RIKEN RESEARCH

NOVEMBER
2007 Volume 2 Number 11

Blood origins

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Fires of creation probed by quarks

PHENIX detector spots melting particles

Scientists have confirmed that a powerful particle accelerator has recreated the intense conditions that existed just microseconds after the beginning of the universe. The experiments have also revealed a surprise about quarks, the fundamental building blocks of every atomic nucleus.

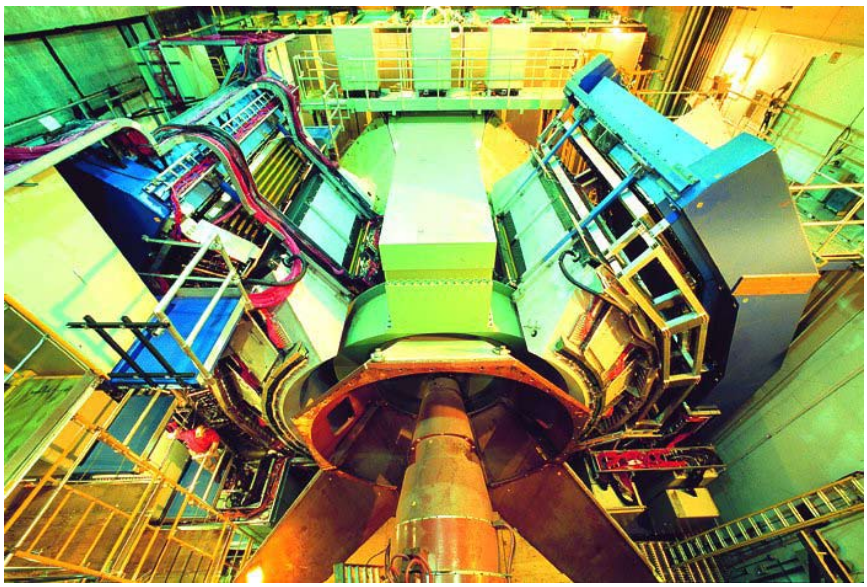
The protons and neutrons inside atoms are made from trios of quarks, which are normally held together by gluons. But immediately after the big bang, these nuclear ingredients existed as a hot quark–gluon plasma (QGP). Understanding how this soup condenses into the discrete particles that make up ordinary matter can help to reveal how the subatomic world works.

In order to generate and investigate quarks of various flavors—known by names such as 'charm' or 'strange'—the Relativistic Heavy Ion Collider (RHIC) at the Brookhaven National Laboratory (BNL) in Upton, US (see Center Profile p.15), smashes particles together at almost the speed of light. Previous results from RHIC had indicated that a very hot, dense form of matter, was formed in such collisions between gold atoms. But was it a QGP?

To find out, the scientists conducted a series of experiments in 2004/5 to create and study an unusual particle called J/ψ, made up of a charm quark paired with its opposite number, the anticharm quark.

The theory that describes how quarks behave, called quantum chromodynamics (QCD), suggests that the J/ψ particle might melt away in a hot QGP. If the gold–gold collisions had indeed created such a primordial state, the yield of J/ψ from the experiments should be suppressed by melting.

However, QCD is notoriously difficult to solve, and there is still much debate about what temperature J/ψ will melt at—hence the need for experimental investigation.



Brookhaven National Laboratory

Figure 1: The PHENIX detector at the Relativistic Heavy Ion Collider (RHIC) at Brookhaven National Laboratory (BNL).

Hot stuff

The scientists first smashed beams of protons together, and watched what happened using the PHENIX (**P**ioneering **H**igh **E**nergy **N**uclear **I**nteraction e**X**periment) detector[1] (Fig. 1).

J/ψ particles themselves only survive for an instant before they decay into a spray of other particles: either an electron–positron pair, or a muon–antimuon pair. Once PHENIX spots these particles, scientists can work out exactly how original J/ψ particles behaved based on their trajectory and energy.

The team saw thousands of J/ψ particle decays, and since proton collisions are not energetic enough to create a QGP, this established the 'normal' level of J/ψ production one would expect from a collision.

"The proton–proton data provides a crucial baseline for the gold–gold measurement," explains Yasuyuki Akiba of RIKEN's Nishina Center, Wako, part of the PHENIX team. "And the proton–proton data are interesting in their own right," he adds. "They can test the theoretical models of J/ψ production."

When the team switched protons for gold atoms, the heavier missiles created more intense explosions (Fig. 2). They saw that, as expected, some of the J/ψ particles from the initial collision were melting away, lowering their overall numbers[2]. "This supports the theoretical prediction that J/ψ will melt in a QGP, and thus provides strong evidence for QGP formation at RHIC," says Akiba.

Quark surprise

Surprisingly, the scientists also found that the central, hotter region of the collision actually hosted more J/ψ particles than the cooler outskirts.

"In the naïve models, the suppression should be stronger in the central region," says Akiba. That's because the hottest part of the fireball should melt more of the J/ψ particles.

So the extra J/ψ particles suggests that charm and anticharm quarks produced at the heart of the collision could be recombining

Jeffrey Mitchell

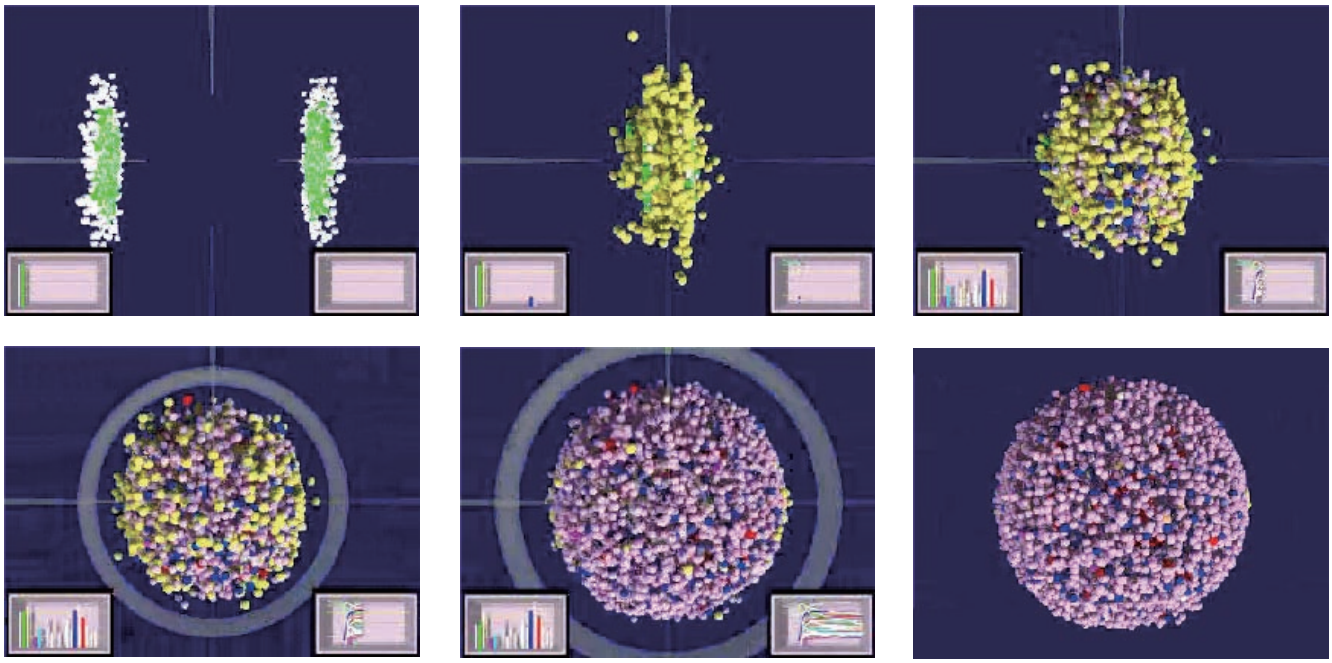


Figure 2: Gold-on-gold collision at RHIC.

into J/ψ, boosting its yields compared to the cooler outskirts of the collision.

