RIKEN RESEARCH

APRIL
2008 Volume 3 Number4

The unique modes of quasi-crystals

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Immune cells stimulated by calcium levels

Calcium sensors may play a pivotal role in the allergic response

A team of Japanese researchers is unraveling the role played by calcium ion influx in mast cells and other immune system cells.

Mast cells contain granules consisting of a potent combination of proteins and other bioactive compounds that are released when the cell is stimulated by the binding of immunoglobulin E (IgE) antibodies and an allergy-triggering antigen to specific receptors on the cell surface. This process and the immunological events that accompany it cause the physiological changes characteristic of an allergic response, including swelling, redness and itching.

The team, led by Tomohiro Kurosaki at the RIKEN Research Center for Allergy and Immunology in Yokohama, has focused their work on STIM1: a protein located on the endoplasmic reticulum, a membranous structure within the cell.

Previous studies by Kurosaki and his colleagues have demonstrated that the STIM1 protein physically relocates from the endoplasmic reticulum to regions just under the cell membrane where it is involved in the activation of specific calcium channels known as calcium release-activated channels. This process is known as store-operated calcium influx and is an important mechanism in the activation of mast cells.

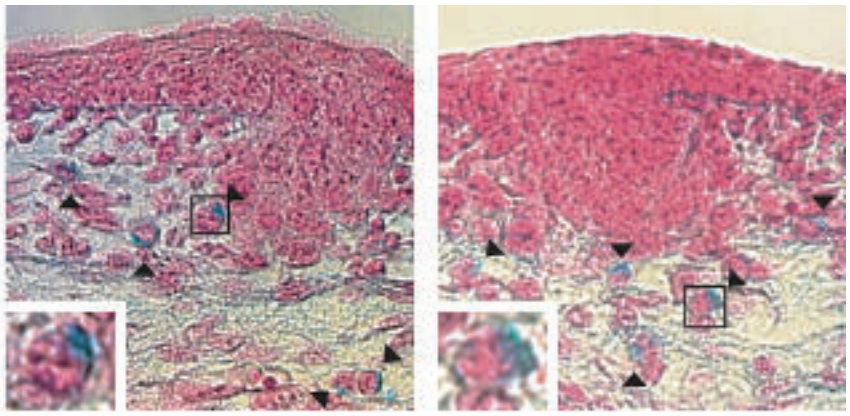


Figure 1: Development of mast cells in normal mouse embryos (left) and embryos lacking the STIM1 protein (right). Arrowheads indicate mast cells stained with alcian blue dye. Insets (bottom left corners) show mast cells in boxes in main images.

Mutation affects calcium influx

Now, using a genetically engineered mouse strain that does not express the STIM1 protein, the researchers have shown that the calcium influx mediated by stimulation of specific receptors, known as FcεR1, on mast cells was severely impaired[1]. But the mice have proven difficult to work with: the mutation preventing the expression of STIM1 is lethal with few fetuses surviving beyond birth.

Comparisons between fetal liver-derived mast cells (FLMC) generated from day 15.5 embryos of the mutant mouse strain and a normal mouse embryos exhibited similar morphology and gene expression profiles. The researchers also found that the density of skin mast cells in the embryos was similar. Taken together, these results suggest that mast cell differentiation is not affected by the absence of STIM1 expression.

To circumvent the lethality of the mutation, the researchers used FLMCs from mice lacking STIM1 to examine calcium influx (Fig. 1). Initially the cells were treated with thapsigargin—a compound that inhibits the calcium pumps in the endoplasmic reticulum—and a calcium-chelating agent to deplete calcium stores. When extracellular calcium was added back to the culture, calcium influx in the FLMCs lacking STIM1 was significantly suppressed compared to levels seen in normal FLMCs. A similar result was seen in FLMCs following stimulation of the FcεR1 receptors, suggesting that STIM1-dependent calcium influx was the main mechanism used during FcεR1 signaling.

In the presence of ionomycin, a drug that raises intracellular calcium levels, FLMCs from normal mouse embryos showed consistently high levels of intracellular calcium while the calcium flux in FLMCs lacking STIM1 was much lower.

When the researchers returned the STIM1 gene to the defective cells using a specially modified virus, they found that mobilization of calcium was restored after stimulating the FcεR1 receptors or treating the cells with ionomycin, thereby confirming the importance of STIM1 in bringing in external supplies of calcium.

Impaired immune function

Kurosaki and team have also shown that FLMCs from the mutant mice have impaired immune function. Mast cell granules contain a variety of proteases and other molecules including histamine and β-hexosaminidase, which are responsible for the physiological effects

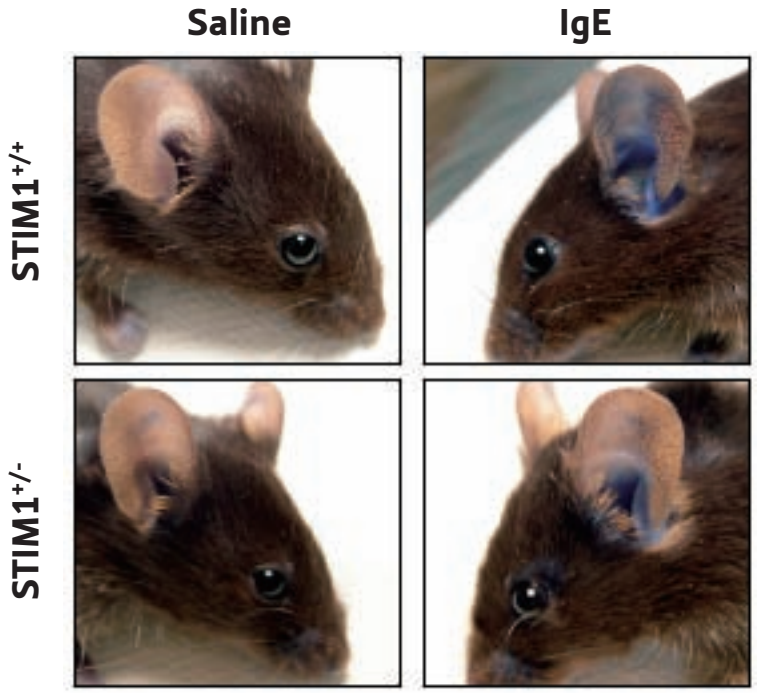


Figure 2: Comparison of *in vivo* anaphylactic responses in mice with either two functional copies of the STIM1 gene (*Stim1*$^{+/+}$) or one functional copy (*Stim1*$^{+/-}$). One ear was injected with IgE antibodies against a specific antigen. The other ear was injected with saline as a control. After 16–18 h the antigen was administered intravenously together with a blue dye and the amount of dye leaking out into the ear tissue was measured.

associated with an allergic response. The activation also triggers the cell to produce and secrete other mediators and hormones that promote inflammation.

After stimulation of the FcεR1 receptors of FLMCs lacking STIM1 there was a significant reduction in the release of the mast cell granules, measured by monitoring levels of β-hexosaminidase. When STIM1 expression was restored to the defective cells, the ability of the cells to degranulate was also partially restored. At a molecular level, activation of transcription factors NFAT and NF-κB—which are responsible for regulation of many mast cell functions—was also impaired.

In vivo observations back up *in vitro* results

Due to the lethality of the mutation, the full effect of deleting STIM1 on the allergic response could not be directly investigated *in vivo*. But in an experiment using mice with only one functional copy of the gene, the researchers were able to show that the sensitivity of immediate-type allergic responses was diminished, when compared to the response exhibited by mice with two functional copies.

This was demonstrated by sensitizing the ear of the mouse through the injection of IgE antibodies against a specific antigen into the outer part of the ear, a process called passive cutaneous anaphylaxis. Sixteen hours after sensitization, the antigen was injected intravenously, in combination with a blue dye. Degranulation of mast cells causes increased permeability of blood vessels in the sensitized site, and the dye leaks into surrounding tissues where it can be biopsied and quantified.

In sensitized mice with only one functional copy of the STIM1 gene, the amount of dye entering the tissues was significantly lower than in mice with two copies (Fig. 2), suggesting that the protein is required for antigen-induced, mast cell-mediated anaphylactic responses *in vivo*.

While there are still questions to be answered about precisely how STIM1 mediates calcium influx, there is no doubt that the protein plays an important role in regulating intracellular calcium levels in mast cells.

"STIM1 may represent a new therapeutic target for allergic diseases," team-member Yoshihiro Baba says.

The next step, says Baba, will be to use a conditional system that only blocks expression of STIM1 in specific cell types, rather than the whole animal. ■

1. Baba, Y., Nishida, K.,Fujii, Y., Hirano, T., Hikida, M. & Kurosaki, T. Essential function for the calcium sensor STIM1 in mast cell activation and anaphylactic responses. *Nature Immunology* **9**, 81–88 (2008).

