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Bright Future for White Organic Light-emitting Diodes

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RIKEN

RIKEN's place in the world

RIKEN has pioneered external evaluations in Japan. Last month the RIKEN Advisory Council (RAC) met for the sixth time since its first meeting in 1993. The 23-member council, including Nobel laureate Dr. Yuan Tseh Lee of Taiwan and 12 other distinguished foreign professors, mulled over reports and presentations from various RIKEN representatives and weighed positive developments against shortcomings. Here, fresh after the conclusion of the week-long meeting, RIKEN President Ryoji Noyori and Dr. Zach Hall, President of the California Institute for Regenerative Medicine and RAC Chair, answer questions about the council and its findings.

No other organization in Japan carries out an evaluation of this scope, scale, and international nature. Please describe the RAC's significance and its goals.

Noyori: The RAC is crucial for our survival. Even the strongest organizations only survive if they continue to adapt. The ability to learn from history and to face reality full on will be the life force of RIKEN. Blindness could trigger our decline. We need to hear the voices of many sectors and many learned people.

Hall: President Noyori chose an extremely distinguished committee including people who have headed major institutions in Sweden, the United Kingdom, France, Taiwan, and the United States. It is an honour to be on the committee. We come because we see RIKEN as an institution that has the potential to lead Japanese science into a new era.

We were very impressed that RIKEN implemented recommendations from the last council. I have been on a number of advisory committees. People sometimes say they want your advice, but when you give it, they do not respond. RIKEN's desire for advice is serious. Our job is not to point it in new directions but simply to offer suggestions. Some details need to be worked out, but we think RIKEN is very much on the right track.

What have been notable achievements for RIKEN since the last RAC in 2004?

Noyori: One of the recommendations was to set up a system of governance that could manage RIKEN through an open and accountable process. In response, we established a powerful advisory system, the RIKEN Science Council, consisting of selected RIKEN scientists, who propose many things from the scientist's perspective. We also have powerful top-down leadership which we strengthened with a president's discretionary fund of JPY 1.2 billion. These two systems come together to decide priorities for research.

Hall: One of the key goals from 2004 was to increase visibility. We have been very pleased with RIKEN's efforts to reach out to the public. RIKEN News has been important. The President too has been a very effective ambassador often making himself available to the public.

One signal achievement of President Noyori has been to instil a sense of unity. The range of sciences that RIKEN oversees is astonishing—from the subnuclear all the way to behavioural and cognitive sciences. You could just let the scientists do their own thing. But we believe, and RIKEN believes, that there are important synergies from having physical sciences and life sciences together. If I may quote President Noyori, "It's ok for an institute to be independent, but it can't be isolated." As an example, I talked to one RIKEN scientist studying molecular trafficking in cells. He was using an extremely sophisticated microscope that he had designed here with a RIKEN physicist. You cannot buy an instrument like that anywhere.

Like all Japanese research organizations, RIKEN has struggled to make its staff more diverse in terms of age, sex, and nationality. How has RIKEN done in meeting this challenge?

Noyori: In terms of graduate students, we are doing well. There are now 1,200 graduate students. We need however to increase the number of women scientists in leading positions as opposed to technical positions. Currently only 7% of senior scientists are women.

The biggest problem is the ratio of foreign researchers. At ten percent, it is higher than the Japanese average of 1.4% for universities and public research centres, but it is still too low. We need to reach twenty percent quickly. At the same time, we should focus on the quality rather than the number of researchers. Professor Hall suggested recruiting 'big shot' researchers from overseas to head the institutes. That's a possibility.

In the end, we should import talented scientists to Japan at the same time we export many talented Japanese overseas.

An x-ray free electron laser, being constructed at Japan's SPring-8 facility pictured here, will keep RIKEN at the cutting-edge of molecular studies into the future.

…so that Japan becomes a stepping stone in a researcher's career just like other major scientific countries?

Hall: That's exactly right. We applaud RIKEN's commitment to these goals. We also recognize the problems of language and of being a relatively closed, homogenous society. RIKEN is very progressive in bringing Japan in line with the international community in recruiting foreign and women researchers. Increasingly science will be done in an international marketplace where people move freely from one country to another. RIKEN needs to take advantage of that.

What are RIKEN's future directions?

Hall: We were delighted to see three new large-scale projects. One is the x-ray free electron laser being developed at SPring-8, which will probably be the best of the three major ones being developed around the world. The second is RIBF [Radioisotope Beam Factory, the world's largest cyclotron system] at the Nishina Centre which will be a major resource in investigating nuclear structure. The big news is that it will be open to researchers outside of RIKEN. The third is a petaflop supercomputer.

These are all exciting large-scale plans that will benefit science in Japan and indeed worldwide.

Noyori: We are making essential infrastructure for the scientific community. This will help RIKEN maximize the visibility of our facilities and our research. Such facilities can only be established at a public research institute like RIKEN.

What still needs to be done?

Noyori: Collaboration and interaction with other sectors, such as the clinical research community, within Japan and with scientists worldwide. The budget is going to shrink, so selection and concentration will be important.

Hall: We want to see RIKEN continue with more collaborations inside the organization and with stronger ties externally. RIKEN has some unique strengths that no other institution in the world has. We see RIKEN as a potential world leader.

Molecules light the way

New compounds promise a bright future for white organic light-emitting diodes

Organic light-emitting diodes (OLEDs) are layered semiconductor devices that produce light upon the application of electricity. The emissive layer is a thin film of an organic compound that is sandwiched between two electrodes; one or both of which are transparent. Other layers of organic materials are often incorporated into OLEDs to facilitate the transport of electrons and holes through the device. It is the recombination of electron-hole pairs in the emissive layer that result in the generation of light.

In comparison with regular LEDs and liquid crystal displays, the superior characteristics of OLED devices—they are thinner, brighter, more efficient and flexible—has spurred the development of this technology. In particular, white organic light-emitting diodes (WOLEDs) offer great potential for lighting applications, ranging from general-purpose illumination to small flat-panel displays found in portable electronics such as mobile phones and digital music players.

To ensure that intense emission is achieved across the whole visible spectrum, most WOLEDs are composed of more than one light-emitting component. There are some examples of single-emitting-component WOLEDs based upon polymers, but none of them emit 'pure' white light.

An illuminating discovery

Now, researchers at RIKEN's Discovery Research Institute in Wako and Jilin University in China have developed[1] a new class of materials known as π-conjugated organic compounds, which can, individually, emit pure white light. This discovery has enabled the team, led by Zhaomin Hou, to build single-emitting component WOLEDs, an advance that Hou argues has "many advantages, such as better stability, better reproducibility and a simpler fabrication process."

The organic molecules are built around a central enyne unit—a carbon-carbon double and triple bond linked directly to one another. This holds together two substituents, carbazole groups, which are known for their interesting optoelectronic properties. These compounds are made in remarkably high yields using catalysts that contain either a lanthanum or lutetium atom—two of the so-called lanthanide elements—which are decorated with organic groups.

The chemical synthesis begins with a single starting material that has a reactive alkyne (carbon-carbon triple bond) group at one end. In the presence of the lanthanide catalysts, the alkyne molecules are joined together in pairs to form the enyne compounds. Two structurally related enyne compounds can be made selectively depending upon the composition of the catalyst.

When the lutetium catalyst is used, the groups attached to the central carbon-carbon double bond point away from the same side of the molecule resulting in a U-shape. In contrast, the lanthanum catalyst gives a similar compound, but the double bond substituents stick out from opposite faces and the molecule adopts a relatively linear, albeit slightly kinked, shape.

