says Usui.

Now neuroinformatics has become an international undertaking; the International Neuroinformatics Coordinating Facility (INCF) was established in 2005. In addition, the Neuroinformatics Japan Center (NIJC), whose former director was



Shun-ichi Amari) was established in the RIKEN Brain Science Institute (BSI) to promote and coordinate neuroinformatics activities within Japan and to represent Japanese efforts in INCF. NIJC started preparations for establishing an INCF Japan-Node, INCF's base in Japan, which was inaugurated in February 2006.

Usui explains that what is important in neuroinformatics is combining various pieces of knowledge on the brain and constructing mathematical models to describe its essence, because mathematics is the common language of science. "Through the process of running simulations with these mathematical models, to confirm their applicability to the functions of the brain, we aim to understand the mechanism of the brain," says Usui. He adds that the ultimate goal of neuroinformatics is to describe the whole brain functions on a computer. In this sense, it could be said that researchers around the world have now started creating Astro Boy's brain.

Promotion in an all-Japan framework

Simulation based on a mathematical model enables us to verify the validity of the model by comparing the simulated results to the experimental ones. Furthermore, the simulation also helps us predict the existence of unknown cells. Usui describes how under the national project on Neuroinformatics in vision, one of the model simulations successfully predicted the existence of 'collision-avoidance cells', which calculate the moment when a gannet plummets into the sea for fish and send collision avoidance signals just before diving. Activation of these cells triggers the gannet to furl its wings and enter the sea smoothly. The existence of such cells was verified by experiments on macaque monkeys. "Through repeatedly running simulations and performing experiments, we can unveil the mechanisms of the brain," says Usui.

Simulation can also be used to predict the side effects of drugs. A clinical trial on a heart arrhythmia drug indicated a side effect in which afterimages remain in the visual field of the patient. "Using simulation," explains Usui, "We successfully pinpointed the exact cause; the phenomenon is caused by the drug acting on a certain type of ionic channel activated in a photoreceptor, which we

managed to demonstrate by experiment. If we can use simulation techniques to effectively predict side effects, the cost of developing new drugs could be drastically reduced."

However, Usui points out that it has been almost impossible for other scientists to use such simulation models to advance their own research. "This is because these kinds of simulation programs have not been put in the public domain," says Usui. Other scientists will find it very difficult to develop programs only on the basis of the information disclosed in papers. "In addition," he points out, "We often found that programs were mislaid or lost following a researcher's retirement."

Usui and his team members have established the Visiome Platform, a digital research resource archive for vision science, and it is now available for public access (Fig. 1). "Our strategy is to integrate papers, experimental data, and references relating to mathematical models and their simulation programs together, so that they can be accessed from the Internet," he says. This will enable researchers all over the world to download various simulation programs to their own computers, making the most use of the programs. "Researchers would be able to follow what we have done, and then indicate drawbacks or problems with the mathematical models,

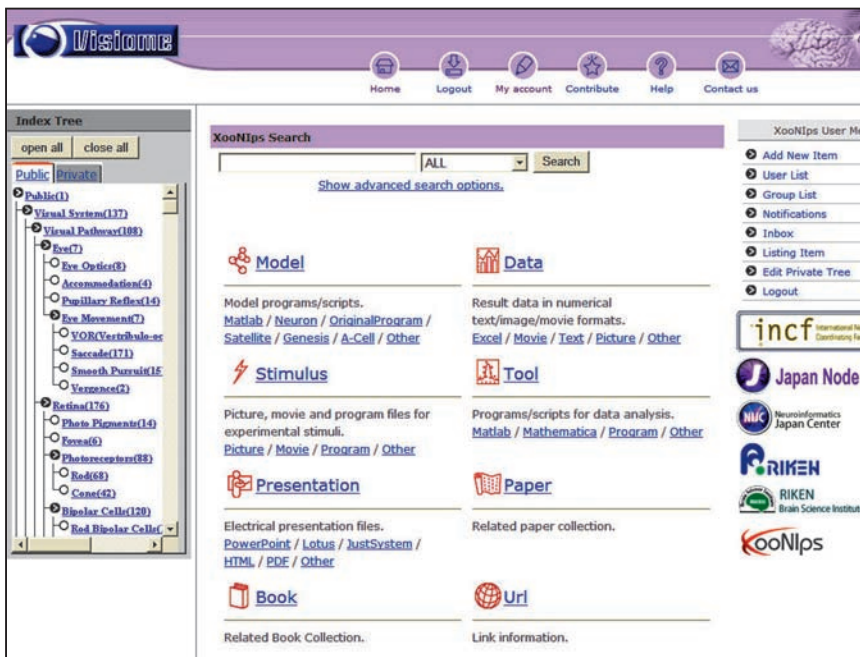


Figure 1: Visiome platform.