About the researcher

Tomohiro Kurosaki was born in Okayama, Japan, in 1955. He received his MD in 1980 from Okayama University Medical School and his PhD in 1987 from Kyoto University. After obtaining his PhD, he received a postdoctoral fellowship at the Sloan-Kettering Institute in New York. He then joined Lederle Laboratories where he remained until 1996 as a senior research scientist, while holding the position of adjunct assistant professor in Yale University in the United States. After returning to Japan, he directed and taught at the Institute for Liver Research at Kansai Medical University. He joined RIKEN in 2001 and has been director of his own research group. His laboratory focuses on understanding the molecular composition of preBCR/BCR signaling complexes and the mechanisms of signaling pathway crosstalk that lead to crucial cell fate decisions during B lymphocyte differentiation. He has also applied insights gained from the studies of B cells to another important immune effecter cell, the mast cell.

Exotic material keeps frustrated electrons flipping

Magnetic, temperature and structural studies have yielded new insights on the material sodium iridium oxide

RIKEN scientists have discovered a new state of matter with unusual magnetic properties—its constituent electrons are in a continuous state of flux, even at incredibly cold temperatures.

As electrons spin, they generate a magnetic field which can point 'up' or 'down'. Within solid materials, an electron will generally try to adopt the opposite spin orientation to its neighbor, just as two bar magnets will flip around so that north and south poles line up next to each other.

In more common lattice structures, where atoms stack up like oranges on a greengrocers stall, it's easy for electrons to achieve this ordered arrangement. But in certain materials, the arrangement of atoms can make it impossible for the electrons to line up with all of their neighbors, and they are said to be 'frustrated'.

One example of a frustrated material contains a network of atoms arranged into corner-sharing triangles. This is called a *kagome* structure after a type of Japanese basket that has the same pattern (Fig. 1).

The electrons' response to this frustration is to constantly flip their magnetic fields to reduce the repulsion between them. In this 'quantum spin-liquid state', the quantum effect is expected to stop flipping electrons from freezing out into a static arrangement even at absolute zero (-273.15 °C—the coldest temperature possible). Several materials have been claimed to contain possible quantum spin-liquid states, but none have been confirmed.

Hidenori Takagi and Yoshihiko Okamoto of RIKEN's Discovery Research Institute, Wako, and colleagues, have now found that sodium iridium oxide ($Na_4Ir_3O_8$) exhibits quantum spin-liquid behavior, even when cooled to -271 °C[1]. This was confirmed by magnetic, temperature and structural studies, involving both neutron and x-ray diffraction.

The material contains a network of iridium atoms that form a three-dimensional pattern of corner-shared triangles—dubbed a hyperkagome lattice (Fig. 2), which can be viewed as a slightly twisted—but different structure—to the *kagome* structure, explains Takagi. Theoretical calculations are consistent with this type of structure showing spin-liquid behavior.

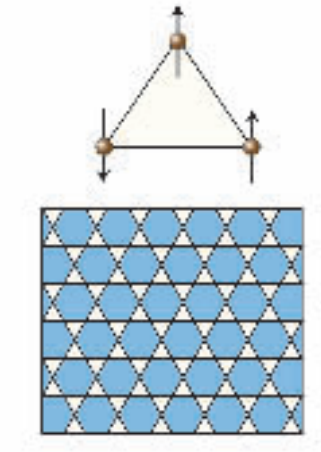


Figure 1: In the triangular arrangement of iridium atoms in $Na_4Ir_3O_8$ (top), each electron's magnetic field will always match one of its neighbors. The pattern of iridium triangles running through the materials lattice matches the traditional Japanese *kagome* basket (bottom).

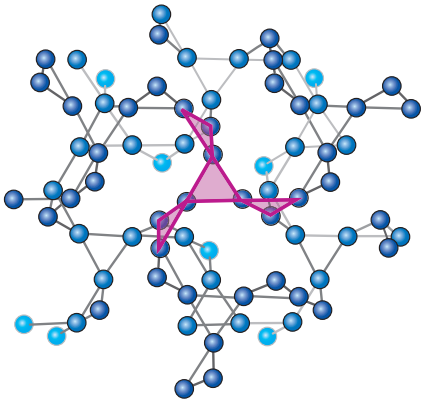


Figure 2: An illustration of the hyperkagome lattice.

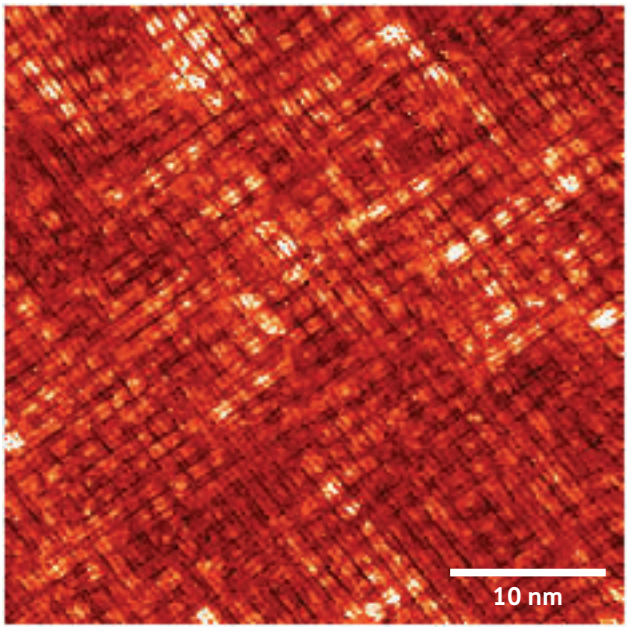
"We believe it is the strongest candidate [for a quantum spin liquid]," says Takagi.

The scientists say that the material is "a fascinating playground for quantum magnetism", and now hope to study the spin-liquid state further. This should to help build up a detailed description of the phenomenon using quantum theory, describing on a subatomic level exactly how the spinning electrons interact with each other. ■

1. Okamoto, Y., Nohara, M., Aruga-Katori, H. & Takagi, H. Spin-liquid state in the S = 1/2 hyperkagome antiferromagnet $Na_4Ir_3O_8$. *Physical Review Letters* **99**, 137207 (2007).

'Virtual' reality check for superconductors

New clues important to our understanding of superconductivity are provided by precise measurements of electronic states



Nature Physics

Figure 1: Periodic variations of the electronic states at the surface of a superconductor. The actual quasiparticle signatures are embedded in signals originating from unrelated surface effects and need to be filtered out using mathematical techniques.

Researchers at RIKEN's Discovery Research Institute in Wako, in collaboration with researchers from Cornell University in the US, and Kyoto University, have refined a method that measures small electronic excitations in superconductors. Comparisons of these properties for different materials have provided valuable clues towards our understanding of superconductivity.

The classical theory of superconductivity describes the superconducting state arising through the pairing of electrons into pairs. The properties of these electron pairs, however, are difficult to model mathematically. Physicists therefore prefer to describe them as a virtual single 'quasiparticle'. "Although these quasiparticles are fictitious, they really govern the electronic states of superconductors, particularly at low energies," explains Tetsuo Hanaguri from the research team.

Many details of the electronic states of quasiparticles and the precise amount of energy it takes to break up the electron pairs are difficult to measure, and remain poorly understood. This 'break-up energy', referred to as the 'superconducting gap', is traditionally considered as being directly related to the critical temperature where superconductivity persists. The larger the gap, the greater the difficultly to break up the electron pairs, thus the higher the critical temperature is for superconductivity. However, this relation has never been confirmed for the so-called 'high-temperature' superconductors, whose mechanism of superconductivity remains a mystery.

Reporting in the journal *Nature Physics*[1], the RIKEN researchers have now measured the properties of the quasiparticles using a scanning tunneling microscope that scans the surface of a superconducting material with an atomic resolution and records tiny variations in the electronic structure (Fig. 1). However, the observed periodic variations in the electronic properties are difficult to analyze as a number of effects contribute to these regular patterns. Therefore, Hanaguri and colleagues developed a novel mathematical technique to successfully pick out the quasiparticle signatures.

This mathematical technique allows the researchers to characterize several materials and compare their superconducting properties. Surprisingly, the relative variation in the superconducting gap was found to be the same for two different high-temperature superconductors, although their critical temperature differs by a factor of three. This shows that, contrary to conventional assumptions, the superconducting state is influenced by more than just the size of the superconducting gap.

To better understand the relation between superconducting gap and superconductivity, Hanaguri says that further measurements are needed to determine the effect of temperature and magnetic field on the quasiparticles. Ultimately, these measurements may provide vital clues on the fundamental mechanisms governing high-temperature superconductors. ■

1. Hanaguri, T., Kohsaka, Y., Davis, J. C., Lupien, C., Yamada, I., Azuma, M., Takano, M., Ohishi, K., Ono, M. & Takagi, H. Quasiparticle interference and superconducting gap in $Ca_{2-x}Na_xCuO_2Cl_2$. *Nature Physics* **3**, 865–871 (2007).

Gamma-ray cloudbursts shed light on lightning

High-energy gamma rays from thunderclouds may help us to predict when lightning will strike

A team including researchers at RIKEN's Discovery Research Institute in Wako and the University of Tokyo has observed a burst of high-energy gamma radiation emerging from a thundercloud over the Sea of Japan[1]. The discovery could help to reveal the complex electrical processes that cause lightning.