A colorful combination

In solution these compounds fluoresce blue. However, when deposited as a thin film, additional emissions in the green and red regions of the visible spectrum combine to produce white light. These longer wavelength emissions originate from the formation of closely associated pairs of electronically excited molecules, known as excimers, confined together

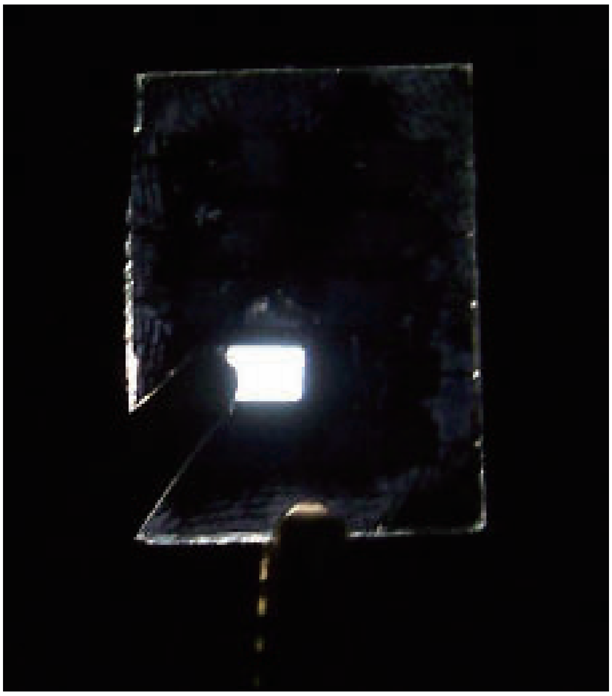


Figure 1: A photograph of the single-emitting-component WOLED in action.

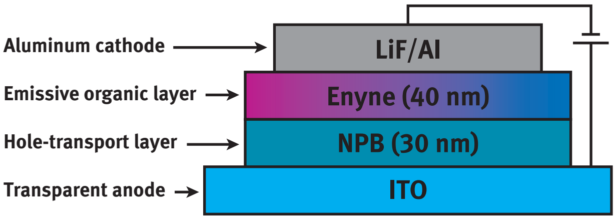


Figure 2: A schematic diagram showing the layered structure of the new WOLEDs.

in the solid state. “Honestly speaking, this is a serendipitous discovery,” admits Hou. “It was an unexpected surprise to us that a simple π-conjugated organic compound, which shows intense blue fluorescence emission in solution, can emit pure white light in a solid-state device.”

To construct a working device, a thin layer of the emitting compound is sandwiched between a transparent indium-tin-oxide (ITO) electrode and a reflective aluminium-based one. The devices (Fig. 1) typically measure 2 x 3 mm, are 300–400 nm thick, and only require small amounts of the organic compound—approximately one hundredth of a gram.

The first generation of devices consisted of a single 60 nm film of the organic molecules produced by vacuum deposition. When a voltage was applied to these devices, white light was emitted. The device characteristics could be further improved by adding a second layer of an organic material that acts as a hole-transport layer. A commonly used compound for this purpose is known as NPB and is commercially available. According to Hou, “NPB can improve many properties of an electroluminescence device, such as increasing the brightness and efficiency, and lowering the turn-on voltage.”

The path to enlightenment

As expected, the second-generation double-layer devices (Fig. 2) incorporating a layer of NPB did exhibit better device performance. Not only did the intensity of the emission increase, but purity of the white light also improved. In this field, color is often defined using CIE (*Commission Internationale de l’Eclairage*) coordinates and those obtained for this device (0.32, 0.33) are almost the same as those of pure white light (0.33, 0.33).

Although the brightness of these devices is no match for traditional light bulbs, they are comparable with present day television and computer displays. Hou also points out that the fluorescence intensity achieved is among the highest reported for single-emitting-component WOLEDs. These WOLEDs are not ready for the marketplace just yet. In the current generation of devices, the turn-on voltages are still a little high and the long-term stability and lifetime of the WOLEDs has not yet been addressed. “Further studies are required for commercial application,” says Hou.

Building upon their success so far, Hou and colleagues plan to broaden the scope of their investigation. “We plan to synthesize a series of derivatives having different substituents, based on the π-conjugated enyne core structure reported here, to try to gain more information about the structure-property relationship of this new class of compounds,” says Hou. “Based on this knowledge, we will design and develop more efficient materials for WOLEDs.”

1. Liu, Y., Nishiura, M., Wang, Y., & Hou, Z. π-Conjugated aromatic enynes as a single-emitting component for white electroluminescence. *J. Am. Chem. Soc.* **128,** 5592–5593 (2006).

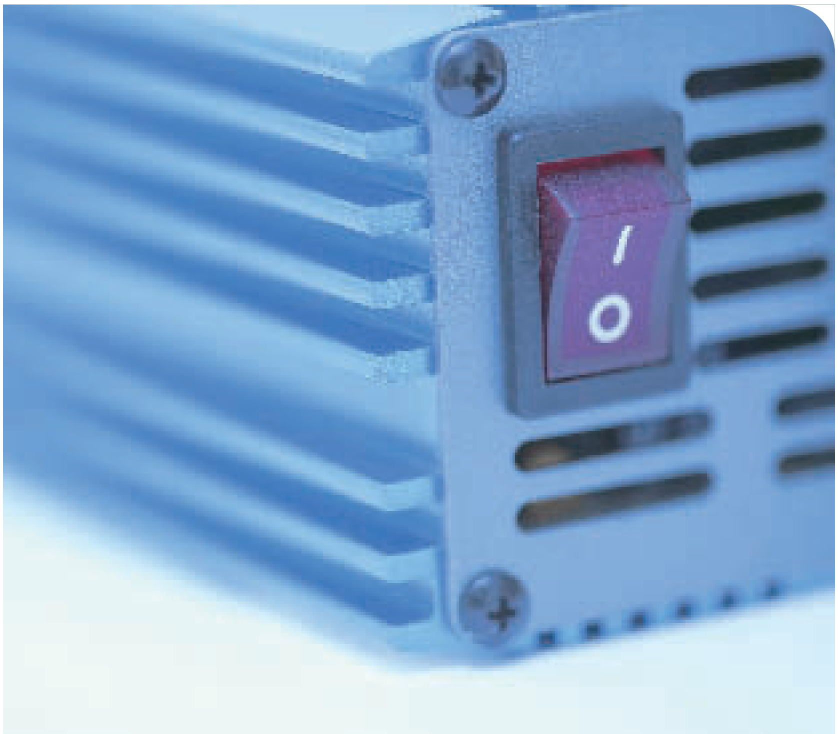
About the Author

Zhaomin Hou graduated from China’s University of Petroleum in 1982, majoring in applied chemistry, and earned his doctorate at Kyushu University in 1989. He became a postdoctoral fellow at RIKEN in 1990. After a two-year fellowship at the University of Windsor in Ontario, Canada, he became a research scientist at RIKEN in 1993, becoming Chief Scientist and Director of the Organometallic Chemistry Laboratory in 2002. Currently, Hou also teaches at Rikkyo University and Saitama University in Japan and Peking University in Beijing. http://www.riken.jp/lab-www/organometallic/engl/index_e.html.

The shifting currents of superconductors

Odd oscillations revealed in simulations

Some superconductors just cannot make their minds up when it comes to electrical current. RIKEN researchers have found that the flow of charge through certain types of fabricated superconducting materials can spontaneously flip between two different values, an unusual effect that could prove useful in developing new electronic devices.



For simple metal wires, a fixed voltage produces a predictable electrical current. Turning up the voltage proportionally increases the flow of charge, just as a higher pressure will force more water through a pipe.

But some semiconductor materials have a strange property called negative differential resistivity—as the voltage increases, currents rise, then fall and finally rise again. This behavior allows some diodes to generate an oscillating current from a fixed voltage. These devices are used to make radio waves, for example, in the car radars that help drivers reverse into tight parking places.

Now scientists at RIKEN's Frontier Research System in Wako have looked at the equivalent effect in superconducting materials, which can carry current with virtually no resistance. Superconductors are used in a variety of applications, including ones with large magnetic fields used in medical imaging devices.

They used computer simulations of superconducting materials that have a regular pattern of man-made defects within their crystal structures. These nano-fabricated 'pinning sites' help to trap magnetic flux within the superconductor, which ultimately helps to improve the flow of current. This in turn boosts the performance of sensitive instruments made from the material.

The team found that a single, fixed voltage could actually induce one of two different current flows through the sample. Under certain conditions, the current will actually cycle between the two values in a regular way, they report in *Physical Review Letters*[1].

This indecisive behavior could actually be useful because it provides a way to switch sharply between different states. Under certain conditions, these two states are stable, and these could eventually be used to represent bits of data in a computer, for example, that are either 'on' or 'off'. "This binary logic is far more difficult to achieve with linear circuit elements," says Franco Nori, part of the research team.