"The data is not inconsistent with a very intriguing possibility that J/ψ can be formed in recombination," adds Akiba, "but, at present, the data cannot rule out other possibilities."

Elliptic flow

The researchers have now just finished collecting a new set of data on gold–gold collisions which will allow them to measure J/ψ production much more precisely, and perhaps pin down whether this recombination is taking place.

They hope to track the characteristic motion of J/ψ particles produced by recombination of quarks, dubbed 'elliptic flow'. This should allow them to distinguish between the swirl of particles created by recombination, and the longer-lived J/ψ particles that had simply failed to melt in the QGP and thus would show no elliptic flow.

"Elliptic flow is the name for the collective motion of particle observed at RHIC," says Akiba. "This flow is generated in the evolution of the dense matter produced at RHIC, and therefore one can get the properties of matter from the pattern of elliptic flow."

"If all of [the] J/ψ particles that we observe at RHIC are those that survived the melting effect of the QGP, the elliptic flow strength of J/ψ should be very small," predicts Akiba. "On the other hand, if a significant fraction of [the] J/ψ particles is produced by regeneration, we should observe a strong elliptic flow of J/ψ. We have just started the data analysis looking for the elliptic flow of J/ψ particles in the new data set," he adds.

Another experiment, planned to start in November 2007, will smash gold atoms into deuterons, a heavy form of hydrogen that consists of a proton and neutron bound together. While no QGP is expected to form in the collision, it should reveal the influence of gold atoms themselves on J/ψ suppression.

Calculating the balance between melting and recombination effects on J/ψ particles should reveal more about the primordial QGP, effectively providing our best glimpse into the hot foundry of creation at the beginning of the universe. ■

1. Adare, A., Afanasiev, S., Aidala, C., Ajitanand, N.N., Akiba, Y., Al-Bataineh, H., Alexander, J., Aoki, K., Aphecetche, L., Armendariz, R. *et al.* J/ψ production versus transverse momentum and rapidity in $p + p$ collisions at $\sqrt{s} = 200$ GeV. *Physical Review Letters* **98**, 232002 (2007).

2. Adare, A., Afanasiev, S., Aidala, C., Ajitanand, N.N., Akiba, Y., Al-Bataineh, H., Alexander, J., Al-Jamel, A., Aoki, K., Aphecetche, L. *et al.* J/ψ production versus centrality, transverse momentum and rapidity in Au + Au collisions at $\sqrt{s_{NN}} = 200$ GeV. *Physical Review Letters* **98**, 232301 (2007).

About the researcher

Yasuyuki Akiba was born in Tokyo, Japan, in 1959. He graduated from the Faculty of Science, the University of Tokyo in 1982, and obtained his PhD in 1988 from the same university. He was a research associate at the Institute of Nuclear Study, University of Tokyo (1988–1997) and at the High Energy Accelerator Research Organization (1997–2003). He came to RIKEN in 2003, and became a vice chief scientist in the same year. His research focus is high-energy heavy ion physics. In 2004, he became a deputy spokesperson of PHENIX experiment.

A concerted effort

Ultrafast fluorescence measurements used to resolve controversy over proton transfer in a chemical reaction

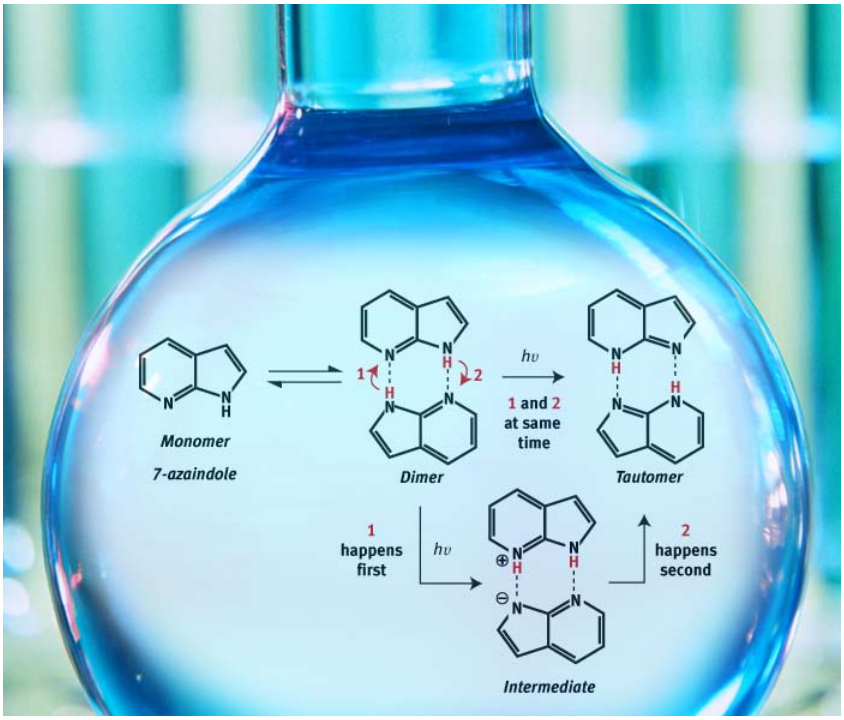


Figure 1: 7-Azaindole pairs up in solution through hydrogen bonding interactions to form structures known as 'dimers' that undergo a double proton transfer reaction (processes 1 and 2 shown in red) when excited by ultraviolet light ($h\upsilon$) to form so-called tautomers. There has been controversy about whether the two proton transfers occur at the same time (top pathway) or sequentially through an intermediate structure (bottom pathway).

Chemical reactions are processes in which one substance is transformed into another and involve the motion of atoms and electrons. Because these processes occur on short time-scales that are measured in femtoseconds (millionths of a billionth of a second), it is difficult to study what actually happens during a chemical reaction.

Of particular interest are reactions that involve the transfer of a hydrogen nucleus (a proton) between two molecules—an important process in biological systems. Tahei Tahara from RIKEN's Discovery Research Institute in Wako has been studying proton transfer reactions for many years and views them as a challenge at the limits of science. "Because hydrogen is the lightest atomic species, it usually moves very quickly and is difficult to catch," comments Tahara.

A model system (Fig. 1) in which proton transfer has been extensively studied is 7-azaindole. In solution, this compound exists in two different forms; discrete individual molecules (monomers), and pairs known as dimers. The dimers can be pushed into a higher energy 'excited' state by shining ultraviolet light on them, and subsequently undergo a double proton transfer reaction to form a structure known as a tautomer.

When Tahara published his first results on this system ten years ago, he says that, "the work triggered very intense world-wide debate." The controversy stemmed from whether the two proton-transfer steps occurred sequentially in a step-wise reaction, or simultaneously in a 'concerted' process. Tahara has always argued that the concerted process is the correct one, a hypothesis that is further supported by his recent findings published in the *Proceedings of the National Academy of Sciences of the USA*[1].