"Free electrons, originally produced by cosmic rays, can be accelerated by the strong electric fields in thunderclouds," explains project scientist Harufumi Tsuchiya. "If they reach relativistic energies, they can knock other electrons out of their atoms, causing a 'runaway electron avalanche.'"

When one of the high-energy electrons is deflected by the nucleus of an atom, it loses energy in the form of gamma rays called Bremsstrahlung—literally 'braking radiation'. Bursts of these gamma rays have been detected by near-Earth satellites above thunderclouds, and very short bursts are often recorded near the ground. Longer bursts lasting up to a few minutes appear to be very rare events, and physicists are unsure where they come from or what they consist of.

To answer these questions, the researchers built new radiation detectors based on devices on board the Suzaku cosmic x-ray satellite. The detectors were installed on the roof of the Kashiwazaki–Kariwa nuclear power plant in Niigata. On 6 January 2007, during a violent winter thunderstorm, they recorded a large radiation spike lasting over a minute, which could not be attributed to background radiation or electrical noise.

The spectrum of radiation included high-energy gamma rays that could not have been produced by thermal processes—which would require temperatures of billions of degrees Celsius. Therefore the burst must have been caused by Bremsstrahlung processes.

The burst was recorded approximately 70 seconds before a large flash of lightning, leading the researchers to speculate on whether the two events are related. In theory the runaway electrons could produce a large number of slower electrons, leading to electrical imbalance and lightning. "If thunderclouds frequently generate gamma ray bursts prior to lightning discharges, detailed observations of such rays would allow us to predict when lightning will occur," claims Tsuchiya.

However, more observations are needed to prove such a link. "We believe the burst behaves like a searchlight beam, illuminating only a limited area on the ground," says Tsuchiya, "so we were probably fortunate that the beam happened to pass over our detector." To test this hypothesis, the researchers plan to spread several detectors over a large area, so that they might trace the movement of a gamma ray burst. ■

1. Tsuchiya, H., Enoto, T., Yamada, T., Yuasa, T., Kawaharada, M., Kitaguchi, T., Kokubun, M., Kato, H., Okano, M., Nakamura, S. & Makishima, K. Detection of high-energy gamma rays from winter thunderclouds. *Physical Review Letters* **99**, 165002 (2007).

Quasi-crystals avoid repetition

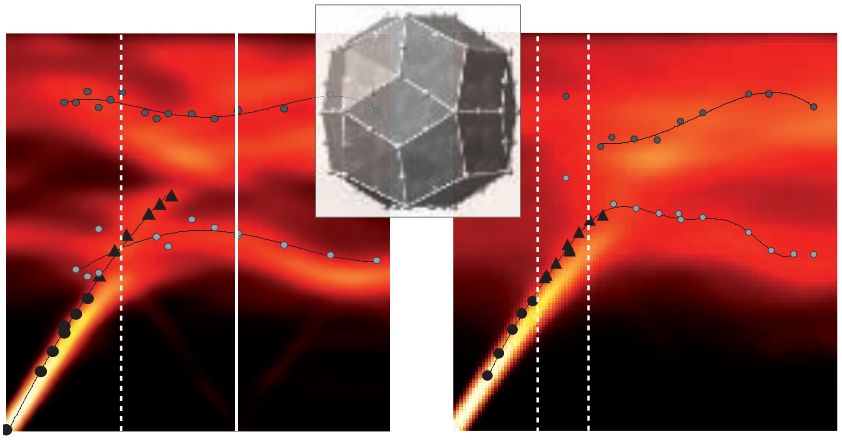
X-rays, neutrons and theoretical modeling are used to explore the physics of quasi-crystals

In a crystal, the same atom or group of atoms is repeated with perfect periodicity. Quasi-crystals, on the other hand, are materials without periodicity. Whether the absence of periodicity in a quasi-crystalline material fundamentally affects its properties, however, is still an open question.

Now, as reported recently in *Nature Materials*[1], an international team of scientists, including Alfred Baron of RIKEN's SPring-8 Center in Harima, has combined high-resolution neutron and x-ray scattering experiments with theoretical calculations to better understand the physics of quasi-crystals.

Most of the physics of solids rests on a simplifying assumption, known as Bloch's Theorem, that can only be applied to crystalline materials. This theorem reduces the task of calculating the properties of macroscopic materials with approximately 10^{21} atoms to calculating the properties of one repeating unit of atoms. Baron explains: "When Bloch's theorem no longer applies, the problem becomes much more complex. Quasi-crystals are then interesting both intrinsically, and as a first step away from periodic crystalline order."

To tackle the question of how the properties of quasi-crystals may differ from perfect crystals, the researchers focused on a material called i-ZnMgSc. This material consists of 'triacontrahedral' clusters (Fig. 1, center) each containing 158 atoms and arranged on a quasi-periodic network. i-ZnMgSc is of interest because it has a nearly identical counterpart,or 'approximant', made up of similar clusters arranged on a periodic lattice. Thus, comparing the two structures allows researchers to isolate the effects of periodicity—or the lack of it—on materials properties.



Nature Materials

Figure 1: The 'triacontahedral' cluster (center) that makes up the i-ZnMgSc quasi-crystal and a crystalline structure—called an approximant—that is chemically similar. The two adjacent panels are a map of the atomic vibrations in the approximant (left) and the quasi-crystal (right). The panels compare atomistic simulations of the atomic vibrations (false color) and the experimental measurements (symbols).

Baron and co-workers used specialized techniques to measure atomic vibrations in i-ZnMgSc and its approximant. The atoms in a material vibrate around their equilibrium positions with patterns and frequencies that are intimately related to the material's atomic structure, and in particular, the periodicity of this structure. With neutrons, and more recently with x-rays, these vibrations can be measured with very high accuracy.

The team mapped out the energy of the atomic vibrations for the quasi-crystal and the approximant and compared their results with atomic-scale calculations (Fig. 1). Both the calculations and the experiments show important, though subtle, differences between the two materials. In particular, certain vibrations that are well defined in the approximant have a different energy—or do not even appear—in the quasi-crystal. These results could have relevance to the use of quasi-crystals in several fields, including photonic crystals and thermoelectrics. ■

1. de Boissieu, M., Francoual, S., Mihalkovi, M., Shibata, K., Baron, A. Q. R., Sidis, Y., Ishimasa, T., Wu, D., Lograsso, T., Regnault, L-P., *et al*. Lattice dynamics of the Zn–Mg–Sc icosahedral quasicrystal and its Zn–Sc periodic 1/1 approximant. *Nature Materials* **6**, 977–984 (2007).

Silver keeps the electrons spinning

Silver can transport spin-polarized electrons, making it ideal for the non-magnetic components in 'spintronic' devices

The future of computing may emerge not from electronics, but from 'spintronics'. This new technology relies on the transport of electrons whose quantum spin states—or internal angular momentum—are all the same. YoshiChika Otani and Takashi Kimura at the University of Tokyo and the RIKEN Frontier Research System in Wako have been searching for the best materials to carry this 'spin polarization', and it appears that silver is a strong candidate[1].

Many useful spin polarization phenomena arise in hybrid devices comprising both magnetic and non-magnetic materials. However, when spin-polarized electrons pass from a magnet into a non-magnet, they quickly lose their spin polarization in a process called spin-flip scattering. Therefore, one of the most crucial parameters for spintronics is the spin diffusion length of the non-magnet: the length that electrons travel before all their spin polarization is lost.

The RIKEN team built devices called lateral spin valves to test the spin diffusion lengths of different non-magnetic metals: copper, aluminum, and now silver. They found that the spin polarization of electrons remained very high after passing through a silver wire—implying that silver has a long spin diffusion length.

The result contradicts previous work by a group in the US[2], who predicted that silver has a very short diffusion length. Otani and Kimura believe this is because the US team did not take account of spin diffusion at the interfaces between the silver wire and the magnetic detectors used in their experiment.

By including the diffusion processes in their calculations, Otani and Kimura have proven that silver actually has a longer spin diffusion length than any other material studied so far. "What we found was quite different, demonstrating that our common understanding about the spin diffusion process was correct," says Otani.

In related work, the RIKEN team recently developed the first method that provides complete control over the direction of spin polarization in copper, by using two spin injection needles[3]. Otani and Kimura believe their device could work just as well, if not better, with silver. However it is more difficult to fabricate devices from silver, so they hope to experiment with other materials soon.

"Our future target is to develop 'spin current circuits' that manipulate the spin polarization as well as spin angular momentums," says Otani (Fig. 1). "This may be applied to the next generation of memory or logic circuit technology."