The researchers think that the behavior could be triggered when a uniform current breaks down into separate strands, or filaments within the material, which have different current densities. Understanding the effect gives scientists the ability to 'sculpt' the shape of the current-voltage response of the material, and this should allow them to manipulate magnetic flux in these devices in the same way that semiconductors manage the flow of electrons, Nori adds. ■

1. Misko, V. R., Savel'ev, S., Rakhmanov, A. L. and Nori, F. Nonuniform self-organized dynamical states in superconductors with periodic pinning. *Phys. Rev. Lett.* **96**, 127004 (2006).

What's in noise?

Experimental evidence confirms that two fundamentally different sources of noise in quantum computers share the same origin

Amongst the promises of quantum computing is the expectation to perform certain computations much faster than any conventional computer could. However, one of the problems that plague quantum computers is the lifetime of quantum states that are used for the mathematical algorithms, the qubits.

Detrimental to the lifetime of those qubits is noise, tiny fluctuations influencing the quantum states of the devices. "Once the origin of noise is identified, the noise can be reduced. This will help to capitalize on the advantage of solid-state qubits to build chips for quantum computers," explains Oleg Astafiev from RIKEN's Frontier Research System in Wako. Joint with the NEC Fundamental and Environmental Research Laboratories in Tsukuba, the group has been long studying the noise in a particular set of qubits—those formed by the interface of two superconductors, known as the Josephson junction (Fig. 1).

At those junctions, two types of noise occur. One originates from the fluctuations of electronic charge in the device. The intensity of this noise decreases with frequency as $1/f$. The second type of noise is associated with the quantum state itself and scales with f. In a previous work of the same research group, indications suggested that these two types of noise might have a common origin. This result was unexpected and led to intensive theoretical studies. "But it was difficult to convince theoreticians that the two noises are really coupled," says Astafiev. The aim was therefore to conclusively prove this hypothesis.

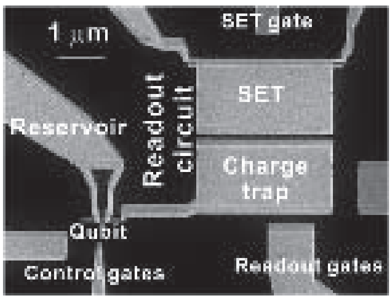


Figure 1: Micrograph of the Josephson charge qubit with readout circuit (SET is a single electron transistor).

The evidence for this coupling lies in the temperature-dependence of the $1/f$ noise, which the research team demonstrated experimentally. These experiments are not as straightforward as one might expect and several precautions have to be taken to correct for various effects that influence the measurements at different temperatures. However, reporting in the journal *Physical Review Letters*[1], the group presents firm evidence that these two noises have indeed a common origin.

The pressing question now is to uncover the reason behind this intriguing coupling. It will be no easy task. "We are planning to continue the experiments that can clarify the origin of the noise," says Astafiev. "I think it is hard to imagine that just one or a set of experiments will provide a definite answer. Maybe this can be achieved through close collaboration of experimentalists and theoreticians." ■

1. Astafiev, O., Pashkin, Yu. A., Nakamura, Y., Yamamoto, T. & Tsai, J.S. Temperature square dependence of the low frequency 1/ƒ charge noise in the Josephson junction qubits. *Phys. Rev. Lett.* **96**, 137001 (2006).

Cool molecule reveals its true nature

Elusive quantum state observed in designer molecule

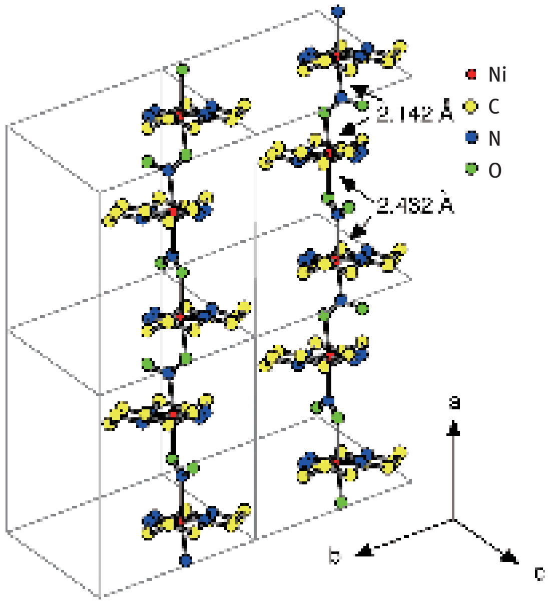
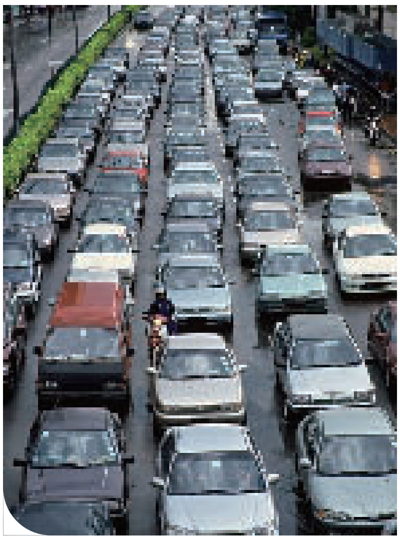


Figure 1: The molecular structure of NTENP, $Ni(C_9H_{24}N_4)NO_2(ClO_4)$.

When things get small, materials change their physical properties significantly. In particular at lower dimensions, the behavior of electrons can be very different. Imagine driving on a highway without the possibility of overtaking other cars—if some cars are slower than others, a traffic jam occurs. Indeed, the most efficient organization in such an environment is if all cars synchronize and drive at exactly the same speed. The same occurs to electrons in one-dimensional systems at low temperatures; they synchronize themselves and rearrange into complex quantum states.

One such quantum state for one-dimensional systems was described by S. Tomonaga and J. M. Luttinger, and is now known as the Tomonaga-Luttinger liquid (TLL). Previously, this quantum state has been observed mainly in carbon nanotubes and quantum wires.

However, when a magnetic field is involved, the physics become more complex. For antiferromagnets with an energy gap—magnetic systems where the magnetic field is alternating between ‘up’ and ‘down’ states—the TLL competes with other quantum states. Only at higher magnetic fields is the TLL expected to form. “To date, however, all experimental evidence in these gapped antiferromagnets has been either controversial or circumstantial,” says Hiroyuki Tsujii from RIKEN’s Discovery Research Institute in Wako. Together with researchers from Osaka University, the University of Florida and the Advanced Science Research Center in Tokai, the RIKEN group went on the hunt for this elusive quantum state.



The key to a conclusive observation of the TLL lies in the material itself, as the symmetry of the molecule has to be precise in order to obtain clear experimental evidence. An attractive candidate is NTENP (Fig. 1).

However, synthesis and characterization of NTENP was not the last hurdle in the search for TLL. The right equipment needed to be built first. In the experiments, tiny changes in the specific heat of the molecule have to be measured at high magnetic fields and low temperatures. “Crucial has been the development of the low-temperature calorimeters, which are capable of reaching 34 mK in magnetic fields up to 20 T,” explains Tsujii.

Using this new equipment, the measurements performed at the National High Magnetic Field Laboratory in Florida, USA and at Osaka University, show striking evidence for the TLL state[1]. Based on these promising results, the next step is to expand our knowledge of the TLL state and as Tsujii says, “To measure the specific heat at higher magnetic fields to extend the phase diagram as well as to check how the TLL behavior persists.”

1. Hagiwara, M., Tsujii, H., Rotund, C.R., Andraka, B., Takano, Y. Tateiwa, N. *et al.* Tomonaga-Luttinger liquid in a quasi-one-dimensional S=1 antiferromagnet observed by specific heat measurements. *Phys. Rev. Lett.* **96**, 147203 (2006).

How proteins work to make us move

Researchers begin to tackle the molecular basis of muscle function

An international team led by a RIKEN researcher has begun to unravel some of the complex molecular details as to how muscles function.

The area is a hot topic of research because understanding how muscles work could lead to better treatment for medical conditions such as muscular dystrophy and some forms of heart disease. It could also provide a basis for developing more efficient artificial limbs and prosthetic devices and even for the production of biomotors for robots and microscopic devices.