By exciting the 7-azaindole dimer with different wavelengths of ultraviolet light and monitoring the fluorescence, Tahara and colleague, Satoshi Takeuchi, show conclusively that no intermediate structure is formed, thereby ruling out the possibility of a step-wise process. Significantly, their experiments demonstrate that a feature of the fluorescence decay that was attributed to a separate proton transfer actually corresponds to the conversion of the dimer from one excited state to another.

Because the 7-azaindole dimer is very similar in structure to the base pairs found in DNA, Tahara expects that this work may help to understand the chemical mechanism of how ultraviolet light affects DNA. In addition, Tahara and co-workers are now intending to observe nuclear motion in real-time using sub-10-femtosecond pulses of light, which he suggests, "may offer new opportunities for using light to control chemical reactions." ■

1. Takeuchi, S. & Tahara, T. The answer to concerted versus step-wise controversy for the double proton transfer mechanism of 7-azaindole dimer in solution. *Proceedings of the National Academy of Sciences of the USA* **104**, 5285–5290 (2007).

Take your computer for a spin

Large spin Hall effect measured at room temperature

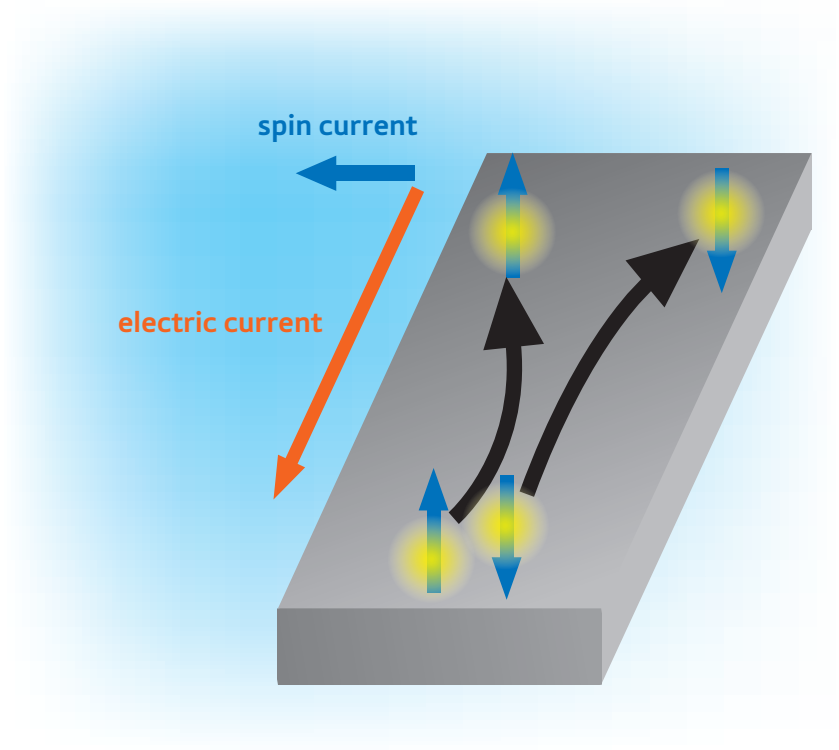
RIKEN scientists have accurately measured a tiny voltage produced by segregating electrons according to their spin[1], a result which could help to usher in a new era of spin-based computing.

Conventional computers process and communicate information by shunting electrons around, but store data in the magnetic properties of tiny segments of a spinning disk drive. Yet that magnetism is also due to electrons—as each charged particle spins, it creates a magnetic moment. Electrons can spin 'up' or 'down', creating opposing poles like a bar magnet, and the burgeoning technology of spintronics uses these two states to represent bits of binary data. As well as storing information, these states can potentially be used to perform calculations.

The spin Hall effect (SHE) provides an important way to control these spinning electrons. The Hall effect itself (identified in 1879 by Edwin Hall) occurs when a magnetic field forces a current of electrons flowing through a flat plate to veer to one side. This causes charge to accumulate on that side of the plate, setting up a voltage across it. In a similar way, the SHE sends spin-up electrons to one side of the plate and spin-down to the other, setting up a 'spin current' (Fig. 1).

Spin current is an important factor in operating future spintronic devices. Ferromagnets are normally used to differentiate spins, but interference between neighboring magnets makes it tricky to build working spintronic devices that way.

"However, if we use SHE, we can generate the spin current without using a ferromagnet," says Takashi Kimura of RIKEN's Frontier Research System, Wako. This could allow much easier integration of semiconductor and spintronic devices in the future.



David Awschalom

Figure 1: The spin Hall effect sets up a spin current by separating electrons according to their 'up' or 'down' spin.

Kimura and the team leader YoshiChika Otani have now found that the spin Hall conductivity—the potential for electrons to migrate due to the SHE—in a platinum wire is a thousand times greater than in previous experiments with semiconductor materials, making it easier to study and exploit the effect. Their electrical measurement technique is also more precise than the optical detection method usually employed.

It's significant that the team has detected this effect at room temperature. It means that SHE is not only a physically interesting phenomenon, but also a useful way of manipulating spins in future spintronic devices, says Kimura.

The team is now trying to identify materials that produce even greater SHE conductivities. "We hope that new devices using SHE are proposed in near future," says Kimura. ■

1. Kimura, T., Otani, Y., Sato, T., Takahashi, S. & Maekawa, S. Room-temperature reversible spin Hall effect. *Physical Review Letters* **98**, 156601 (2007).

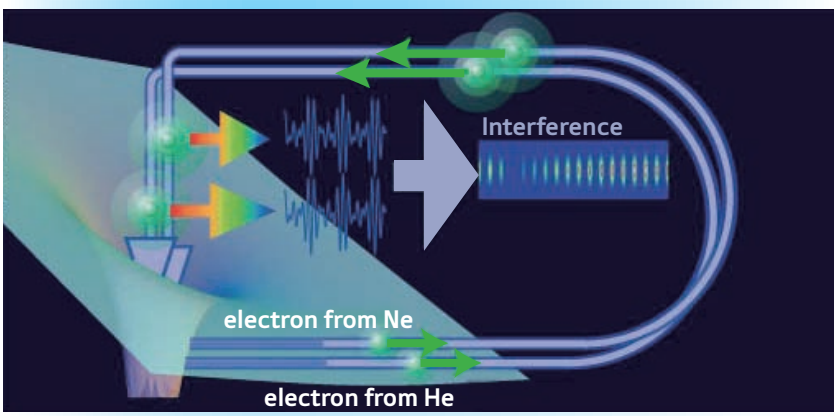
Boosting the harmonics of light–matter interaction

Researchers show that the interaction of a laser pulse with a mix of two gases creates high-energy radiation

A team of researchers from the RIKEN Discovery Research Institute in Wako has shown that the strong light–matter interaction between a short laser pulse and a mix of the two noble gases helium (He) and neon (Ne) can be used to create laser pulses with very high energies and extremely short duration.

Laser light can be described as an oscillating electric and magnetic field. These intense fields, particularly for very short and powerful pulses, can exert significant forces on atoms: forces strong enough to separate and eject an electron from its atom. However, this 'excursion' is only short-lived as the electromagnetic field of the laser beam oscillates rapidly. Therefore, after a short time, the laser field changes its direction and pushes the electron back towards the atom (Fig. 1) where it is recaptured. The electron then releases its energy as a short, intense laser pulse having a harmonic frequency that is a multiple of the original laser frequency.