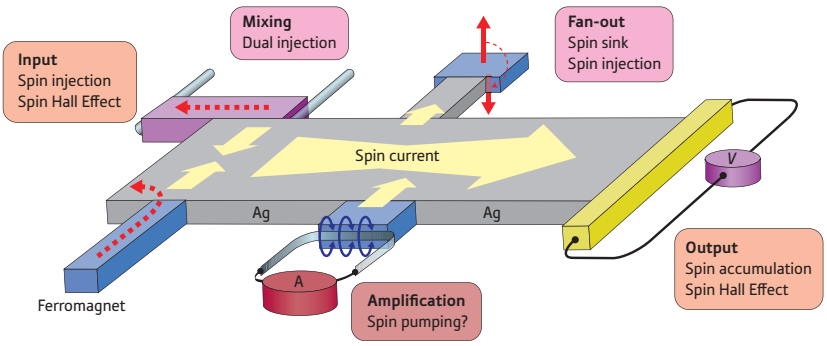


Figure 1: Building-blocks for a spin current circuit. Diagram shows a theoretical silver (Ag) spin current circuit, which exploits phenomena such as the Spin Hall Effect—the scattering of electron spins in a direction perpendicular to an electric field.

1. Kimura, T. & Otani, Y. Large spin accumulation in a permalloy-silver lateral spin valve. *Physical Review Letters* **99**, 196604 (2007).
2. Godfrey, R. & Johnson, M. Spin injection in mesoscopic silver wires: experimental test of resistance mismatch. *Physical Review Letters* **96**, 136601 (2006).
3. Kimura, T., Otani, Y. & Levy, P.M. Electrical control of the direction of spin accumulation. *Physical Review Letters* **99**, 166601 (2007).

On the road to a vaccine against tumors

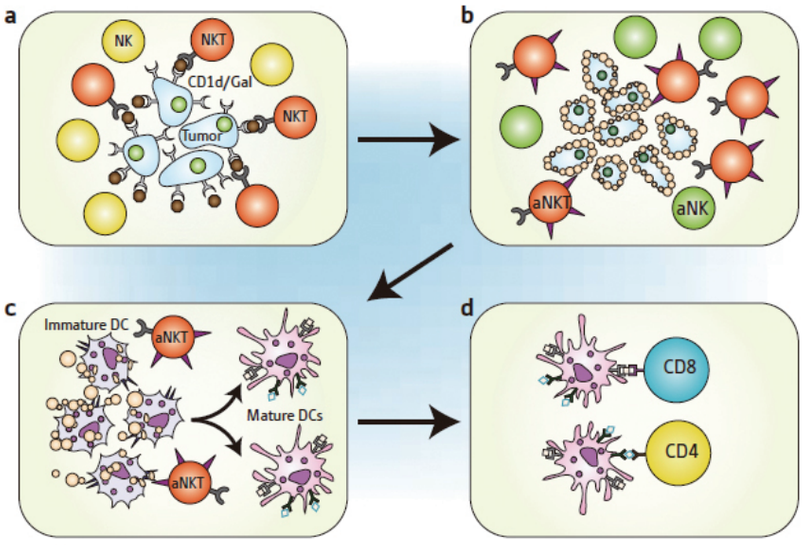
Researchers find how to generate an immune response in mice

A research team from RIKEN's Research Center for Allergy and Immunology (RCAI) in Yokohama has discovered a means of inducing persistent immunity to tumors in mice. In the long term, the work could lead to a vaccine against certain tumors in people.

Unlike infectious organisms and foreign tissue, tumor cells do not elicit a powerful immune response naturally. In particular, tumors do not activate the production of immune $CD4^+$ and $CD8^+$ T-cells geared to fighting them. This typically needs two signals. In addition to a compound known as an antigen which is specific to the tumor and reacts with a T-cell receptor when presented by dendritic cells (DCs), it also requires a co-stimulatory molecule that tumors appear to lack.

In a recent paper in the *Journal of Experimental Medicine*[1], the research team—comprising members from RCAI and The Rockefeller University in New York—detailed a method for inducing immunity in mice to four common tumors lasting up to 12 months.

A glycolipid compound derived from marine sponges known as α-galactosylceramide (α-GalCer) can activate the immune system's natural killer (NK) and natural killer T-(NKT) cells against tumors, but alone does not protect mice from cancers such as B16 melanoma. The researchers found, however, that a low dose of B16 tumor cells loaded with α-GalCer and injected intravenously will induce a protective immune response to B16 melanoma. The same was true for three other mouse tumors which normally generated a poor immune response.



Immunological Reviews

Figure 1: Mechanism of the mouse immune response against tumors. (a) Tumor/Gal activates NKT/NK cells. (b) The activated NKT/NK cells then kill tumor cells. (c) Next, DCs engulf tumor debris and cross-present on CD1d to NKT cells, which matures the DCs. (d) Mature antigen-capturing DCs induce long-lived, adaptive T-cell immunity.

To trace what was taking place, the team tracked labeled α-GalCer-loaded tumor cells under the confocal microscope. They found that α-GalCer did indeed activate NK and NKT cells to kill tumor cells (Fig. 1a, b). Debris from the dead cells was captured by DCs in the spleen. These DCs then changed or matured to mount an immune response by presenting tumor antigen peptide in such a way as to stimulate the production $CD4^+$ and $CD8^+$ T-cells against that particular tumor (cross-presentation 1) (Fig. 1c). In addition, the mature DCs presented the original α-GalCer to NKT cells again, stimulating further response (cross-presentation 2) (Fig. 1d). Immunity against individual tumors persisted for at least six months.

"We now have a mouse model for generating an immune response to tumors," says project coordinator Shin-ichiro Fujii. "We can use it to focus on questions of basic science, such as what triggers the immunity. We would also like to extend the research into human patients." ■

1. Shimizu, K., Kurosawa, Y., Taniguchi, M., Steinman, R.M. & Fujii, S. Cross-presentation of glycolipid from tumor cells loaded with α-galactosylceramide leads to potent and long-lived T cell-mediated immunity via dendritic cells. *Journal of Experimental Medicine* **204,** 2641–2653 (2007).

Good housekeeping

A protein with an important role in regulating gene expression may have other duties relating to chromosome maintenance

Most genetic information is directly encoded by the sequence of nucleotides in a chain of DNA, but further instructions may also be provided by adding chemical modifications to those nucleotides, just like inserting footnotes can alter the meaning of a text. One important modification is DNA methylation, which generally has the effect of 'silencing' transcriptional activity of marked genes—a secondary but essential level of regulation.

DNA methylation patterns can be transmitted from parent to child, an important process known as genomic 'imprinting'. Maintaining these patterns is an active process, as each cycle of DNA replication results in the production of chains that are only hemimethylated, and full methylation is subsequently restored by the enzyme DNA methyltransferase 1 (Dnmt1).

Other proteins are known to assist this process. Recent work from a group led by Haruhiko Koseki of the RIKEN Research Center for Allergy and Immunology in Yokohama, and Masaki Okano of the RIKEN Center for Developmental Biology in Kobe, has highlighted the important role of one particular protein, Np95, in directing Dnmt1 to hemimethylated DNA targets[1].

Koseki's group initially found that Np95 associates with imprinting-related proteins, and subsequent experiments in mouse embryonic stem cells (ESCs) extended these findings, demonstrating that Np95 co-localizes with Dnmt1 and other associated proteins at hemimethylated chromosomal regions after DNA replication (Fig. 1). Eliminating the expression of Np95 altogether resulted in a marked reduction of DNA methylation in cultured ESCs, and led to full developmental arrest in mouse embryos.

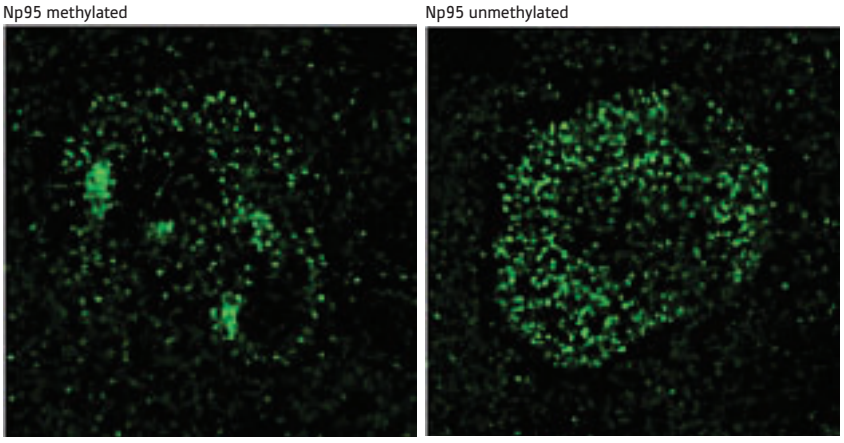


Figure 1: In cells undergoing DNA synthesis in the presence of methylated nucleotides (left), Np95 (green) specifically localizes to the chromosomes, revealing preferential association with hemimethylated DNA. In cells treated with unmethylated nucleotides (right), no such localization is seen and the Np95 is diffused throughout the nucleus.

Methylation does more than silence genes; it also helps stabilize DNA elements known as retrotransposons, which are otherwise capable of physically 'jumping' into other chromosomal regions—and potentially disrupting other genes. Koseki's group found that Np95 helps to lock down these retrotransposons. "At the least, Np95 is essential to maintain genomic imprinting, which in turn permits normal development of embryonic and extraembryonic tissues," he says. "But it could be possible that this process may also be important to ensure genomic stability."