At a molecular level, muscle contraction is a complicated interplay between two proteins, myosin and actin. Myosin molecules have a bulbous head (the motor domain) (Fig. 1) tacked onto a rod-like tail (the lever arm). Actin molecules join together in long chains to form a double-stranded helical filament. By alternately attaching to and detaching from the actin filament in a ratchet-like process, a myosin head 'walks' up its length, in the process pulling back on the filament and contracting the muscle. The energy for this process comes from splitting a phosphate group from the body's standard energy molecule adenosine triphosphate (ATP).

The research group, based at RIKEN's SPring-8 Center in Harima, investigated the details of the molecular attachment process to the actin filament[1]. From earlier work using crystallography and electron microscopes, the researchers determined an area or 'patch' on the head of the myosin molecule where the actin filament was bound. This patch is surrounded on three sides by molecular loops sticking out from the myosin head. These loops appeared to play a key role in binding the myosin head to the actin filament.

The researchers made changes to the structure of each of these loops, and then assessed the impact of their interference on the binding process. The loops surrounding the patch are guided into alignment with the actin filament by means of a weak interaction between the myosin head and the filament.

At this point, each of the loops becomes involved in specific strong binding with the actin filament. The result is to change the shape of the myosin head, closing a cleft in one place, while in another uncovering the bound ATP molecule and providing a pathway for its terminal phosphate group to split off. Thus, as the proteins bind together, the myosin is prepared to cleave its ATP molecule which provides it the energy to detach and thrust its head further up the length of the actin filaments.

"This study is just the beginning of the understanding of actin activation," says Hirofumi Onishi of the SPring-8 Center. "The binding to actin triggers the whole of the later movement of the head. I want to continue this line of work using the same strategy." ■

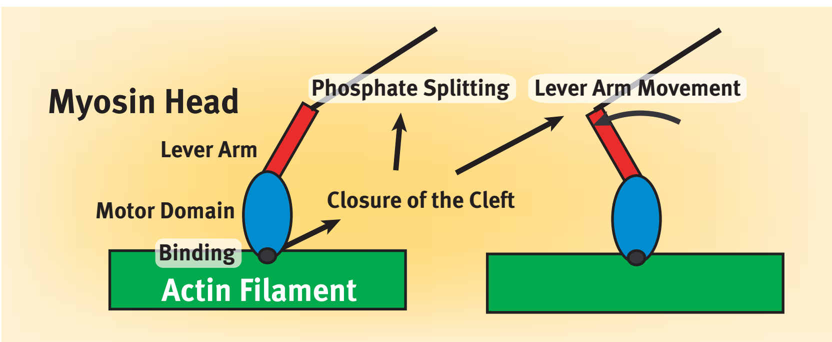


Figure 1: Muscle contraction at the molecular level.

1. Onishi, H., Mikhailenko, S.V. & Morales, M.F. Toward understanding actin activation of myosin ATPase: the role of myosin surface loops. *Proc. Natl. Acad. Sci.* USA **103,** 6136–6141 (2006).

Shedding light on how sensors work

Researchers from RIKEN and two Japanese universities have confirmed the molecular details of how a significant group of light-sensing proteins work

Photosensitive compounds not only play a key role in the conversion of light into energy in biological systems, but they are also important for sight and vision, and act as triggers for many activities. So, understanding how such compounds function has great relevance to fields as diverse as medicine, robotics and environmental science.

In many photoreceptor compounds, such as the rhodopsins found in human eyes, the absorption of light triggers a series of far-reaching structural changes. But this is not the case in the compounds known as BLUF proteins which are sensitive to blue light and control the function of photosynthetic genes in microbes. Here, the changes induced are much less drastic, and lead to absorption of light at longer, that is slightly redder, wavelengths.

One suggestion, based on structural data, is that blue light causes a reshuffling of the hydrogen bonding within the BLUF protein so that one of its amino acid components, a glutamine, rotates by nearly 180 degrees (Fig. 1). The Japanese research team, including Taka-aki Ono from the RIKEN Discovery Research Institute in Wako, set out to test if this hypothesis were correct. Their results are reported in the *Journal of the American Chemical Society*[1].

The conventional way of determining the structure of proteins involves crystallizing them and then looking at the deflection patterns produced by probing the resultant crystals with x-rays. When the researchers did this under conditions without light, however, they found the critical glutamine residue had already taken up the position predicted after treatment with blue light.

Suspicious that this result may be an artefact of the crystallization process, the group employed other techniques, including vibrational spectroscopy, to determine the position of the BLUF glutamine in the dark and in solution rather than crystallized.

Their measurements confirmed the difference between the dark and light forms of the BLUF proteins with respect to the critical glutamine. And the researchers reinforced their conclusions by constructing a mathematical model which simulated the data they obtained.

Further investigation of the BLUF protein is planned, says Ono. The team hopes to unravel how the changes induced by light lead to control of the photosynthetic genes. ■

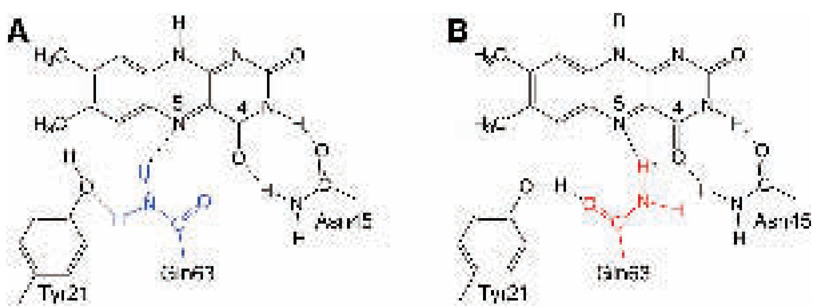


Figure 1: Possible structures of the active site of a BLUF protein in the dark (A) and after treatment with blue-light (B). The side group of the glutamine (Gln63) has rotated into a different position.

1. Unno, M., Masuda, S., Ono, T. & Yamauchi, S. Orientation of a key glutamine residue in the BLUF domain from AppA revealed by mutagenesis, spectroscopy, and quantum chemical calculations. *J. Am. Chem. Soc.* **128,** 5638–5639 (2006).

Moody mice and humans not necessarily poles apart

Transgenic 'moody' mice provide model for testing drugs to treat bipolar disorder and investigate its causes in humans

Brain researchers from RIKEN have developed a useful mouse model for the debilitating human mental condition of bipolar disorder. In doing so, they have strengthened a proposed link between bipolar disorder and disruption of the function of mitochondria—the energy production centres—in nerve cells in the brain.

The work should lead to better targeted research to unravel the genetic and molecular details of what leads to bipolar disorder, and potentially to the development of future therapies.

Earlier research has shown there is a strong inherited or genetic component of bipolar disorder. Recent studies have demonstrated that bipolar disorder is associated with altered mitochondrial function in the brain, and that patients with mitochondrial diseases also sometimes have mood disorders. Taken together, these pieces of evidence suggest that genetic mutations which disrupt the workings of the mitochondria in the brain may be responsible for mood disorders.

So, researchers from the RIKEN Brain Science Institute in Wako focused their studies on a human mitochondrial disease, chronic progressive external ophthalmoplegia, which is both caused by genetic mutation and linked to mood disorders. The researchers were able to generate transgenic mice with a similar condition. Their research is reported in *Molecular Psychiatry*[1].

It is difficult to determine moods in non-human animals, and to compare them with their human equivalents. The research team therefore decided to judge whether the genetic changes in their transgenic mice led to a state like a human mood disorder on the basis of three criteria—similarities in behavior, a common mechanism which explains the disorder in both mouse and human, and the same reactions to treatment with the same drugs.