or combine the program with other programs, thereby advancing their own research programs,” says Usui. “We want to construct a system in which the latest knowledge is combined on this kind of database so that researchers in the field can share research information through the Internet. Through this process, the knowledge will be integrated to promote the development of neuroinformatics.”

Usui and his team members have developed XooNips, a base platform that inherits the basic specifications and functions of the Visiome platform and puts it in the public domain in Japan (<http://xoonips.sourceforge.jp/>). “We have asked expert researchers in various fields to establish and maintain their databases platform under the Japan-Node,” says Usui (See Fig. 2). The databases will be useless unless they are developed by top researchers of the respective research area, so the members are top scientists representing brain science in Japan. Focusing on Japan’s distinguished research area, INCF Japan-Node has started promoting neuroinformatics in an all-Japan framework.

Other countries participating in the INCF are also considering using

XooNips. Furthermore, XooNips is attracting attention not only in brain science but also in other fields. Today, librarians in universities are establishing an Institutional Repository, or a system in which to store research archives. For example, Keio University has launched a XooNips-based database, ‘KOARA (Keio Academic Resource Archive)’. In addition, other universities and colleges are also considering using XooNips. “This is something we never expected to happen,” Usui adds. Through these means, the methodology of neuroinformatics will contribute to storing, commoditizing, and integrating currently segmentalized academic achievements.

Unveiling the mystery of the brain

“There is a phenomenon in which a person’s voice is heard differently when the person changes the shape of his or her lips,” says Usui. “This shows that visual perception can affect our perception of sound.” He explains that vision researchers, who want to study this phenomenon, have had to study the auditory system and build up their own auditory model from scratch. “This does not seem very efficient,” he adds. “When the platform we suggest is put in place,

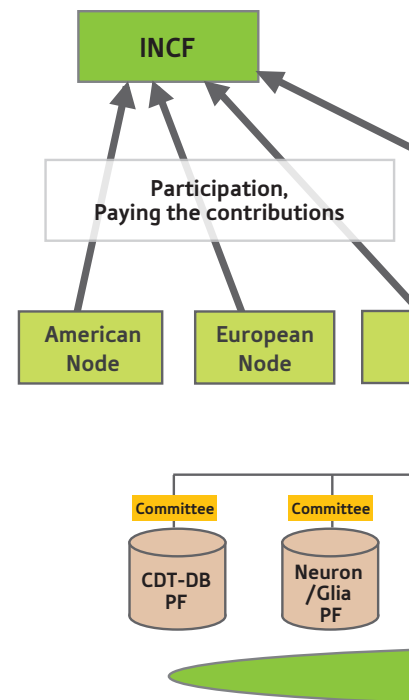


Figure 2: INCF Japan-Node scheme (July 2007).