This process of 'higher harmonics frequency generation' occurs for both types of atoms in the gaseous mix. As helium and neon have slightly different electronic properties, the harmonics generated by these two atoms differ slightly in energy so interact with each other in a process known as interference. Crucially, interference leads to conditions that "not only allow the determination of the oscillation phase of the generated harmonics but also enable us to see the motion of the electrons and atoms," explains Tsuneto Kanai from the RIKEN team. These findings were published recently in the journal *Physical Review Letters*[1].



Physical Review Letters

Figure 1: The steps leading to higher harmonics generation. A high-intensity laser pulse tears electrons away from the helium and neon atoms. After a short time, the electrons are driven back to the atom, where they are recaptured. The electrons then release short pulses of high-energy radiation that interfere with each other, creating a spectrum of high harmonic frequencies.

The team observed excursion times as low as a few hundred attoseconds—the shortest duration of a particle motion observed to date: an attosecond is one billionth of one billionth of a second. Such short pulse durations of the higher harmonics create exciting possibilities for further studies, particularly as the relative mixture of the two noble gases provides the means to tune the energy and intensity of the generated harmonic radiation.

Kanai is therefore convinced that "this new light source will provide us with new insights into fundamental processes in nature and their possible use for applications." For example, it will allow the study of the molecular dynamics in gases with attosecond resolution. More complex mixtures of molecules might lead to further improvements. Therefore, this pioneering work marks only the beginning of an entirely new research field. ■

1. Kanai, T., Takahashi, E. J., Nabekawa, Y. & Midorikawa, K. Destructive interference during high harmonic generation in mixed gases. *Physical Review Letters* **98**, 153904 (2007).

Microwaved electrons

Microwave radiation is found to efficiently excite electrons at the surface of liquid helium

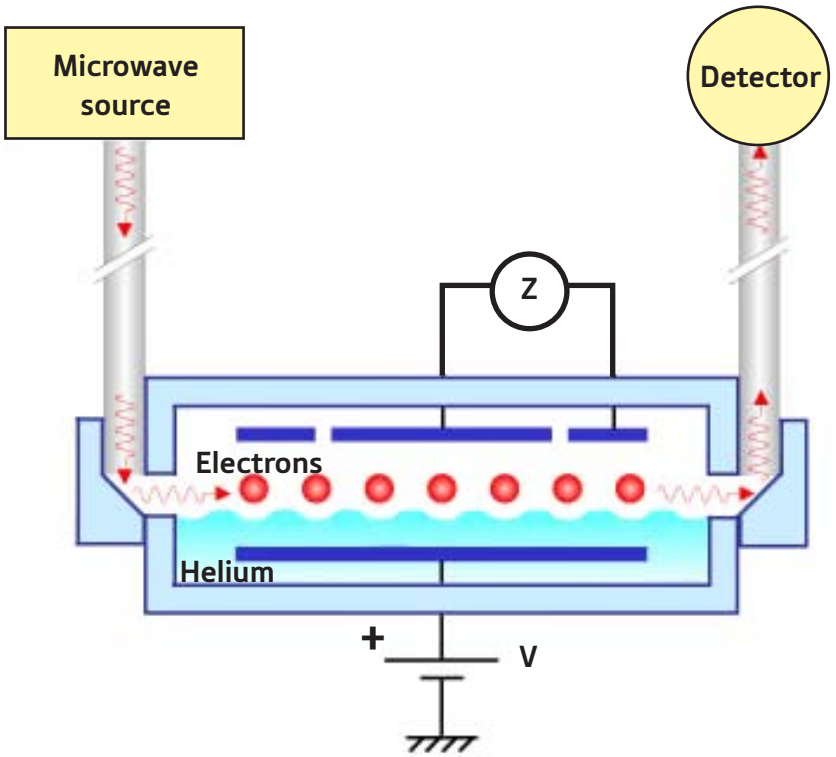


Figure 1: Microwave excitation of electrons (red) floating on liquid helium (light blue). The change in electrical resistance across the electrons provides information on the amount of microwave radiation absorbed.

Physicists have long known that, when cooled to very low temperatures, electrons can be placed on the surface of liquefied helium. Now, researchers from the RIKEN Discovery Research Institute, Wako, in collaboration with colleagues at Japan's Keio University, Yokohama, have discovered they can effectively excite these electrons using microwave radiation.

At these extremely low temperatures—just above absolute zero—the electrons are stabilized by tiny electrical fields at the surface of the liquid helium, leading to an arrangement of electrons into regular two-dimensional patterns. Recently, scientists in the US proposed that these ordered charges could be used for quantum computing applications, which triggered intense studies in laboratories around the world. To achieve the necessary control of the electron states, the use of microwave radiation was suggested as a way to excite the electrons from one energy state to the other and thereby modify their quantum computing behavior.

Reporting in the journal *Physical Review Letters*[1], the researchers have studied the influence of microwave radiation on the electrons by measuring the electrical resistance across the floating electrons (Fig. 1). Increased resistivity is a sign of excited and heated electrons. Such measurements provide a relatively accurate picture of the state of the electrons, as "this system is an extremely clean and transparent electron system that provides a direct relationship between experiment and theory," comments Kimitoshi Kono from the RIKEN team.

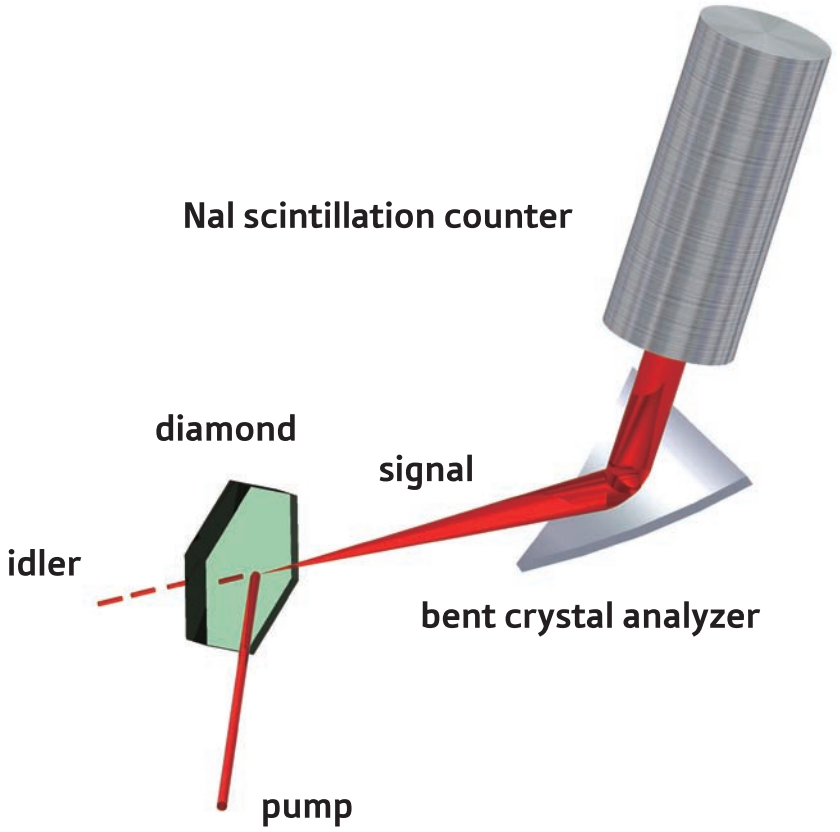
Surprisingly, the researchers found that as the temperature is lowered the change in resistivity of the electrons increases significantly through microwave irradiation. The measured values are much higher than estimated in previous theoretical studies. In fact, the sensitivity of the system's electric current to the microwave radiation is so high that it could even be used as an efficient microwave detector. Regardless, this change in resistivity is a clear sign of an increased electron temperature and therefore of excitation of electrons into higher energy states. In particular, the researchers found that electrons are scattered away from the surface, which significantly reduces the suitability of such microwave-controlled electrons for quantum computing.