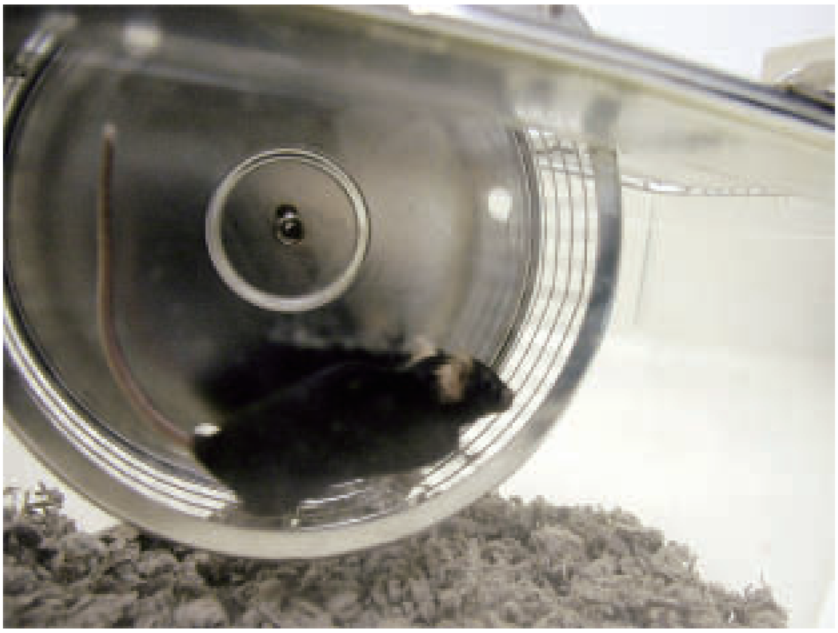


Figure 1: The researchers analysed wheel-running activity of their transgenic mice to determine alterations in behavior.

The researchers, in collaboration with colleagues from the Nagoya University Graduate School of Medicine, found their transgenic mice not only had similar genetic mutations in the nerve cells of the forebrain as humans with bipolar disorder, but also showed characteristic altered behavior (Fig. 1). In addition, the transgenic mice reacted to antidepressants and to mood stabilizing drugs in a similar way to humans with bipolar disorder.

The researchers now aim to use their model to identify the details of the molecular pathway by which the mutation has its impact, says team leader, Tadafumi Kato. "We also want to use the mice to evaluate candidate drugs for therapy, and we hope to identify the neural circuit directly linked to bipolar disorder." ■

1. Kasahara, T., Kubota, M., Miyauchi, T., Noda, Y., Mouri, A., Nabeshima, T. & Kato, T. Mice with neuron-specific accumulation of mitochondrial DNA mutations show mood disorder-like phenotypes. *Molecular Psychiatry* advance online publication, 18 April 2006 (doi: 10.1038/sj.mp.4001824).

Takao K. Hensch
Experiences shape the brain

A neuroscientist trying to unveil the mechanisms of early brain plasticity uncovers implications for better education, innovative drug design and neuroethics

When Takao K. Hensch started French lessons at a local elementary school in New York, he was surprised to see how his classmates struggled with a second language. For him, it was a straightforward task and he quickly acquired the communication tool without too much difficulty.

Soon, Hensch realized his ability was not gifted, but derived from something special in his environment. His father was German and his mother Japanese, speaking to him strictly in their native tongue. At school, he spoke with friends and teachers in English. As a result, Hensch naturally mastered the ability to switch from thinking in one language to another according to his conversation partner. “My unique background gave me a different perspective from that of my friends,” says Hensch, who himself is an American citizen. “Having realized that, I grew fascinated by the mystery of the brain.”

Years later, Hensch has become one of the world’s outstanding young neuroscientists, and now heads the Critical Period Mechanisms Research Group and Human Learning Group at RIKEN’s Brain Science Institute (BSI) in Wako, near Tokyo. The 39-year old researcher investigates how sensory experiences shape the mammalian brain during vital periods in early life, and has reported unexpected findings about how the brain learns. His work not only suggests various applications for educational policies and new drug design to treat developmental disorders, but also draws attention to emerging ethical issues associated with our growing ability to manipulate brain function.

The brain’s ability to rewire its circuits

The brains of mammals have a particular capacity, known as plasticity, that enables them to change the wiring of their neuronal circuits through experience – and to keep learning new things throughout life. This plasticity is greatly enhanced shortly after birth during a ‘critical period’ that lasts from a few weeks to many years, depending on the type of species and brain region. Environmental and external stimuli are key factors influencing brain plasticity, and some behaviors and perceptions, including language learning and visual acuity, are strongly determined during this limited time in early life. For example, it is difficult for adults to become perfectly bilingual unless they have spent their childhood in a two-language environment.

At the beginning of his career, says Hensch, “I wanted to understand various levels of brain function.” As an undergraduate at Harvard University, he researched brainstem mechanisms of sleep rhythms. In 1988, he moved to the University of Tokyo for his Master’s degree, where he studied under Masao Ito, a world authority on the cerebellum and later founding director of BSI. Hensch then spent a Fulbright year in Germany before earning his Ph.D degree at the University of California, San Francisco (UCSF). Ito then called on him to establish a lab at the newly forming RIKEN BSI in 1996, when he was just 29.

“The success of Takao’s research has been really remarkable, and I am proud of this because it demonstrates how excellently RIKEN BSI system works when run by competent researchers,” says Ito, now Group Director at BSI’s Neuronal Circuit Mechanisms Research Group.

At RIKEN, Hensch focused on his long-standing interest in the development of visual circuits as a classical model of critical period plasticity[1]. Historically, closing one eye of a kitten during this time in development – even for just a few days – greatly weakens the response of neurons in the visual cortex and results in permanent amblyopia (‘lazy eye’), while the open eye’s responses are enhanced. In contrast, covering an eye in adulthood doesn’t disrupt its visual acuity. This ground-breaking discovery 40 years ago surprised many and earned a Nobel Prize, but how the phenomenon is established has remained largely mysterious.

Opposite thinking

The brain’s neural networks consist of excitatory and inhibitory circuits. Because the excitatory cells constitute 80% of cortical neurons, many neuroscientists including Hensch had assumed that excitatory connections would have a dominant role in promoting plasticity during the critical period. However, numerous experiments failed to show this. Then Hensch hit upon an unconventional hypothesis. As he puts it, “We thought the minor inhibitory circuits might exist not only to prevent excessive excitation, but rather play a specific role in creating the balance required to drive plasticity.”

Pioneering the use of mice as a model and incorporating cutting-edge cellular and computational perspectives, Hensch

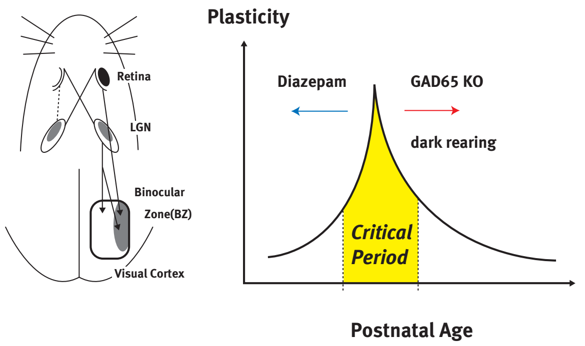


Figure 1: Critical period for plasticity is triggered by inhibitory (GABA) circuits within visual cortex.

attempted to uncover the role of inhibitory transmission in cortical plasticity by disrupting genes for candidate proteins. He says he has been grateful to be working at RIKEN, where his team could profit further from the ongoing construction of a mouse genome encyclopedia through collaboration with the Genome Science Laboratory.

Hensch and his colleagues eyed GABA (γ-aminobutyric acid), the primary inhibitory transmitter in the brain (Fig. 1). Two types of gene encode enzymes that produce GABA. Deletion of one of these, GAD67, leads to death at birth, but Hensch found that the other type, GAD65, was the trigger for plasticity. When one eye was closed during the typical critical period in mice lacking GAD65, visual acuity remained normal, indicating that plasticity had not occurred[2]. The team further successfully restored plasticity to the knockout animals by injecting benzodiazepines (a positive modulator of GABA receptors) directly into the visual cortex. With this tool, Hensch's team showed in 2000 that the level of inhibition within cortex triggers the critical period at any time in life[3], suggesting for the first time that the profile of plasticity could be freely and directly manipulated.

They continue to provide new insights downstream of this inhibitory trigger. By adjusting GABA transmission, he altered the spacing of anatomical ocular dominance columns (clusters of preferentially right or left eye inputs)[4], and his team identified proteases as an important mediator of the very earliest structural changes at the level of dendritic spines[5]. Hensch further applies his accumulated expertise to examine the relationship between sleep rhythms and experience-dependent plasticity, because both systems share the same circuits in cortex and thalamus.

> **"My unique background gave me a different perspective from that of my friends. Having realized that, I grew fascinated by the mystery of the brain."**

His remarkable achievements have led to his appointment as Professor of Molecular and Cellular Biology at Harvard University from the 2006-2007 academic year. Hensch will jointly hold a position as Professor of Neurology at Harvard Medical School, where he hopes to contribute to a planned project on autism at Children's Hospital Boston. His lab at BSI will continue to explore the link between sleep and plasticity.