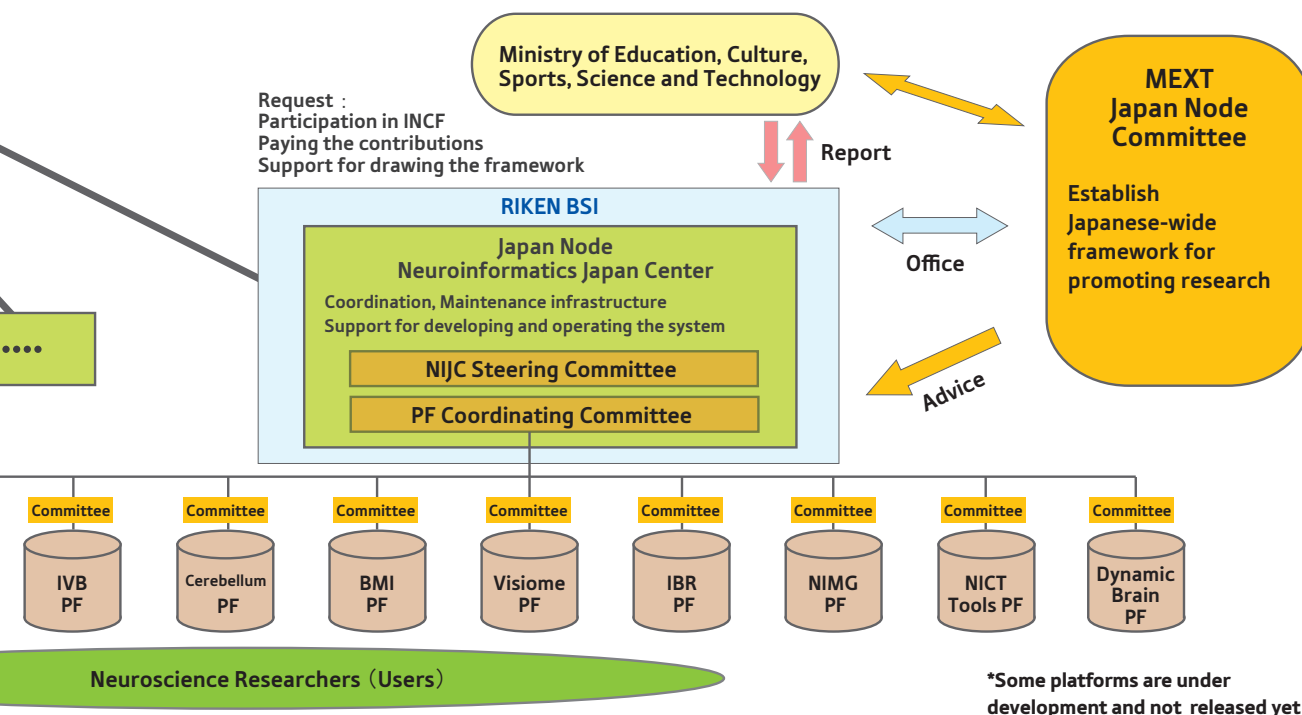
vision researchers can, for example, download a model of the auditory system from their platform and combine the model into their vision models to simulate the interaction between the visual and auditory systems.”

This approach will enable researchers to step closer to the ‘binding problem’, one of the most difficult brain-related questions. For example, information on colors and shapes are processed in different areas in the brain. However, it is not known how the information is combined such as, for example, how a moving red ball and a blue box are recognized in the brain. This remains a big mystery.

“Today, brain science is rapidly progressing especially in the analysis of DNA and proteins at the molecular or neuron level,” says Usui. “However the most mysterious mechanism in the brain is how the information is processed in different areas and how it is integrated and recognized.”

Towards a Neuro-Renaissance

“I have devoted myself to what I find interesting,” says Usui, looking back on his life. In 1992, he even participated in the space experiment with a carp that



astronaut Mamoru Mouri conducted during the mission of the Space Shuttle Endeavor. The experiment was intended to clarify how the vestibulo-ocular system causes space sickness. Usui talks about how attractive it is to study the visual system. “Our ability to see is amazing,” he says. “There is no other miracle like this.” As an example, he describes how each eye receives information about the external world as a two-dimensional image. In addition, the left and right retinas only capture two images that are insufficient for the brain to reproduce a three-dimensional world. Thus, the brain complements the necessary information on the basis of various assumptions, and then reconstructs the three-dimensional image. “Also our ability to recognize colors is also something of a miracle,” he adds. Physically, no color exists in the real world. “We perceive a light with a certain wavelength as a sensation of color. In other words, what we see is only an image created by the brain.”

Usui continues, “We plan to exploit neuroinformatics on a long-term basis; our generation creates mathematical models for various brain functions, then, the next generation will integrate them. This is the timescale that we

are trying to work toward to establish Neuroinformatics.” He draws an analogy between these efforts and those of Gaudy in building Sagrada Familia—an unfinished church still under construction 100 years later. “Both require a long-term commitment and evoke a sense of romanticism in mankind.”