Intriguingly, Koseki's and his colleagues also found evidence suggesting that Np95's function may not be limited to restoring DNA methylation, but could encompass other chromosomal maintenance tasks as well—a possibility he is keen to investigate further. "Hemimethylated DNA is not simply a transient status that appears after DNA replication … it may potentially form a specific signal that could be sensed by Np95," he says. "We presume that Np95 may form a platform that helps to organize not only DNA methylation but also other types of modifications." ■

1. Sharif, J., Muto, M., Takebayashi, S., Suetake, I., Iwamatsu, A., Endo, T.A., Shinga, J., Mizutani-Koseki, Y., Toyoda, T., Okamura, K. *et al.* The SRA protein Np95 mediates epigenetic inheritance by recruiting Dnmt1 to methylated DNA. *Nature* **450**, 908–912 (2007).

Small changes, big impacts

Molecular-scale rearrangements influence how receptors transmit their message, adding another layer of complexity to the regulation of cell signaling

The pathways by which signals are transmitted within cells are extremely convoluted, involving sequential interactions between large numbers of individual proteins. Modeling these pathways is a daunting enough challenge, but recent studies designed to actively monitor individual protein molecules have hinted at additional levels of complexity.

"Single-molecule studies suggest that proteins [undergo] complex structural and reaction dynamics," explains Yasushi Sako, a biophysics specialist at the Discovery Research Institute in Wako who specializes in biomolecular imaging. "We wanted to investigate the possibility that complex protein dynamics are involved in molecular-level signal processing." Sako and colleagues focused on epidermal growth factor receptor (EGFR), a membrane protein that transmits signals responsible for cell division. Several proteins bind to EGFR following activation, including Grb2, which serves as an 'adaptor' that enables other signaling proteins to associate with the receptor.

Sako and colleagues took advantage of sophisticated new imaging methods that made it possible for the first time to examine the interaction of Grb2 with full-length, intact EGFR, yielding valuable insights into the kinetics of association between these two proteins[1]. The group attached individual receptor molecules to a solid support, and then exposed the receptor molecules to different amounts of fluorescently tagged Grb2; by monitoring the appearance and disappearance of fluorescence at individual receptor locations, they were able to quantitatively measure Grb2 binding and release.

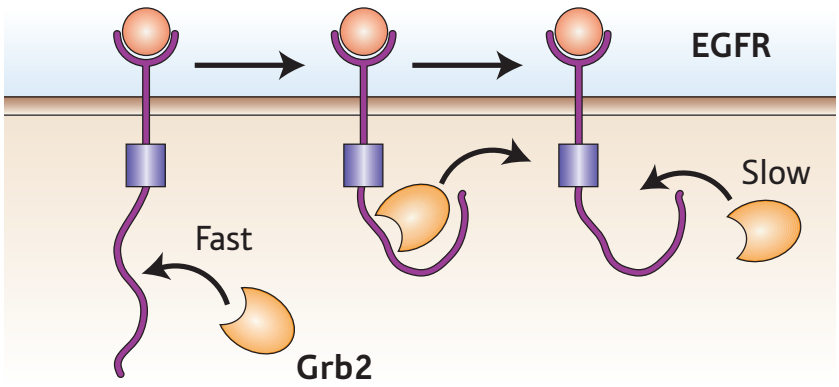


Figure 1: The initial 'fast' association of EGFR with Grb2 is believed to lead to a conformational change in the receptor; when the first Grb2 molecule dissociates, the receptor initially maintains this new 'slow' conformation, which markedly reduces the affinity of Grb2 and reduces the rate of subsequent binding interactions.

Instead of a basic on–off interaction between the two proteins, the interaction data suggested a far more complex picture, where the rate of association with EGFR is strongly dependent on the concentration of Grb2. "This means that the protein EGFR can sense the concentration of its association partner," says Sako. Their findings further suggested the receptor does not constantly maintain a single fixed structure, but instead transitions through multiple structural 'substates', and that these fluctuations in turn affect the kinetics of subsequent interactions between receptor molecules and Grb2 (Fig. 1).

The resulting model reveals an additional level of fine control over the process of signal transduction at the molecular scale, and Sako suggests that a better understanding of the structural changes involved could be a boon for future bioengineering projects. "If we know the mechanism of the molecular-level signal processing and can design the reaction behavior of proteins at will," he says, "that would be big progress toward realizing sophisticated protein nanomachines." ■

1. Morimatsu, M., Takagi, H., Ota, K., Iwamoto, R., Yanagida, T. & Sako, Y. Multiple-state reactions between the epidermal growth factor receptor and Grb2 as observed by using single-molecule analysis. *Proceedings of the National Academy of Sciences USA* **104**, 18013–18018 (2007).

How light can scramble time

Researchers solve the mystery of how biological clocks are disrupted

Hiroki R. Ueda

A team led by researchers from RIKEN has revealed how daily or circadian rhythms in mammals can be reinforced, shifted or disrupted by exposure to a burst of bright light. The work solves a 30-year-old mystery, and may well find application in the treatment of circadian disorders such as jet lag, lack of alertness in shift workers, delayed sleep phase syndrome and some forms of mental illness.

A network of genes ensures the rhythms of organisms—sleep and wakefulness, changes in body temperature and the secretion of certain proteins—are attuned to daily cycles. These genes generate proteins that interact in complex interlocking feedback loops to produce the rhythms. Groups of cells exhibiting circadian rhythms are found in many parts of the body.

The researchers found that a critical light pulse at midnight can uncouple and randomize the circadian cycles of individual cells thus damping the rhythm of the whole group of cells. Their data did not support a more popular hypothesis, that the pulse suppresses the rhythms of all the cells simultaneously.

In a recent paper in *Nature Cell Biology*[1], the researchers from RIKEN's Center for Developmental Biology in Kobe and several Japanese universities outline how they created light-sensitive circadian clocks in mouse fibroblast cells in the laboratory. The team introduced the light receptor melanopsin together with a bioluminescent reporter compound that emits light when the key clock gene *PER2* is active. The system can be used to track the phase and amplitude of circadian rhythms by measuring the average output of light over time.

The researchers then plotted the impact on phase and amplitude of pulses of light of differing lengths introduced at different times during the cycle. From this work, they determined which pulses were most effective in disrupting the rhythm altogether.

The team next measured individual cells within a group, and found that disruptive light pulses desynchronize their cycles with respect to one another, but without damping each individual cycle. A computer model developed to mimic this desynchronization process generated results which closely matched the experimental data.

The researchers also showed light could desynchronize the activity of key clock genes in live rats. This was linked with a decrease in general movement in 30% of the rats.

The team hopes to apply its findings to human behavior, says Hiroki Ueda, the research team leader. "Our mathematical model could lead to a deeper understanding and better treatment of circadian rhythm disorders." ■

1. Ukai, H., Kobayashi, T.J., Nagano, M., Masumoto, K., Sujino, M., Kondo, T., Yagita, K., Shigeyoshi, Y. & Ueda, H.R. Melanopsin-dependent photo-perturbation reveals desynchronization underlying the singularity of mammalian circadian clocks. *Nature Cell*

Instructing neuronal connections

Researchers unravel how specific connections result in the layering of neurons in the brain

Information in the brain travels along neuronal axons that form junctions, or 'synapses', with tree-like dendrites of other neurons. Normally, the myriad of neuronal pathways develop into highly organized layers called lamina—distinct areas where axons physically meet dendrites, providing a structural basis for integrating information. How such patterning of neurons actually occurs has long eluded brain scientists.

Now, a team led by Shigeyoshi Itohara at the Brain Science Institute in Wako, has determined that adhesion molecules on terminally projecting axons instruct the laminar configuration within 'target' dendrites—branches of neurons that receive signals from axons[1]. The researchers found that individual dendrites are divided molecularly and functionally into 'sub-dendritic segments', each of which corresponds to information input from a specific group of axons.

Netrin-G1 and netrin-G2 belong to a family of molecules that promote attraction between cells. Previous studies have demonstrated that netrin-G1 and -G2 proteins bind specific receptors, NGL-1 and NGL-2, respectively. Itohara's team initially demonstrated selective expression of netrin-G1 and -G2 on axons that project onto individual layers of the brain cortex and hippocampus (Fig. 1); even layers physically juxtaposed to one another express only one of the netrin-G proteins. Interestingly, the team also found similar laminar patterns of netrin-G partner proteins NGL-1 and NGL-2 on target dendrites.

These one-to-one expression patterns of netrin-G and NGL protein suggested that a 'lock-and-key' configuration of the proteins might account for lamina-specific organization within sub-dendritic segments. To address this possibility, the team analyzed mice lacking either netrin-G1 or -G2 and found, surprisingly, disruption of laminar neuronal patterns but normal gross brain structure and arrangements of neurons. Closer examination revealed that in the absence of its netrin-G partner, the cognate NGL protein was now distributed diffusely along a given dendrite rather than restricted to a specific segment.