Bridging the gap between Japan and the world

Outside the lab, Hensch works hard to provide policymakers and parents with accurate information on brain science and education. He warns that it is unwise to worry too much about 'missing' the critical period, as it is wrong to say that later learning is hopeless. "What happens after the critical period is simply a change in the brain's learning strategy," he says. As a father of three, Hensch applies his work to recognize and enrich each boy's personality and strengths.

Education aside, Ito says Hensch has been 'instrumental' in the internationalization of BSI. Although he thinks that Japan' s brain researchers are outstanding, Hensch is irritated by the geographical and mental distance between Japan and other countries, especially the United States. He is beginning to work closely with RIKEN's President Ryoji Noyori on plans for a Science-Culture Exchange Center at RIKEN. "Researchers in the U.S. think that the East Coast is enough. I want to change this mindset," Hensch says.

In 1999, Hensch launched an annual summer school at BSI, inviting about 50 top-level students each year from around the world to experience Japan and the institute. Thanks to his efforts, several dozen non-Japanese participants or friends have later returned to RIKEN as full-time researchers. Hensch has already encouraged Harvard to provide course credits, travel and accommodation expenses for its students joining the program. "What I can do alone is limited, but these students are the future. They can promote what they have learned here and are contributing greatly to the internationalization of RIKEN." ■

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About the researcher:

Takao Kurt Hensch was born in Tokyo in 1966, and moved to New York in 1969. In 1988, he graduated from Harvard University majoring in biological sciences, and then spent two years at the University of Tokyo Medical School. In 1990-1991, he studied at the Max-Planck Institute for Brain Research in Germany and returned to the US for a Ph.D in neuroscience from the UCSF in 1996. The same year, he was appointed Laboratory Head for Neuronal Circuit Development at the Frontier Research System prior to the launch of BSI. In addition, he now serves as director of two research groups (see the text). In the fall of 2006, he will become Professor of Molecular and Cellular Biology at Harvard University and Professor of Neurology at Children's Hospital Boston, Harvard Medical School. He has won a number of awards, including Japan's Minister of Science, Education, Culture, Sports, Science and Technology (MEXT) Prize in April 2006 and the first US Society for Neuroscience Young Investigator Award from abroad in November 2005.

Elucidating principles of the brain mathematically

Shun-ichi Amari

Group Director of Brain-Style Computing Group
Leader of Amari Research Unit and Director of Neuroinformatics Japan Center
Director of Brain Science Institute
RIKEN Wako Institute

No brain-measurement equipments, no chemical agents, and no laboratory mice can be found in the laboratory led by Shun-ichi Amari, Leader of Amari Research Unit and Director of Brain Science Institute. Instead, he uses mathematics as his research tool. "Experimentation has revealed in sequence the activities of nerve cells and the functions of genes and proteins in the brain. However, experiment-based data is not all that is necessary to elucidate the mechanism of the brain. Science, like physics or chemistry, starts with the discovery of facts based on experiments, discloses the essence behind a number of facts, and finally expresses that essence in mathematical form. Thus I am sure that the mechanism of the brain can be expressed mathematically," says Amari, who has been pursuing a mathematical model of the brain for the last 40 years. However, I wonder if the day will ever come when we can elucidate the mechanism of the brain and understand what the human being is in mathematical form?

Information processing mechanism of the brain

Amari used the following example to explain the remarkable capabilities of the brain. "Suppose you see an acquaintance whom you have not seen for a long time. I am sure you have no difficulty in remembering them, even if that person has put on a little weight. It may seem to be a simple process, but it is no easy matter for a computer to simulate the process, because a huge number of steps are required in processing the data."

The brain is very slow in processing data, about one-millionth the speed of current computers. In contrast, the brain needs far fewer steps to instantaneously recognize a person. But what makes that possible?

"It is the force of numbers," answers Amari. In the whole human brain, there are more than 100 billion nerve cells, each of which is connected to another 10 thousand nerve cells. "The brain can process information instantaneously because the vast number of nerve cells it contains exchange information in a parallel manner. In this process, each nerve cell acts in a rather fuzzy manner, and its function is not as specific as the function of a computing device. However, the neural circuits as a whole eventually derive appropriate answers."

Amari has tried to elucidate such a complicated system by using mathematics. "Mathematics is a kind of culture that human beings have created as a means to understand the essence of things. Today, in the face of various life phenomena, especially the brain, we are trying to understand this very complicated system by using mathematics. However, we need to establish a new mathematics because conventional mathematics has no chance. Efforts to understand life phenomena and the brain will surely serve as the impetus for creating a new mathematics and new fields of science."

What is the essence of learning?

"A new mathematics that will allow an understanding of the brain cannot be established in a day. Thus we have not only relied on conventional mathematical theories but have also drawn on the whole of our 'mathematical sense' to move forward our own research," says Amari. One specific research subject based on this approach is learning.

For example, people are able to recognize handwritten characters after receiving training in which various examples of handwritten characters are presented in the manner of 'this is A, and this is B.' "Then, surprisingly, a 'sensation' is created in the brain that will enable you to recognize A or B even if they are slightly different from the original characters. In other words, human beings have the ability to learn the essence or mechanism behind various examples. This is the very nature of learning."

However, what is happening in the brain during the process of learning? As training proceeds, the manner of information exchange in the neural circuit gradually changes at synapses, which are the junctions between nerve cells. For example, some pieces of information will run more smoothly, whereas others won't. Thus it is thought that this is how the learning process of a task proceeds.

Then, can we expect that the more complicated the neural circuit is and the higher the number of nerve cells, the faster the learning process proceeds? How many examples do we need for training?

"If the neural circuit is too complicated, a large number of synapses will require adjustment. Furthermore, if the complicated neural circuit exerts all its powers but has an insufficient number of examples, a phenomenon will take place in which handwritten characters such as A or B can only be recognized when the original sample characters are presented. This is because the neural circuit has been too meticulous to detect the rule behind the examples. We are trying to analyze mathematically the complexity of the neural circuit and the relationship between the number of examples and the progress of learning in an attempt to derive general rules. I am sure that the abstracted rules can be applied to both humans and computers."

Singularity in the learning process

Among the many areas of mathematics, Amari puts the emphasis on geometry, which is the branch of mathematics used to explore the properties of figures and space. He has also used figure space to express the relationship between the neural circuit and learning in an attempt to find the rules.

For example, the distance between nerve cells is considered to be wide when they are connected through synapses in which the change in information flow significantly affects the progress of learning, whereas the distance is considered to be narrow when they are connected through synapses in which the change has an insignificant effect on the progress of learning. Thus the whole neural circuit can be expressed as a 'curved (deformed)' space with the same number of dimensions as the synapses. This space can change into various shapes depending on the complexity of the neural circuit and the number of samples.

"We are dealing with the space in order to explore the relationship between the neural circuit and learning. The research subject I am currently fascinated with is the occurrence of a singularity phenomenon, where a point in the space is extremely contracted. This means that the learning process does not proceed, regardless of any measures taken to change the flow of information through the synapses."

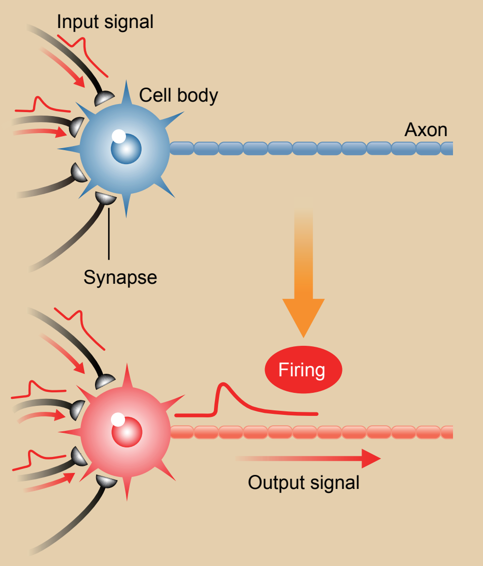

Figure 1: Firing mechanism in nerve cells.
A nerve cell is connected to and receives signals from about 10,000 nerve cells through synapses.
The nerve cell fires when the summed intensity of the input signals to the nerve cell exceeds a certain value, sending a signal to other nerve cells.