So when does he expect to reach the ultimate goal of neuroinformatics, that is, the creation of a man-made brain as represented by Astro Boy’s brain? “I recognize it is not such an easy goal to reach,” he concedes. “I even think that we might never be able to reach that far. This is why doing research in neuroinformatics is just like chasing an eternal dream of mankind.”

What will be the benefit of such an ambitious dream? “Science, philosophy, and religion are all deeply related to the brain. I hope that our efforts in advancing neuroscience will help to harmonize these creations of our brains and, as a result, provide mankind with a clue as to how to live a peaceful and enjoyable life on this precious Earth.” He adds, “This is our eternal dream. I wish such days may come in the future and open the door to the ‘Neuro-Renaissance’ age.”

1. Usui, S. Neuroinformatics - focused on vision system. Ohmsha (2006) (in Japanese).
2. Usui, S. Virtual brain project – Neuroinformatics aspect. *Seitai no Kagaku* 57, 310–314 (2006) (in Japanese).

About the researcher

Shiro Usui was born in Quigdao China in 1943. He graduated from the University of California, Berkeley, in 1974, and obtained his PhD in electrical engineering and computer science. He then became a research assistant at Nagoya University. He moved to the Toyohashi University of Technology in 1979, as a lecturer, and has been a professor since 1986. In 2003 he moved to the RIKEN Brain Science Institute, as head of the Neuroinformatics Laboratory, and became the director of the Neuroinformatics Japan Center in 2007. His research interests are Neuroinformatics, computational neuroscience and physiological engineering in vision science. He is the author of Neuroinformatics, Mathematical Models of Brain and Neural Systems, and several other books. He is a fellow of the IEEE and the IEICE and was the president of the Japanese Neural Network Society during 2005 and 2006.

RIKEN leads project to build world's fastest supercomputer

RIKEN has taken on the challenge of developing the world's fastest and most efficient supercomputer.

The computer is to boast a performance of 10 petaflops (that is, 10^{16} floating-point operations per second) in a general-purpose, compound configuration. RIKEN is to jointly develop the supercomputer with three major manufacturers, Fujitsu Corp., NEC Corp., and Hitachi Ltd, and if all goes according to plan, the new machine will be in operation by 2012.

The supercomputer will be a compound general-purpose configuration, and the project will incorporate the integrated

development of both supercomputer and software. The system will feature both a scalar and a vector section, and it will incorporate cutting-edge technology, including 45 nm semiconductor processes and optical interconnection, to achieve compact size and relatively low electric-power consumption for a computer of this capability.

RIKEN will act as project headquarters for the academic-industrial collaboration. When complete, the supercomputer facility will be opened up for use by academic, industrial, and governmental bodies for everything from basic research to commercial

applications. Its general-purpose nature will allow it to be used in a wide range of fields of scientific research, from life sciences to nanotechnology.

The project was instigated on orders from the Ministry of Education, Culture, Sports, Science and Technology, to develop the "world's leading general-purpose supercomputer and the software to use it". The Ministry also called for the establishment of the world's most advanced supercomputing Center of Excellence, with the new supercomputer at its center. The Next-Generation Supercomputer R&D Center was established by RIKEN in January 2006. ■

Powerful yet soft—RI-MAN, the caring robot

RIKEN and Tokai Rubber Industries Ltd (TRI) have teamed up to create a workable robot that can flexibly interact with humans and carry out a variety of heavy physical tasks, including lifting and carrying people.

Its creators at the RIKEN-TRI Collaboration Center for Human-Interactive Robot Research expect the humanoid robot, dubbed RI-MAN (for robot interacting with human) to find applications in nursing care for the elderly.

By combining the know-how in motion-type system control of researchers at the RIKEN Bio-Mimetics Control (BMC) Research Center with TRI's advanced capability material, 'smart rubber', the group built the robot, which can interact gently and flexibly with humans. Its arms and torso are equipped with soft tactile sensors that measure the magnitude and position of a contact force, and feedback from these sensors enables the robot to interact safely with humans.