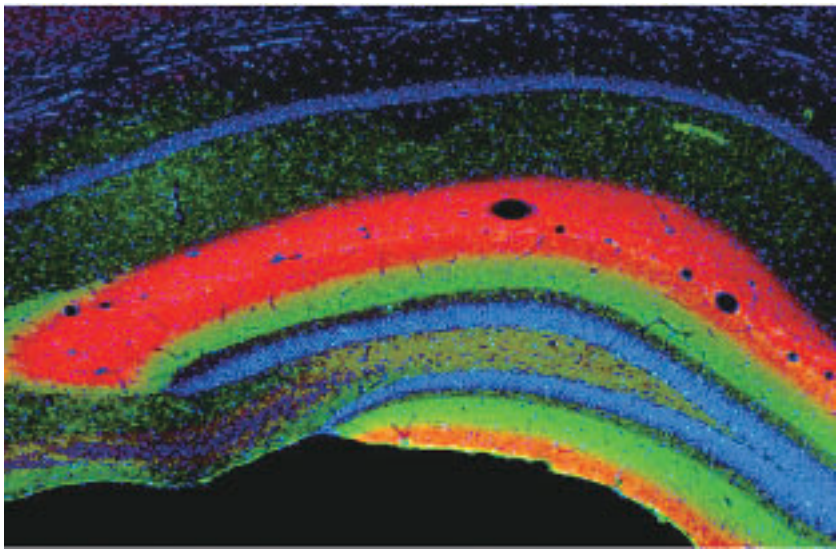


Figure 1: A section of the hippocampus stained to show the unique laminar structure determined by specific connections between neurons.

Itohara and team concluded that the interaction between axon-expressed netrin-G and dendrite-expressed NGL functionally and physically divides dendrites into segments. In other words, 'trans-neuronal' mechanisms, rather than cell-intrinsic factors, account for neuronal circuit specificity within a single neuron.

"We are working hard to investigate the role of netrin-G/NGL interactions on structure and function of the neurons, and to understand how netrin-G1- and -G2-dependent neuronal circuits integrate information," says Itohara. For now, the team's data point to an essential role for netrin-G/NGL interactions in determining specific interaction between axon projections and dendrites, which give the characteristic laminar organization of the brain. ■

1. Nishimura-Akiyoshi, S., Niimi, K., Nakashiba, T. & Itohara, S. Axonal netrin-Gs transneuronally determine lamina-specific subdendritic segments. *Proceedings of the National Academy of Sciences USA* **104**, 14801–14806 (2007).

Forgetful mice show the way to treating Alzheimer's

RIKEN researchers find link with protein build-up

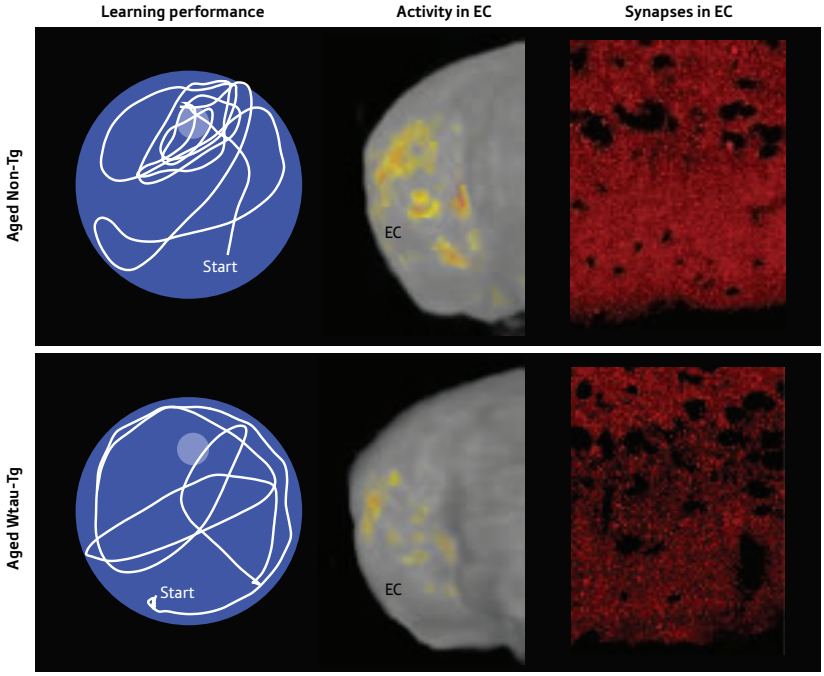


Figure 1: Aged transgenic (Wtau-Tg) mice have greater difficulty in finding the platform in the Morris water maze (left); show less activity in the entorhinal cortex (EC) (centre); and display fewer synapses (right).

The accumulation of a phosphate-laden, soluble form of tau protein in an important memory center of ageing mice is associated with loss of nerve cell connections or synapses and deterioration of memory, RIKEN researchers have found. Not only does this constitute the first sign of the onset of Alzheimer's disease (AD), they suggest, but reduction or prevention of the build-up of such hyperphosphorylated tau may well lead to an effective treatment.

Two consistent biochemical hallmarks of AD in the brain are the presence of deposits of misfolded proteins known as amyloid beta plaques and insoluble aggregates of hyperphosphorylated tau proteins inside nerve cells called neurofibrillary tangles (NFT). Tau proteins help stabilize the internal skeleton of cells by interacting with microtubules. They are regulated by phosphates that can attach at various points along the molecule. Both NFTs and amyloid beta plaques form well before the onset of AD, and the role they play has been the subject of intense scrutiny.

In a recent paper in *The EMBO Journal*[1], researchers from RIKEN's Brain Science Institute in Wako detail their work using transgenic mice to which a gene for human tau protein had been added together with a promoter to stimulate its activity in the nerve cells of the forebrain after birth. The researchers found that the human tau protein became hyperphosphorylated as the mice aged, but did not form NFTs. There was also no evidence of nerve cell loss.

Using the Morris water maze, whereby mice learn the position of a submerged escape platform in a tank of water by remembering cues to its position, the researchers determined that the transgenic mice also displayed impaired learning ability as they grew older compared with normal mice (Fig. 1). And with manganese-enhanced MRI imaging, a new technique for analyzing brain activity in small animals, they were able to match this with reduced activity and fewer synapses in the entorhinal cortex of the brain, critical to spatial memory. All of this occurred without NFT formation and before any possible appearance of amyloid beta plaques.

"Once NFTs form, we cannot rescue the nerve cells," says research team spokesman, Akihiko Takashima. "But before the formation of NFTs, tau proteins form small soluble aggregates, and we know of several enzymes that can inhibit this. So we are now trying to detect the aggregates by means of the small compounds which bind to them or through positron emission tomography."

1. Kimura, T., Yamashita, S., Fukuda, T., Park, J-M., Murayama, M., Mizoroki, T., Yoshiike, Y., Sahara, N. & Takashima, A. Hyperphosphorylated tau in parahippocampal cortex impairs place learning in aged mice expressing wild-type human tau. *The EMBO Journal* **26**, 5143–5152 (2007).

Neural architecture

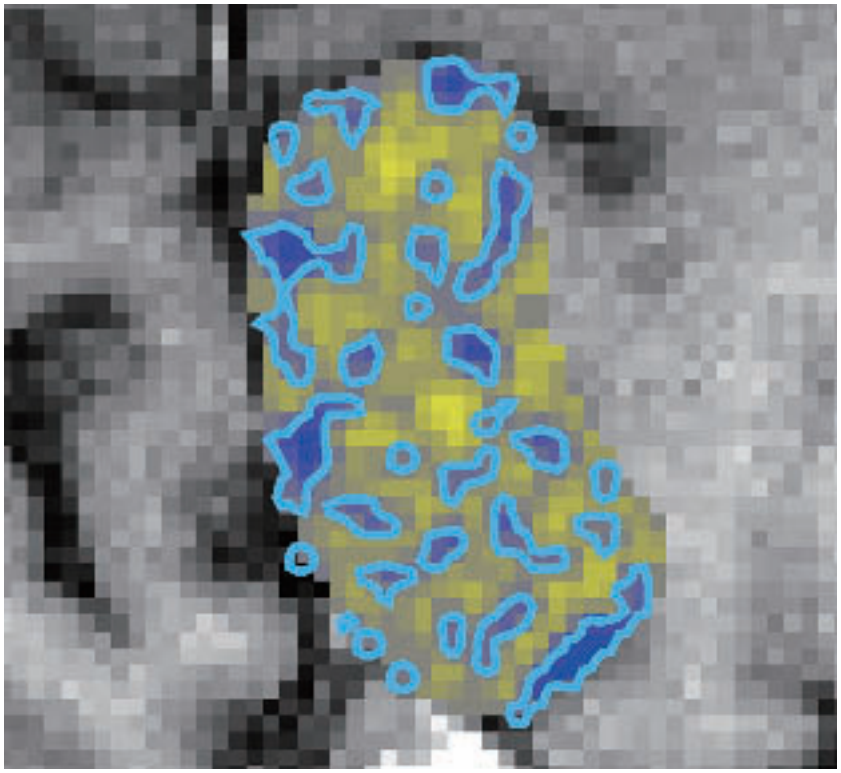
The neurons in the primary visual cortex processing high- and low-frequency images are distinct

Neuroscientists from the RIKEN Brain Science Institute, Wako, and New York University have used functional magnetic resonance imaging (fMRI) to study the organization of neurons in the primary visual cortex (V1) of humans and establish that the temporal frequency of a stimulus activates specific V1 neurons.