Unfortunately, "this is an important limitation towards the realization of quantum computers," says Kono. To further pursue quantum computing applications, physicists must confine the lateral motion of electrons. For example, nanostructures around the surface could create suitable electric potentials to suppress increases in electron temperature. Therefore, Kono remains convinced that "quantum computing is still possible in this system." ■

1. Konstantinov, D., Isshiki, H., Monarkha, Y., Akimoto, H., Shirahama, K. & Kono, K. Microwave-resonance-induced resistivity: evidence of ultrahot surface-state electrons. *Physical Review Letters* **98**, 235302 (2007).

X-rays in full color

Conversion of x-ray beams into longer wavelengths creates a new spectroscopic tool



Physical Review Letters

Figure 1: Optical parametric down-conversion. A high-intensity x-ray beam (pump) scatters off a diamond crystal and is split into a long-wavelength idler and a short-wavelength x-ray signal beam.

X-rays—beams of light with short wavelengths and high energy—are a commonly used diagnostic tool, not only in medicine, but also in materials science. Two researchers from RIKEN's SPring-8 Center in Harima have demonstrated the conversion of x-rays into longer wavelengths that preserves some of their useful properties, such as high spatial resolution.

Normally, image resolution is limited by the wavelength of the light being used. Light with a very short wavelength, such as x-rays, therefore yields higher imaging resolution than, for example, visible light. On the other hand, since x-rays have high energies (equivalent to shorter wavelengths) they are not always suitable to study low energy (or long-wavelength) properties of materials.

Writing in the journal *Physical Review Letters*[1], Kenji Tamasaku and Tetsuya Ishikawa, present an experimental demonstration of how some of the advantages of x-rays can be brought towards other wavelengths. They used an optical effect, known as 'parametric down-conversion' that can be realized with high-intensity x-rays. "The important point of x-ray nonlinear optical effects, such as parametric down-conversion, is that one can generate an arbitrary wavelength from the visible to the x-ray region for further study," says Tamasaku.

In this process, an x-ray beam, the 'pump', is split into two beams, the 'signal' and 'idler', by scattering off a regular crystal such as a diamond (Fig. 1). The wavelength of the signal beam is in the x-ray region, whereas the wavelength of the idler beam is much longer, in the extreme ultraviolet light region. The precise relationship between signal and idler wavelengths is given by physical laws such as the conservation of energy. The idler beam in particular is of interest for high-resolution spectroscopy applications.

In their experiments, Tamasaku and Ishikawa have clearly and successfully demonstrated this effect for the first time. Their achievement is rooted in the very high x-ray intensities that can be achieved with the SPring-8 synchrotron radiation facility—necessary for an efficient conversion of the pump beam.

The extreme ultraviolet wavelength region is of particular interest to probe the nature of atomic bonds. As the creation of the idler is directly related to the local environment of the x-ray pump, a high spatial resolution can be achieved in experiments. Therefore, "it will be possible to obtain information about the bonds between individual atoms," explains Tamasaku. The parametric down-conversion pioneered by the RIKEN researchers might therefore become an important analytical tool. ■

1. Tamasaku, K. & Ishikawa, T. Interference between Compton scattering and x-ray parametric down-conversion. *Physical Review Letters* **98**, 244801 (2007).

Putting fluorine in its place

A three-component catalytic system enables the formation of carbon–fluorine bonds at precise positions in organic molecules

Organic molecules produced by living systems are often referred to as 'natural products', and are a rich source of biologically active substances that can sometimes be used as drugs themselves or, alternatively, offer a convenient starting point for designing and making others. These compounds generally have hydrocarbon skeletons and contain a small number of atoms of other elements—so-called heteroatoms.

Whereas nitrogen and oxygen, and, to a lesser extent, sulfur and phosphorus, are relatively common heteroatoms found in natural products, many of the other elements that comprise the periodic table rarely feature. A case in point is fluorine, which, points out Mikiko Sodeoka from RIKEN's Discovery Research Institute in Wako, "is not popular in chemicals produced by organisms."

Substituting a hydrogen atom with fluorine can, however, often confer beneficial properties on a particular compound, such as a drug, by increasing its stability or making it more easily absorbed in the body. Consequently, as many as 20% of therapeutic pharmaceuticals and 30–40% of agrochemicals, made by the chemical industry, contain a fluorine atom.

Many researchers have, therefore, investigated reactions to make carbon–fluorine bonds in an efficient and selective manner. Sodeoka and co-workers[1] have made many contributions in this area and the most recent describes a new three-component catalytic system that enables the fluorination of a family of molecules known as aryl acetic acids.

After screening a range of reaction conditions, it was found that a cocktail of three different chemicals could be used, in conjunction with a fluorinating agent (N-fluorobenzenesulfonimide (NFSI)), to replace a hydrogen atom with a fluorine atom in a range of aryl acetic acid substrates (Fig. 1). Each component of the ternary mixture has a specific function: an acid activates the NFSI, a metal-ligand complex activates the substrate, and the base removes the hydrogen atom that is being substituted.

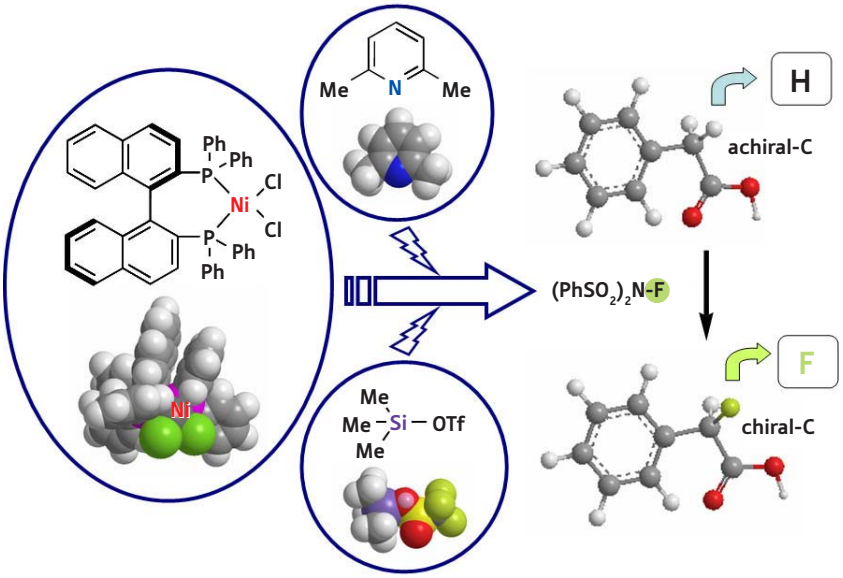


Figure 1: A three-component catalyst system comprising (i) a nickel (Ni) metal ion complexed to an organic ligand, (ii) a nitrogen (N)-containing base, and (iii) a silicon (Si)-containing acid can be used, in conjunction with a fluorinating agent, to switch a specific hydrogen atom (white) in an aryl acetic acid substrate with a fluorine atom (yellow green).