In some cases of handwritten character recognition, the discriminating power was found to stay constant regardless of any increase or decrease in the flow rate of information. This leads to the discovery of a phenomenon in which the learning process comes to a halt because no way is found to proceed.

In fact, such phenomena were reported in computer image recognition systems, but the cause has remained unknown. “The culprit was found to be the existence of singularities. We have successfully derived the conditions for singularities not to form in order to develop measures to prevent them.”

Proposed ‘Information Geometry’

A nerve cell can generate electrical signals, receive signals from many other cells, and generate electrical signals when the intensity of signals from other cells exceeds a threshold (Fig. 1). This is called ‘firing.’ How is this firing involved in processing information?

“For example, in an experiment where the same figures are repeatedly presented, each firing seems to occur quite randomly. However, it is not completely random, and the phenomenon is governed by rules. The key to analyzing these rules, we think, is ‘probability.’ For example, once a firing occurs, the probability of occurrence of a subsequent firing, or the probability of occurrence of a firing in a certain period of time increases.”

It is thought that the number of firings and their timing are a method to express information. For example, when information is sent to a muscle to tell it to ‘exert a strong force,’ many nerve cells fire repeatedly in a short period of time. In contrast, when information is sent to a muscle to tell it to ‘exert a weak force,’ the number of firings is reduced. The regularity of the firings also conveys different information with different meanings.

Furthermore, the comparison of two of three nerve cells may show that their activities are quite different. However, simultaneous consideration of all three nerve cells may lead to the discovery of some relationship among them.

To analyze these types of activities in nerve cells, mathematical approaches involving probability and statistics are very useful. In this area, Amari has also advanced the research by applying geometry to the analysis of probability and statistical distributions (Fig. 2).

“In the 1980s, I put forward a proposal that we establish an ‘information geometry,’ that is, a branch of geometry that can deal with information based on integrated mathematical theories.”

But why geometry? “Geometry, which can express phenomena in figure space, is the most intuitive of all the fields of mathematics, and helps us to visualize a concept,” says Amari, who has held prominent positions such as Founding Board Member and President of the International Neural Networks Society, and who is thus a global leader in the field of theoretical research on the brain.

Thinking process that goes between the conscious and unconscious

Amari tells us about his future goals. “For example, even simple organisms can make their own choice whether to get away from or come closer to an external stimulus when it is given. However, how is the information expressed during the thinking process, or how is the final decision made? We want to create a mathematical theory that can describe the dynamics of this

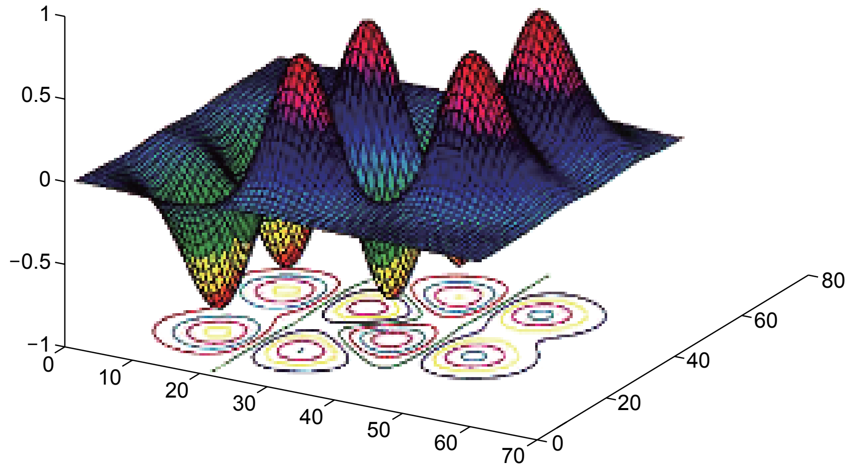

Figure 2: **A research example of spatio-temporal firing patterns in nerve cells.**

process. Furthermore, I am sure that we cannot get by with avoiding the issues of consciousness and mind if we try to explore the thinking process of human beings."

The thinking process of human beings is divided into two categories: information processing in the realm of the conscious, and in the realm of the unconscious. For example, handwritten character recognition is dealt with in the realm of the unconscious, and words alone can never describe how the recognition is performed.

"When we try to solve mathematical problems, many things pop up in the realm of the conscious such as 'this approach may contribute to solving the problem,' or 'we are coming to a dead end at this point.' In other words, the brain processes information in the unconscious realm and brings the results into the conscious realm. However, what we write on a test paper is limited to what we think logically in the conscious realm. Thus we extract some parts and express them logically to make up a program for processing information. Of course, human beings can process information in a logical way, but we need to pay special attention to the information that is processed in the unconscious realm."

"I believe that human beings have ability to see into the essence of a complicated system like the brain, even though it is immensely complicated."

Future of brain research

The advance of research into a mathematical model of the brain will clarify what can be done or what cannot be done in a system like the brain. This knowledge will serve as an important means to understand what a human being is, and can also be applied to using technology to create a system like the brain. For example, it will be able to contribute to building a robot that, like a human being, can make the right decisions and act on them in various situations. However, how will research proceed in the future?

"Physics, including the theory of relativity and quantum theory, has finally resulted in a single set of equations. However this does not hold true for a mathematical model of the brain. I believe it is necessary to establish multi-strata theories that can explain various aspects of the brain from the microscopic world to the macroscopic world, and to systematize them."

Finally Amari talked confidently about prospects for the future. "I think a mathematical model of the brain will be completed by the middle of this century at the latest. I would say that we have reached the level of 30 to 40%. In the rapidly-advancing field of brain research, we need more breakthroughs because we are facing a difficult period. However, I think the future is bright because of the recent trend toward collaboration between theoretical and experimental research. I am optimistic for the future because I believe that human beings have the ability to see into the essence of complex phenomena, even though they are immensely complicated. In physics and chemistry, people have succeeded in mathematically systematizing complicated phenomena even though they seemed extremely complex. I am sure that this approach will hold true for the brain."

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About the researcher

Born in 1936 in Tokyo. In 1958, he graduated from the University of Tokyo, majoring in applied physics, and earned his Ph.D in engineering in 1963. He became assistant professor at Kyushu University in 1963, and at the University of Tokyo in 1967. In 1981, he was appointed professor at the University of Tokyo and retired from the position in 1996. He became group director of RIKEN Brain Science Institute in 1996 and has been heading the institute since 2003.

RCAI–JSI International Symposium on Immunology 2006

From June 16 to 18, the RIKEN Research Center for Allergy and Immunology (RCAI) held an international symposium on immunology in Yokohama in collaboration with the Japanese Society for Immunology (JSI). This symposium was first held last year, with the goal of enabling young Japanese scientists and students to meet leading researchers and learn about advanced areas of immunology. This year's conference was organized by Masaru Taniguchi, the director of RCAI, and Toshio Hirano, the president of JSI. It was a great success with more than 500 people in attendance. There were excellent presentations by thirty invited guests, including seventeen from the US and Europe. This year there was also a poster session to allow young scientists and students to make their own presentations and discuss their work with eminent scientists from around the world.

The organizing committee decided that the title for this second symposium should be 'Regulation of Immune Responses in Allergy and Inflammation,' reflecting the recent direction of immunological research. Now that the individual constituents of the immune system have been fully analyzed, immunology researchers are studying how the overall immune system is regulated in humans. The symposium therefore focused on important immunoregulatory components such as dendritic cells, regulatory cells, Th1/Th2 balance, signaling molecules, and chemical mediators in allergy and inflammation, as well as biological aspects of allergy and inflammation. Thought-provoking talks were given by speakers including the prominent biochemists Shu Narumiya and Takao Shimizu, and the audiences asked many perceptive questions. At the poster session, fifty posters were displayed, and participants were able to have many useful discussions in a more informal atmosphere.

Hamagin Hall in Yokohama was almost full for the whole of the symposium, and everyone who came got useful new information to take back to their laboratories. Hirano, the joint organizer, says that, "Research on regulation of immune responses has become a growing interdisciplinary field, and we expect more advances will be forthcoming at the third symposium next year."

Dr. Juan Rivera (NIH, USA) talking with a Japanese researcher during the poster session.