The V1 is an area at the back of the brain where the first stage of visual processing takes place. Although this is one of the most heavily studied parts of the visual cortex, little is known about how its neurons are arranged. In general, neurons with similar selectivity for visual stimuli cluster together. For example, V1 neurons that process stimuli from each eye are grouped into pillars, called ocular dominance columns.

V1 neurons are highly sensitive to the contrast, orientation, and spatio-temporal frequency of a visual stimulus. Temporal frequency is an important determinant of how moving images are processed by the brain and is a measure of how often an image appears in the visual field. This attribute is also of particular interest to RIKEN researcher Pei Sun and his team, headed by Keiji Tanaka and Kang Cheng, who have determined that images appearing less frequently over time are handled by neurons that arrange themselves differently to those that are activated by more frequently appearing images.

The fMRI technique allows the function and anatomical structure of the brain to be studied live and works by measuring the level of oxygen in the blood immediately after a neuron has been active, giving a pattern of which neurons have been triggered by a stimulus.



Nature Neuroscience

Figure 1: The pattern of temporal-frequency domains in the human primary visual cortex shows distinct characteristics. Low temporal-frequency domains appear to be continuous (yellow) whereas the high temporal-frequency domains are more isolated (blue).

The team has shown that separate domains in human V1 respond preferentially to low- and high-temporal frequencies. The former appear to be continuous, whereas the latter seem to be more like isolated islands with no particular orientation (Fig. 1).

This study provides direct physiological evidence that different temporal frequencies are preferentially processed by spatially segregated streams in human V1. The work recently published in *Nature Neuroscience*[1] is the first to show neuronal organization specific to temporal frequency in primate V1.

Evidence of these separate neural regions will assist further study into human perception of moving images and help to develop a map of the neural architecture of the brain. Pei plans to develop the fMRI technique as "it could link animal and human behavioral studies, giving a better picture of how information is processed by the brain," he says. ■

1. Sun, P., Ueno, K., Waggoner, R.A., Gardner, J.L., Tanaka, K. & Cheng, K. A temporal frequency-dependent functional architecture in human V1 revealed by high-resolution fMRI. Nature Neuroscience 10, 1404–1406 (2007).

Probing nature at the nanoscale with the world's most powerful synchrotron light source

RIKEN SPring-8 Center

The RIKEN Harima Research Institute, in Harima Science Garden City near the city of Aioi, Hyogo Prefecture, makes its home at SPring-8, the most powerful source of synchrotron light in the world. The facility's 1,436 m storage ring encircles a mountain, Mount Mihara-Kuriyama, and within its confines some very exciting science is being done.

Built in 1997 by RIKEN and the Japan Atomic Energy Research Institute, SPring-8 (short for Super Proton Ring-8 GeV) has maintained its leadership position among third-generation synchrotrons for over 10 years, a longevity unheard of in the world of high-energy physics. The 'number one' rating, however, is a bit misleading, as Tetsuya Ishikawa, director of the SPring-8 Center, points out. "Because of technological advances made here at SPring-8, for some classes of experiments, synchrotrons don't have to be this big anymore to get the same synchrotron-radiation energy, he said.

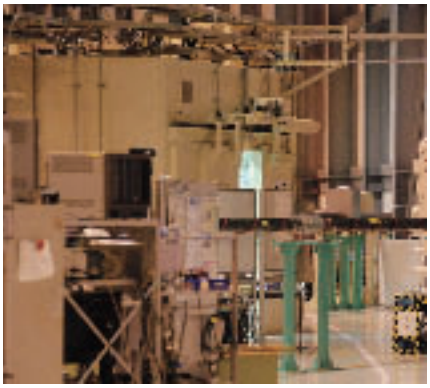
The RIKEN SPring-8 Center operates 7 of the 62 beamlines at the facility, conducting research into X-ray spectroscopy, synchrotron-radiation physics, synchrotron-radiation crystallography, structural genomics, X-ray optics and structural biology.

A storage ring works by maintaining electrons in a circular path, close to the speed of light. At this velocity, when the electrons' path is bent, they emit very intense light, known as synchrotron radiation, made up of radio waves, infrared light, visible light, ultraviolet light and X-rays.

The key innovation at SPring-8 has been the in-vacuum undulator, an array of permanent magnets with alternating polarity, through which electrons run at velocities close to the speed of light. Each period of the magnets bends the electron trajectory to emit synchrotron radiation, which constructively interferes giving it exceedingly high brilliance. Quasi-monochromatic light at specific wavelengths is generated at intensities about a billion times greater than conventional X-ray sources.

"The key advantage of the in-vacuum undulators is that we can make the magnetic period shorter. This makes relatively low-energy electrons emit high-energy photons," Ishikawa says. He adds, before SPring-8, it was very difficult to deliver 0.1 nm wavelength X-rays using a small accelerator. But now, even a 3 GeV machine can deliver this level of radiation. Such X-rays are also extremely brilliant, and they exhibit a sharp directionality that is superior to laser sources. All

The construction site for theXFEL laser



Inside the storage ring building

of this makes them extremely useful for a variety of scientific tasks.

The facility will soon be getting an upgrade in the form of the XFEL, or X-ray Free Electron Laser. The XFEL is generating excitement in the research community as it promises radiation a billion times brighter than existing X-ray sources, with pulses 1,000 times shorter, a level that will allow real-time observation of objects at atomic-level resolution.

The new laser's extremely fast femtosecond pulses will permit direct examination of the movements of atoms in motion within crystal lattices, and its ultrashort wavelength will permit observation of individual atoms.

Tetsuya Ishikawa

This will allow, for example, close observation of proteins that cannot currently be analyzed. About half of the proteins in the cell membrane have not been analyzed, because for this they must be crystallized, which so far researchers have been unable to do. "We'll also be able to learn a lot about the structure of viruses and protein complexes by applying the XFEL," Ishikawa noted.

"With its extremely short pulse duration, about 1 femtosecond, or 10^{-15} seconds, we will be able to take snapshots of very fast movements. The peak intensity of the XFEL is 10^9 times that of SPring-8. So it's going to be a revolution," Ishikawa said. "The important point here is, no one has ever seen this light or worked with it anywhere in the world. No one knows what will happen with the XFEL's light, or what it will reveal."

Excitement is building within the scientific community, and applications are flooding in to SPring-8 to use the new laser, many of them for rather interesting and unexpected investigations.

"Before we built SPring-8, we had discussions for many years about what research we would do with it," Ishikawa said. "And within two or three years, most of the research we had discussed was complete. Then the really interesting stuff started, after we saw what the light could do. We expect the same to happen with the XFEL."

SPring-8's operators are already looking beyond XFEL to consider the facility's longer-term future. This may include upgrading SPring-8 itself, raising its performance by using the XFEL accelerator as an injector. Plans are already being discussed, with a possible completion date of around 2019–2020.

Watching the motion of atoms
Alfred Q. R. Baron

Associate Chief Scientist, Materials Dynamics Laboratory

Alfred Baron, head of the Materials Dynamics Laboratory at the RIKEN Harima Center, and his team are working to understand the motion of atoms in materials.

X-rays are well known as a tool to investigate the average positions of atoms—their wavelength is similar to interatomic distances, allowing investigation of atomic positions on the same scale, using such techniques as X-ray crystallography and powder diffraction. But given a strong enough X-ray source, SPring-8, for example, it is also possible to directly investigate atomic motions. "If you look on extremely short, picosecond (10^{-12} s) and subpicosecond timescales, atoms inside materials are constantly in motion—they never stop moving," says Baron .

Atomic motions are intimately connected with many physical properties of materials. Many changes in material structure (phase transitions) can be linked with a slowing or 'freezing in' of a particular mode of vibration, or phonon. On a more sophisticated level, cooperative effects between atomic and electronic motions drive superconductivity and also, perhaps, more subtle features of technologically relevant materials.

Using the 10 metre inelastic X-ray scattering spectrometer at beamline BL35XU of SPring-8, Baron and his co-workers are investigating new superconductors, liquids, glasses, and other materials to see how their dynamics change under different conditions. The work has yielded some interesting results, including

the first-ever observations of changes in atomic dynamics as a liquid metal shifts from conductor to insulator when heated.

Baron is now working on a new, longer beamline, which will be more powerful by a factor of 20 or more. "Building the longer beamline is the right thing to do, and it is uniquely possible at SPring-8," he says.

A native of the USA, Baron came to Japan 10 years ago, after working as a researcher in the USA and Europe. The time at SPring-8 has been good for him, both professionally and personally, and, if the proposal for the new facility is successful, the project will keep him in Japan for some years to come.