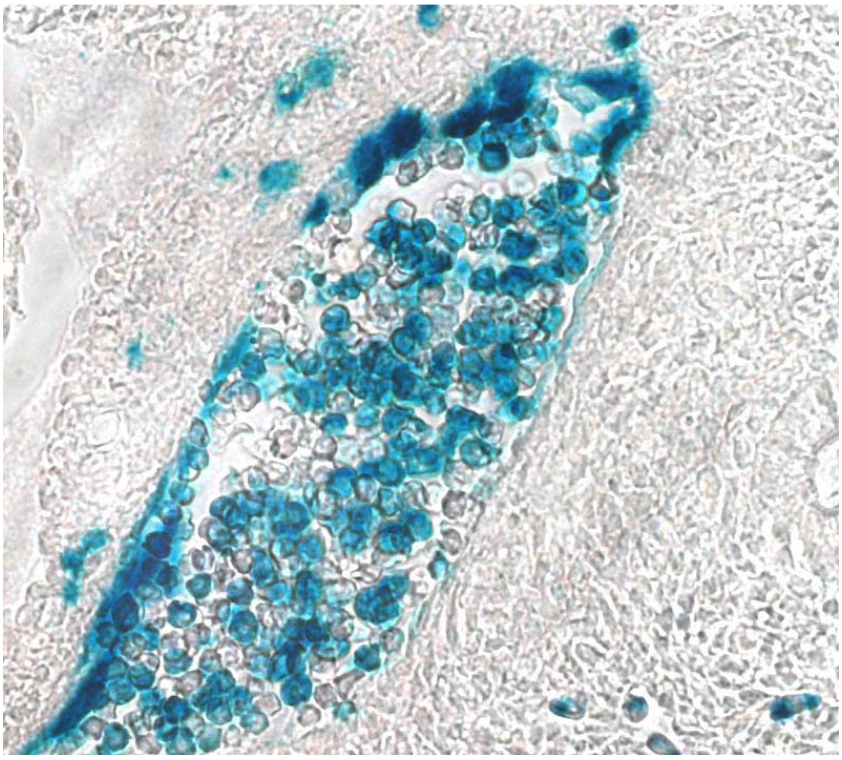
In principle, this fluorination reaction can produce two different mirror-image forms (enantiomers) of a given compound. The process developed by Sodeoka and co-workers is particularly powerful, however, because it can be intentionally biased to produce greater amounts of either of these closely related products—simply by choosing which mirror-image form of the metal catalyst is used in the reaction.

The ability to introduce fluorine atoms into molecules that can be made selectively in either left- or right-handed form is a powerful and generic synthetic strategy which Sodeoka hopes could make a significant contribution to the field of medicinal chemistry. ■

1. Suzuki, T., Hamashima, Y. & Sodeoka, M. Asymmetric fluorination of α-aryl acetic acid derivatives with the catalytic system $NiCl_2$–binap/R_3SiOTf/2,6-lutidine. *Angewandte Chemie International Edition* **46**, 5435–5439 (2007).

Origin of adult blood cells clarified

Precise cell tracing shows that adult blood cells have an extra-embryonic origin



Nature

Figure 1: The progeny of blood island cells (blue) in the wall and lumen of the umbilical vein at day 11. These cells were derived by tagging Runx1-expressing cells at day 7.5.

Developmental biologists have debated the original source blood cells in adult mammals for over thirty years. Now, a team led by Igor Samokhvalov at the RIKEN Center for Developmental Biology, Kobe, has developed a cell tracing method that unambiguously identifies the yolk sac—an extra-embryonic structure—as a source of blood cells in both the embryo and, later, the adult.

The yolk sac, which provides the developing embryo with nutrients, is the first extra-embryonic structure to form during embryogenesis. This structure is also the first place of embryonic blood cell formation (hematopoiesis). A central question in developmental biology about hematopoiesis is the role—if any—the yolk sac-derived blood cells play in the development of adult blood cells.

"The origin of [the] hematopoietic [blood] system was always obscure and controversial; this was the reason I became interested in this area of hematology," says Samokhvalov.

To resolve the controversy, the team labored for two years to develop a cell tracing method to follow yolk sac-derived blood cells through later stages of embryonic development[1]. The ability to study this development non-invasively through time was critical, says Samokhvalov, because removing cells from tissue introduces stresses that can lead to an inaccurate picture of actual embryonic processes.

The method consists of replacing of one copy of a gene called *Runx1*, which is essential for blood development, with another gene that produces a protein creating 'tags' in the cells and all their progeny. The 'new' gene is turned on at the same time *Runx1* normally is—at a mere 7.5 days after embryonic development begins.

Tagging the earliest Runx1-expressing yolk sac cells at day 7.5 of development allowed the team to follow these cells' progeny when they're incorporated into blood vessel walls (Fig. 1), and evaluate their long-term contribution to the adult blood system.

So clear were the results, remarks Samokhvalov, that "our work showed direct contribution of [the] yolk sac to adult haematopoiesis". Indeed, the team's direct and carefully designed cell tracing methodology eliminated ambiguities that could lead to alternative interpretations.

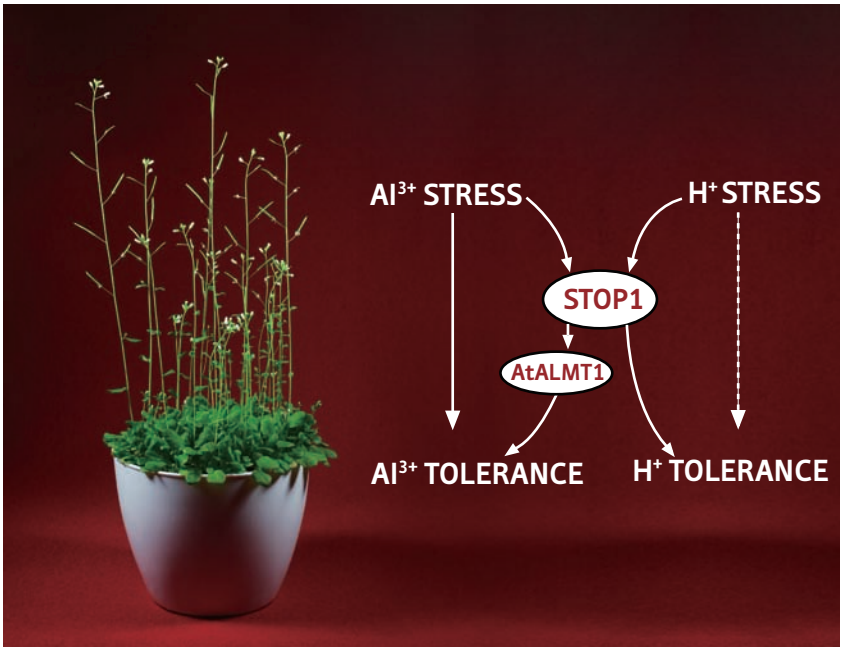
This work settles the long-standing controversy, marking an important step forward in developmental biology. However, the team's data do not rule out the possibility of an additional source of haematopoietic stem cells in the embryo.

Samokhvalov's future plans include determining more precisely the extent of the yolk sac's participation in adult blood development, and whether another source of haematopoietic stem cells occurs in the embryo itself. ■

1. Samokhvalov, I.M., Samokhvalova, N.I. & Nishikawa, S. Cell tracing shows the contribution of the yolk sac to adult haematopoiesis. *Nature* **446**, 1056–1061 (2007).

Putting a STOP to acid stress

A transcription protein called STOP1 helps plants to tolerate aluminum ions and protons



Satoshi Iuchi

Figure 1: The STOP1 protein regulates activity of the *AtALMT1* gene to tolerate aluminum ions (Al^{3+}), and regulates plant tolerance of protons (H^+) by acting on other as-yet-unknown genes.