RIKEN reveals the first ever petaflops computer

A team at the RIKEN Genomic Sciences Center in Yokohama has succeeded in building a petaflops computer system called MDGRAPE-3, specially for simulating the dynamics of proteins and other biomolecules. MDGRAPE-3 was developed in collaboration with SGI Japan and Intel Japan, and is also known as "Protein Explorer."

MDGRAPE-3 is a large system that consists of 201 units of 24 MDGRAPE-3 chips, 64 parallel servers each containing 256 of Intel's newest Xeon 5000-series processors (codename Dempsey), and 37 parallel servers each having 74 Intel Xeon 3.2GHz processors with 2MB L2 caches. Developed by RIKEN, the MDGRAPE-3 chip is the world's fastest LSI chip for simulation of molecular dynamics.

MDGRAPE-3 is unable to run the Linpack benchmark, which is the basis for the TOP500 supercomputer rankings. However, its nominal peak performance of one petaflops means that it is almost three times faster than IBM's BlueGene/L, which TOP500 currently lists as the world's fastest supercomputer.

MDGRAPE-3 can simulate and test the affinity of proteins for pharmaceutical candidate molecules at extremely high speeds. It will therefore be useful in speeding up the development of new drugs. Its ability to reveal the workings of proteins through simulations will also make it invaluable for research on the mechanisms by which some proteins cause diseases, and for development of biological nanomachines.

Collaborative Agreement between RIKEN and CAS Shanghai Branch

On May 23, RIKEN and the Shanghai Branch of the Chinese Academy of Sciences (CAS) concluded a General Collaborative Agreement in which they agreed to continue, expand, promote and facilitate cooperative activities between the two institutions in all aspects of scientific research and development, including chemistry, biochemistry, biotechnology, cancer therapeutic research, bioresources, plant science, immunology, material science, and synchrotron radiation research.

In 1982, RIKEN and CAS Headquarters entered into a Memorandum of Understanding on exchange of researchers and research information. Since then there have been many exchanges of researchers between the two institutions. CAS Shanghai Branch is one of the major branches of CAS, and contains more than ten institutes, including the Shanghai Institutes for Biological Sciences (which in turn contains the Institute of Biochemistry and Cell Biology, the Institute of Plant Physiology and Ecology, the Institute of Neuroscience, the Health Science Center, and other institutes), the Shanghai Institute of Organic Chemistry (IOC), and the Shanghai Institute of Applied Science.

The idea of making this agreement came about when Prof. NOYORI Ryoji, President of RIKEN and a Professor Emeritus of IOC, was invited to give a special lecture at IOC. The agreement was signed by Prof. Noyori and Prof. JIANG Mianheng, the President of CAS Shanghai Branch.

Under this Collaborative Agreement, RIKEN and CAS Shanghai Branch will exchange researchers and staff, scientific and technological information (including giving lectures and holding joint seminars and symposia), and scientific and technological research materials. They are already planning a joint workshop on bioresources in Shanghai this November. They will also undertake joint research projects, which will each require separate specific agreements. RIKEN and CAS Shanghai Branch hope that their collaborative relations will increase and grow in strength, and contribute to the development of further ties between China and Japan.

Back from Beyond – Japan's cyclotron, Part I

RIKEN resurrected its once-discarded, high-energy particle accelerator and placed it at the forefront of nuclear physics in the postwar era

RIKEN's early days in the 1920s and 1930s coincided with a period of rapid progression in nuclear physics. One of the greatest achievements of this era was the development of a cyclotron, a type of a particle accelerator that effectively generates high-energy beams of atomic or subatomic particles, such as ions and electrons respectively. Pioneered by Ernest Lawrence, a physicist at the University of California, in 1931, the device is used to study nuclear physics and in the development of diagnostic and medical procedures.

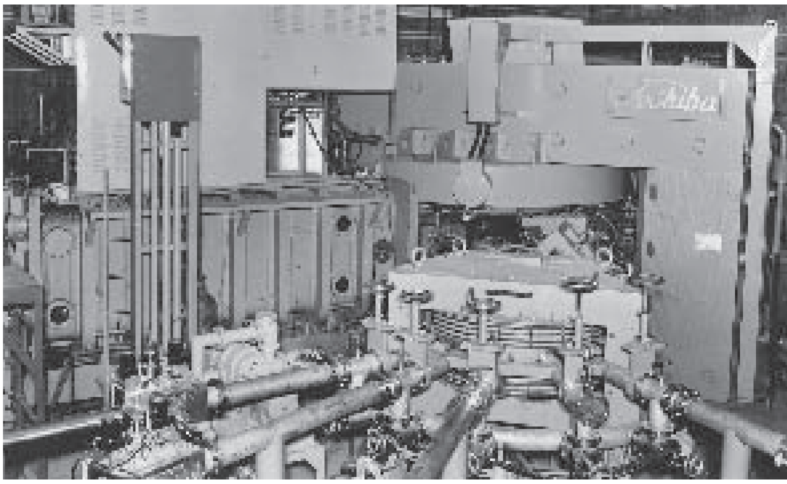
In 1937, Yoshio Nishina, a physicist at RIKEN and pioneer of quantum physics in Japan, led the development of the world's second cyclotron—albeit a small one with a magnetic field of 65 centimeters in diameter. Nishina's team completed construction of a bigger cyclotron (150 cm diameter) in 1943, and, in the following year, successfully tested a powerful beam of deuterons, which produce more energy in fusion reactions than protons.

However, this achievement couldn't have come at a worse time for Japan. Soon after the beam experiment was completed, Japan surrendered in World War II in 1945. Suspicious that Japan was producing nuclear weaponry, the General Headquarters of the Allied Forces dissembled and dumped these two cyclotrons into Tokyo Bay. Physicists from the US lobbied to stop the action, but their efforts were in vain.

Devastated, Nishina nevertheless continued on to become the fourth president of RIKEN after it was dissolved and reorganized in 1948. He worked hard to resurrect RIKEN to its previous standing, but he passed away in 1951. Four months after Nishina's death, Lawrence visited Japan and urged the revival of cyclotron research. Thanks partly to his support, in 1952 RIKEN built its third cyclotron with similar specifications to the first one. In the same year, Japan regained its independence and resumed atomic energy research.

In 1958, when RIKEN was inaugurated as a public corporation, the new president Haruo Nagaoka, a son of Hantaro Nagaoka, campaigned strongly for RIKEN to have a large cyclotron. Researchers thus hammered out a plan to develop a cyclotron equipped with a magnetic field of 160 cm in diameter. Nagaoka wanted to promote the '160 cm cyclotron' as a symbol of the new RIKEN, which moved its headquarters to Wako, near Tokyo, in 1966.

Development of the 160 cm cyclotron began from scratch due to a dearth of postwar expertise, but RIKEN's researchers never compromised their quest to better its performance. In 1966, the new cyclotron was completed and heralded Japan's first capability to accelerate heavy ions—a brave decision on reflection, because, at that time, few thought that heavy ions would be a mainstay of nuclear research in the future.



The 160 cm cyclotron, completed in 1966, was central to the reconstruction of postwar RIKEN and Japan's nuclear physics research.

By early the 1970s, this large cyclotron commenced 24-hour operation with strengthened beam power that allowed international researchers, from different research fields, to jointly use the equipment.

Using the cyclotron, RIKEN researchers zealously studied nuclear reactions and the scattering of helium-3 and heavy ions, while examining in-beam spectroscopy using alpha particles. In 1970, RIKEN commenced joint research with other scientists to produce short-lived radioactive isotopes. This work laid the foundation for developing medical imaging techniques such as Single-Photon Emission Computed Tomography (SPECT) and Positron Emission Tomography (PET).

Diversifying heavy-ion nuclear research using the 160 cm cyclotron bloomed in the 1970s, and led RIKEN to become one of the world's leading research institutes in the field. Its contribution to medicine and physics until the halt of operation in 1990 is immeasurable, as some of this research paved the way for developing the next-generation of cyclotrons down the road. ■

How a cyclotron works: In the device, the charged particles are made to follow a circular path using a magnetic field. Each time those particles compete a lap they are accelerated by a high-frequency alternating voltage applied at the so-called 'potential gap.' Each time the particles cross this gap, they speed up. Then their radius of curvature inside the magnetic field increases, such that the path of the accelerated beam grows into an outward spiral as the particles get faster. Like other accelerators, the high-energy beam can be used to initiate nuclear reactions by striking a target particle.

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