RIKEN and Peking University agree to cooperate with Joint Graduate School and Nishina School programs

RIKEN and Peking University have signed an agreement on strategic cooperation for two programs, the Joint Graduate School program and the Nishina School program. The Joint Graduate School program offers Peking University students an opportunity to conduct research at RIKEN, while the Nishina School program will offer a coordinated graduate program in nuclear physics.

RIKEN President Ryoji Noyori and Peking University President Xu Zhihong signed the agreement in Beijing on February 28, 2008. The agreement will be effective for five years.

Both institutions will benefit greatly from the collaboration. Peking University is one of the finest universities in the world, with excellent students in a wide range of fields, and RIKEN offers world-class facilities and experienced research staff.

Peking University and RIKEN have a longstanding cooperative relationship centered on exchanges of researchers. With the new programs, special exchange student slots will be provided by Peking University, and the work undertaken by the students at RIKEN will be credited toward their graduate degree.

At the Nishina School, a special basic course will be set up for Peking University undergraduate and graduate students to take part in nuclear physics and related research using the RIKEN accelerators, which are among the best in the world. The Nishina School will also hold jointly sponsored symposiums and similar events.

It is hoped that these cooperative programs will nurture excellent young researchers over the long term, and stimulate academic activities throughout the Asian region. The programs are also expected to provide a base for strengthening research education in both Japan and China.

The new programs will start accepting students in September of this year.

Signing the agreement for strategic cooperation on the Joint Graduate School and Nishina School Programs.

Ryoji Noyori receives honorary doctorate from Peking University.

RIKEN opens its terahertz database to public

The RIKEN database on the terahertz wave absorption spectra of a wide range of materials has now been opened for public use.

The database will provide support for industry, with information on a variety of materials, such as 164 kinds of organic substances and 18 kinds of inorganic substances. RIKEN opened the database online at the end of January, 2008.

The Tera-Photonics Laboratory of the RIKEN Frontier Research System's Terahertz-Wave Research Program has been collecting terahertz-wave data on various materials since 1998. Other research laboratories have also helped to create a system that researchers, industrial developers and educational institutions all over the world can use freely online.

The terahertz band is a region of the electromagnetic spectrum between submilli-wave and infrared. The physical properties of the terahertz band have been attracting attention recently in many areas, including basic science and industrial applications. This makes them potentially useful in a range of fields, including medical imaging, airport security, spectroscopy and astronomy, as well as in communications and non-destructive testing in manufacturing. The RIKEN database contains data on the terahertz absorption and transmission spectra of various materials.

Collecting and sharing information is crucial in terahertz-wave research, since the field is still quite new. The RIKEN database will be an invaluable aid for researchers in materials, life and medical sciences.

The data includes not only the shape of the absorption spectrum, but also the conditions under which the material was measured. The shape of the spectrum can change greatly when, for example, the temperature changes, so the measurement conditions will be available with the spectra.

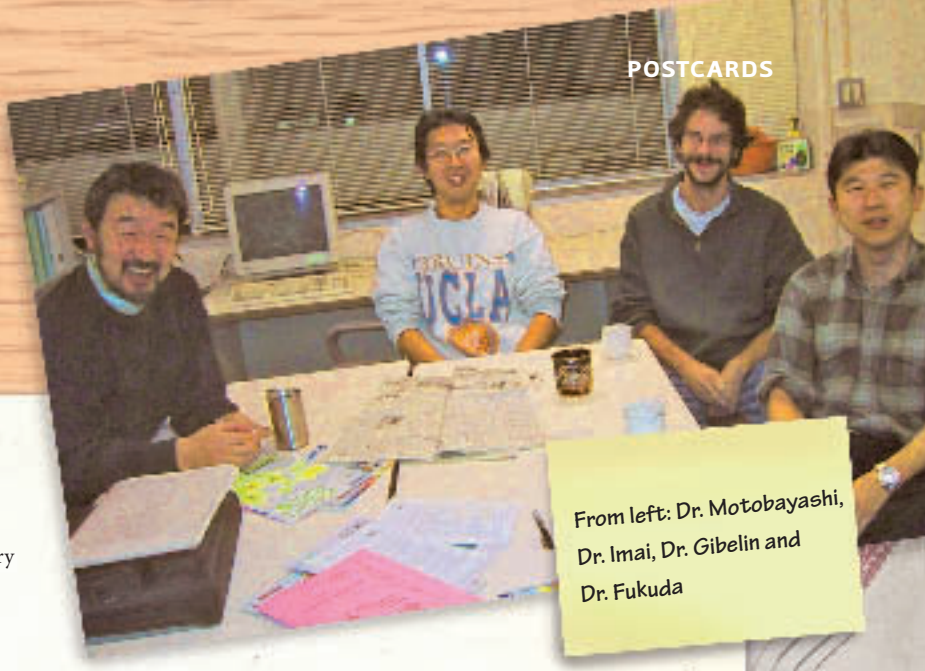
The database, which was featured in an article in *Nature Photonics* (Graydon, O. *Nature Photonics* 2, 68; 2008), is available for researchers all over the world to use and contribute to. It can be accessed at http://www.riken.jp/THzdatabase..

RIKEN calls for research proposals for the prototype XFEL

RIKEN has begun soliciting research proposals for the prototype X-ray Free Electron Laser (XFEL) at the Harima Institute in Hyogo Prefecture. Proposals have been accepted since February.

Japan's government has designated XFEL as one of the key technologies of national importance. The five-year construction project, which began in fiscal year 2006, was preceded by a joint RIKEN/JASRI project. In 2005, RIKEN began building a prototype XFEL at the SPring-8 site prior to the construction of the full-scale, 700 m XFEL machine. The 60 m prototype, which boosts electrons to energies of 250 MeV, succeeded in creating free-electron lasing in the extreme ultraviolet wavelength of 49 nm in June, 2006. Experiments using the prototype XFEL starting in May, 2008, will exploit its extremely intense ultraviolet radiation to explore new frontiers of science. The experiments will also clarify the direction of research for the full-size XFEL machine.

Details concerning submission of proposals can be found on the web site of the XFEL Experimental Facility Group, http://xfeluser.riken.jp.



From left: Dr. Motobayashi, Dr. Imai, Dr. Gibelin and Dr. Fukuda

Dr. Tohru Motobayashi
Chief Scientist
Heavy Ion Nuclear Physics Laboratory
RIKEN Nishina Center for
Accelerator-Based Science
Wako-city, Saitama, Japan.

Dear Dr. Motobayashi,

I'm very excited at the prospect of returning to Japan in the near future and working at the Nishina Center again. As you know, the main French governmental agencies in nuclear physics (CEA-DSM/CNRS-IN2P3/GANIL) have signed a research agreement with RIKEN and other research centers in Japan, so we are busy designing experiments for the new detectors we'll be bringing to install to the cyclotron — probably sometime next year — and for sure later in the Superconducting Ring Cyclotron.

Perhaps I never told you, but the first training (and support) I got at the Cyclotron Center in RIKEN really changed my life. In my fourth year of university when I first came to Japan, I was planning to become a high-school teacher, but I loved the research work at RIKEN so much I became a researcher in nuclear physics. One year after this first experience I thus came back to RIKEN (partly via Rikkyo University and the French-Japanese university agreement of the College Doctoral Franco-Japonais) for the first two years of my PhD, in order to carry out an experiment proposed by my French supervisors Dr. Beaumel and Dr. Blumenfeld at the Riken Cyclotron. My being a foreigner in Japan didn't seem to make a difference to the people at your lab—everybody seemed happy to see a young guy coming in to do research, and really supported me.

Among my best souvenirs, I fondly remember the meetings you held every Saturday afternoon at the Heavy Ion Lab (and in the evening at our favorite Korean barbecue!), when all the researchers discussed the status of their experiments and analysis—all those open discussions helped everyone gain a good understanding of what was going in our work, and sparked a lot of new ideas.

And, of course, I'll never forget the effort you put into being my PhD referee; flying to France for two days to participate in my thesis defense. It really showed how you support your people. All of this has had a huge influence on my current work, studying nuclear structure via exotic, highly unstable nuclei at the G.A.N.I.L (Grand Accélérateur National d'Ions Lourds) accelerator in Caen, France.

My confidence about my work and career is mostly due to the intensive training I received at RIKEN. The international experience I gained there was also important. In today's world, we can only conduct this kind of research via international collaboration, an impression I confirmed by spending two more years as post-doc in Berkeley, California. I have now not only colleagues in Japan but also friends I am eager to work with.

Working in Japan also changed the way I interact with my colleagues—I learned to work within a group and it taught me how to better apprehend other people's opinions and feelings. I guess this is the Japanese way, but it's the way to go when there are people from different cultures on your team.

Anyway, I wish you all the best, and I hope to see you soon in Wako!

Yours truly,

Julien Gibelin
G.A.N.I.L, France.

From left: Dr. Beaumel, Dr. Gibelin, and Dr. Blumenfeld

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
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