The robot's assortment of visual, auditory, tactile, and olfactory sensors is integrated with

motor functions of multiple servo motors by a hierarchical distributed processing system that mimics the human brain. The robot incorporates a 'whole-body manipulation system', in which pairs of embedded motors produce coupled output power to use different parts of the body, much as a person lifts an object with all of his or her muscles. Each of RI-MAN's arms has six joints, each driven by six motors, which operate in pairs in a mechanism called a 'coupled drive', to enable combined bending and twisting motions. This mechanism enables the shoulder and elbow motions needed to lift and hold a person. The robot can carry objects of up to 35 kg.

The robot identifies human faces using visual data from stereo cameras, and can localize the position of a speaker's voice with onboard microphones.

BMC and TRI have been involved in collaborative research since November 2004. ■

from Japan, Canada, Germany, the UK, and the USA, and students from the RCAI International Summer Program.

The first day's talks concerned the development of the immune system and mechanisms of lymphocyte selection. Toshio Suda (Keio University) described the importance of the osteoblast, a cell normally thought of in terms of its role in bone formation, in the stem-cell niche, a specialized microenvironment where the hematopoietic stem cells reside in an inactive state. Juan Carlos Zúñiga-Pflücker (University of Toronto, Canada) demonstrated an important role for Notch signaling in early T cell development. A Notch signal is required for expansion of $\alpha\beta$ T cells and their survival at the single positive stage, whereas the $\gamma\delta$ T cells can survive without Notch once they express a T cell receptor.

Differentiation of lymphocyte subsets and the maintenance of a functional immune system were the focus of the second day's talks. Brigitta Stockinger (National Institute for Medical Research, UK) described physiological inducers for the development of Th17 cells, a recently described subset of helper T cells that produce IL-17. Marc Jenkins (University of Minnesota Medical School, USA) discussed strategies to enumerate polyclonal antigen-specific CD4 T cells in unimmunized mice. From RCAI, Masato Tanaka demonstrated that he had developed a system for tolerance induction in experimental autoimmune encephalomyelitis, a mouse model for human multiple sclerosis.

The next RCAI-JSI International Symposium on Immunology is tentatively scheduled for June of 2008. ■

Development and Maintenance of the Immune System Symposium

On July 26 and 27, the RIKEN Research Center for Allergy and Immunology (RCAI) and the Japanese Society for Immunology (JSI) jointly held an international symposium on immunology at the Pacifico Yokohama Conference Center. The third meeting of this series of symposia was entitled 'Development and Maintenance of the Immune System', reflecting the increasing interest in microenvironments, signaling, and cytokines essential for development and maintenance of the immune system. More than 350 people participated in the meeting, including speakers



RI-MAN weighs in at 100 kg and is 158 cm tall.

Opening to the outside world

Embracing the global spirit of its forerunners, RIKEN continues to seek opportunities to learn from overseas scientists and present new research approaches to the world

Science is borderless. Since it was founded in 1917, RIKEN has kept forging ahead by interacting with the world's top scientists. Despite its tight financial situation in the 1920s and the 1930s, RIKEN sent promising young scientists to study abroad, while attracting the world-famous scientists, such as physicist Albert Einstein and chemist Francis Aston to visit RIKEN.

After World War II, RIKEN entered decade-long hard times, and interactions with overseas researchers were disrupted. Fortunately in the late 1950s, RIKEN researchers began obtaining scholarships from the US and Europe. Momentum for international collaborations heightened in the late 1970s, when RIKEN's international visibility increased after becoming the world's frontrunner in such fields as cyclotron research and solar power energy.

At this time, RIKEN initially sought collaborations with other Asia-Pacific countries, including Indonesia and Australia. RIKEN also worked with US universities on photosynthesis research under an agreement to collaborate bilaterally on energy research (see History of RIKEN, *RIKEN RESEARCH 1* (6), p. 18).

In 1980, physicist Tatsuoki Miyajima became RIKEN's fifth president and he actively proceeded with internationalization. During the early 1980s, RIKEN signed collaboration agreements with the Chinese Academy of Sciences, and the Korea Advanced Institute of Science and Technology, the Pasteur Institute in France and the Max Planck Society in Germany.

In 1986, Miyajima also inaugurated the 'Frontier Research Program,' under which RIKEN recruited many top-level researchers from across the globe (see History of RIKEN, *RIKEN RESEARCH 2* (6), p. 18).