Plant growth can be badly stunted by excess ions in the soil. This effect, called acid soil syndrome, can cause severe agricultural yield losses, especially in areas prone to drought. For this reason, a team of researchers from RIKEN and two Japanese universities are working to identify genes that regulate a plant's tolerance of ions[1].

Much work has been done on aluminum toxicity in plants, but little is known about the genes that control direct tolerance to acid in the form of hydrogen ions, or protons. The researchers prepared thale cress, *Arabidopsis thaliana*, from seeds treated with ethyl methanesulfonate to introduce random point mutations in their genome. The seeds were cultivated in an acidic (proton-rich) environment, and the researchers looked for seedlings that failed to grow roots.

"We carried out screening using 25,000 seedlings," says project leader Satoshi Iuchi from the RIKEN BioResources Center in Tsukuba. "Finally we obtained one mutant that had an acid sensitive phenotype."

The mutant plant, named *stop1* (Sensitive TO Proton), was cloned and subjected to DNA sequencing. The sequencing revealed mutations in a part of the genome that encodes a protein called STOP1, consisting of 499 amino acids. The protein contains four 'zinc-finger' domains that regulate DNA transcription in the cell nucleus.

The researchers next investigated whether the *stop1* mutant strain was sensitive to other toxic ions. It showed no particular sensitivity to cadmium, copper, sodium, lanthanum or manganese, but was extra sensitive to aluminum ions—*stop1* plants showed 80–90% reduced root growth when exposed to aluminum, compared to only 30% in control plants.

Arabidopsis is known to tolerate aluminum by excreting malate, an ionized form of malic acid that is regulated by a gene called *AtALMT1*. This new study confirmed the link—*stop1* mutants failed to express *AtALMT1* in the toxic aluminum, and did not excrete any malate.

However, when *AtALMT1* was deliberately disrupted in the control plants, the proton sensitivity was not affected. Therefore STOP1 must regulate different genes related to proton sensitivity (Fig. 1).

This work puts STOP1 on the expanding list of transcriptional factors that respond to stress and regulate genes to ensure a plant's survival. Iuchi believes genetic modification of proteins such as STOP1 is the best way to improve farming efficiency. "Large amounts of chemical fertilizer are used in agriculture, which causes problems," he says. "If enhanced-tolerance plants can be used, chemical fertilizer usage can be reduced." ■

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A very sociable brain

Brain activity in primates is directly influenced by social context

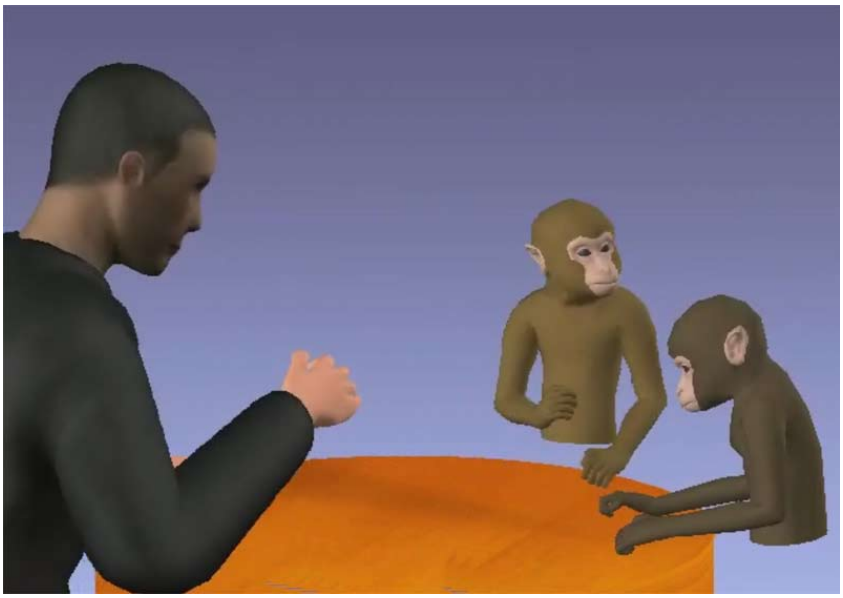
Human society puts heavy demands on the brain. Neurons must adapt rapidly to contextual changes in the social environment. Researchers at the RIKEN Brain Science Institute in Wako are gaining insight into this 'social brain function' by observing Japanese macaque monkeys[1].

"We can understand how our brain recognizes and adapts to social environments by expanding research in primates," says cognitive neuroscientist Naotaka Fujii, "because the social behavior of monkeys is very similar to that of human children."

Fujii's team placed two male monkeys around a square table in chairs that restricted their necks and lower bodies but left their arms and head free to move. Food was placed in random positions on the table, and the monkeys' arm and head movements were closely monitored using a 3D motion capture system. Individual neuron activity was measured by inserting electrodes into the parietal cortex, a region of the brain that processes sensory information to determine the locations and movements of objects. In total, 174 neurons were isolated of which 91 were related to specific actions.

When the monkeys were seated opposite one another, they could only reach half the table each, so could not compete with one another. They effectively behaved as if no other monkey was present, and most activated neurons were associated with the monkeys' own right-arm motion.

However, when the monkeys were seated on adjacent edges of the table, they shared a corner and could fight over food items that were placed there. One monkey appeared to be dominant, taking the food about 90% of the time. The dominant monkey frequently watched the submissive monkey, and became aggressive on the rare occasions that the submissive monkey managed to grab the food (Fig. 1). "When the monkeys are placed in a conflict situation, they tend to be more active to get the reward, even when they are not hungry," says Fujii.



Naotaka Fujii

Figure 1: Computer graphic reconstructed from monkey behavioral data. The experimenter is about to place food on the table. The dominant monkey (left) is watching the submissive monkey (right) but the submissive monkey does not look back due to social suppression.

Brain activity changed dramatically when this social conflict was introduced. The researchers saw decreased activity in neurons related to the monkeys' own right-arm movements, and increased activity in neurons related to other stimuli, such as the actions of their competitor's arms.

"This is the first evidence that neurons are manipulating activity depending on social context at a single cell level," says Fujii. "However, the parietal cortex may not be the only structure that implements the function. We have to expand recording areas to obtain an entire view of social brain functions." ■

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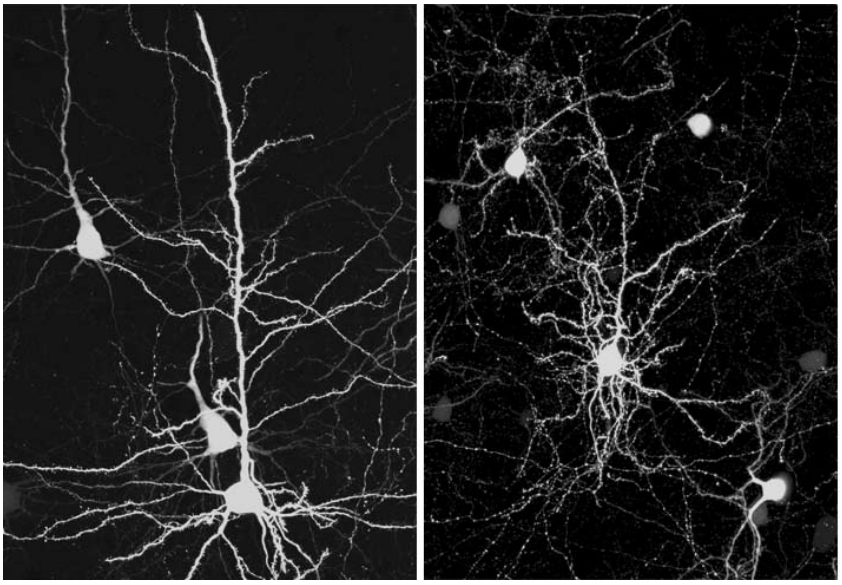
Layering and positioning neurons

Multipolar-to-biopolar neuronal transition is essential during brain development



Development

Figure 1: Normal (left) and defective (right) dendritic development in mice lacking Cdk5. In mature neurons, neurites are referred to as either dendrites or axons.