Miyajima's global spirit was actively pursued by his successors. Sixth president and astronomer Minoru Oda implemented joint research into gamma-ray bursts in the space with the Massachusetts Institute of Technology (MIT) and France's CNES (Centre National d'Etudes Spatiales). Later in 1998, brain science was added to the RIKEN-MIT collaboration.

Seventh president and nuclear physicist Akito Arima generously supported fledgling scientific initiatives in war-torn Vietnam. In 1997 RIKEN opened the Computer Center for Nuclear Science at the Institute of Nuclear Science and Technique in Hanoi to help Vietnamese nuclear physicists conduct theoretical analyses and verify experimental data.

RIKEN's most significant alliances were created with the Rutherford Appleton Laboratory (RAL) near Oxford, UK, and the

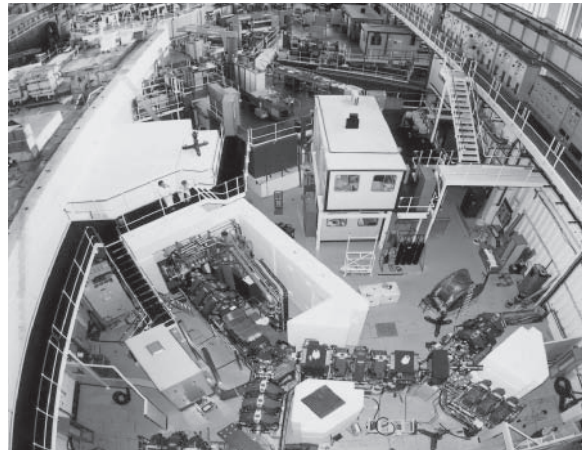


Figure 1: RIKEN's muon facility (equipment in the foreground) was established at the Rutherford Appleton Laboratory in 1995 in the UK.

Brookhaven National Laboratory (BNL) in New York, US.

In the mid-1980s, researchers at RIKEN felt they needed to have their own facility to produce the 'muon'—a heavy elementary particle with a negative electric charge—so they could investigate metal properties without relying on other institutes. Building a facility at RAL, one of the world's leading particle physics research institutes, was considered the best way forward. As its first project to build an experimental base abroad, RIKEN had to overcome difficulties including tax issues and tough negotiations. The first beam of pulsed muons was successfully generated at the new Muon Research Facility in 1994 (Fig. 1). In 1995, the RIKEN Facility Office was also established at RAL.

Lessons learned from the RAL project were applied to RIKEN's next large project based overseas. In early the 1990, when BNL was building the Relativistic Heavy Ion Collider (RHIC) to study the birth of universe, it asked RIKEN to join its two large-scale teams named STAR and PHENIX. RIKEN accepted and saw the opportunity to launch original research, known as 'spin physics,' designed to study the spin properties of particles. RIKEN's proposal was accepted in 1995 and the RIKEN BNL Research Centre was established in 1997.

Currently, RIKEN's international spirit manifests as significant research outcomes both at home and abroad. The number of foreign researchers at RIKEN has increased dramatically from 37 in 1980 to more than 600 at present. At the RIKEN-RAL facility, RIKEN's scientists are exploring new fields such as protein and DNA research, while those at the BNL have developed a novel 'snake' magnet to study the spin properties of sub-particles (see 'Seeking the full story of spin,' *RIKEN RESEARCH 1* (2), p.10). Further down the road, RIKEN knows it will not produce notable findings without contribution from international partners. ■



www.rikenresearch.riken.jp

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.

RIKEN RESEARCH is a website (www.rikenresearch.riken.jp) and print publication intended to highlight the best research being published by RIKEN (www.riken.jp). It is written for a broad scientific audience and policy makers interested in science and aims to raise global awareness of RIKEN and its research.

For further information on the research presented in this publication or to arrange an interview with a researcher, please contact

RIKEN Public Relations Office

2-1, Hirosawa, Wako, Saitama, 351-0198, Japan

TEL: +81 48 467 4094

FAX: +81 48 462 4715

E-Mail: rikenresearch@riken.jp



Percentage of Waste Paper Pulp 100%