A team of Japanese scientists led by Toshio Ohshima, at the RIKEN Brain Science Institute, Wako, has determined that a protein called cyclin-dependent kinase 5 (Cdk5) is required for neurons to develop their proper shape. Morphological defects from a lack of Cdk5 affect the position and function of neurons in many parts of the brain, including the cerebral cortex—or gray matter.

Reporting in the June issue of *Development*[1], Ohshima and colleagues extend their previous work that demonstrated proper migration of neurons to form the normal six layers of the cortex failed to occur in mice lacking Cdk5.

All cells of the body express Cdk proteins which are necessary for controlling when and how long cells divide. However, Cdk5 is different from other Cdk proteins in that it must be activated by specific 'accessory' proteins that are most highly expressed in neurons.

Ohshima and colleagues used several experimental approaches, including introducing a fluorescent 'tag' protein into developing brains to follow neuron migration in real-time, to evaluate the function of Cdk5.

As cortical neuron layers develop, the shape of neurons shifts from cells with multiple neuronal projections, or multipolar neurites, to cells with fewer neurites 'pointing' in opposite directions ('bipolar'). The team found that in brains lacking Cdk5, however, the neurons remain multipolar.

This morphological defect was especially pronounced in so-called 'pyramidal' neurons (Fig. 1), which are specialized neurons with a single apical ('top') dendrite and many basal ('bottom') dendrites (hence their bipolar morphology) that represent nearly 80% of the neurons in the cortex.

Commenting on their work, Ohshima says that he was initially intrigued with Cdk5 because it regulates proteins associated with devastating diseases such as Alzheimer's and Amyotrophic Lateral Sclerosis. Serendipitously, however, the team found developmental defects in mice lacking Cdk5, which prompted further experiments.

The team's new contribution adds to the well-accepted view that Cdk5 function is essential for normal brain development. Of particular note, the team found that pyramidal neurons require Cdk5 for multipolar-to-bipolar transition. But exactly which protein substrates Cdk5 regulates to bring about this transition is still not well understood.

"There are some candidates for Cdk5 substrates, but I have no direct evidence to say which one may be involved in its function," says Ohshima. Indeed, the next step is to uncover the molecular pathway regulated by Cdk5. Using proteomics approaches—a combination of techniques to understand how proteins interact with one another—is one way Ohshima thinks he and his team can move forward. ■

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Towards a treatment for epilepsy

Researchers uncover a mechanism for seizures

Japanese neuroscientists have clarified the molecular basis of the intractable epileptic disorder known as severe myoclonic epilepsy in infancy (SMEI). In the process they have redefined the position and role of an important protein involved in controlling the firing of nerve impulses in the brain. The work also has generated a mouse model of severe myoclonic epilepsy that the researchers hope to use to study the condition and how to treat it.

More than 200 different mutations of the human *SCN1A* gene are known to be associated with human epileptic disorders including SMEI. The gene itself encodes an ion-channel protein, $Na_v1.1$, which forms a pore in the plasma membrane that controls the in-flow of electrically-charged sodium ions into nerve cells. This is a significant step in the generation of nerve impulses. There is a homologous gene, *Scn1a*, in mice.

In a recent paper in *The Journal of Neuroscience*[1], researchers from the RIKEN Brain Science Institute, Wako, and their colleagues, describe how they produced a 'knock-in' mouse, by introducing a disease-causing, nonsense mutation found in SMEI patients into the middle of the *Scn1a* gene. Mouse pups which inherited copies of the mutant gene from both mother and father were markedly smaller (Fig. 1), developed epilepsy and an unstable gait by the second week after birth, and died within three weeks. Pups with only one copy of the mutant gene began epileptic seizures in the third week, and about 40% had died within three months.

Kazuhiro Yamakawa

Figure 1: An *scn1a* knock-in mutant mouse (right) with a normal (wild-type) litter mate (left).

Previous studies suggested that the $Na_v1.1$ protein was distributed rather evenly throughout the brain and could be found in the projections of nerve cells known as dendrites. Using three different antibodies as probes, the RIKEN-based research team corrected this picture. The $Na_v1.1$ proteins are more likely to be found on axons and cell bodies. In particular, they are found on inhibitory nerve cells that express the calcium-binding protein parvalbumin, often in the area known as the axon initial segment where nerve impulses are generated.

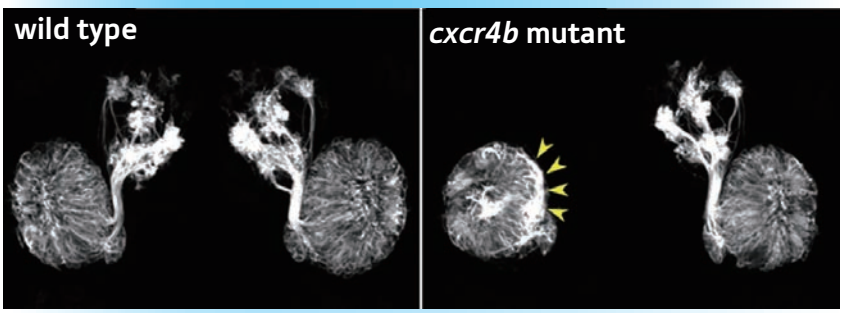
By measuring and comparing the output of excitatory and inhibitory neurons in normal and mutant mice, the research team found that the $Na_v1.1$ channel proteins were needed not to initiate firing of the excitatory nerve, but to maintain the inhibitory pulse, thus preventing epileptic seizures.

"We hope to develop effective therapies for this intractable epilepsy from further work," says project leader Kazuhiro Yamakawa. ■

1. Ogiwara, I., Miyamoto, H., Morita, N., Atapour, N., Mazaki, E., Inoue, I., Takeuchi, T., Itohara, S., Yanagawa, Y., Obata, K., Furuichi, T., Hensch, T.K. & Yamakawa, K. $Na_v1.1$ localizes to axons of parvalbumin-positive inhibitory interneurons: A circuit basis for epileptic seizures in mice carrying an *Scn1a* gene mutation. *The Journal of Neuroscience* **27**, 5903–5914 (2007).

On the scent of how a sense of smell develops

Researchers identify factors needed for proper olfactory development



Development

Figure 1: Live imaging of axon projections from the nasal epithelium into the olfactory bulb in normal (left) and mutant zebrafish lacking functional Cxcr4b (right). The mutant Cxcr4b fish have a variable phenotype, such that some nasal epithelia fail to project axons (yellow arrowheads) and others do not.

Neurobiologists from Japan and the US have identified a signaling system functioning during vertebrate development that controls the proper positioning of cells giving rise to future olfactory neurons, and their eventual correct wiring to the brain.

During development many cells originate in one place but then migrate to another before they mature into their final functional cell type. One example of this process is the development of the placodes—areas of thickening along the embryonic epithelia that gives rise to organs for hearing, seeing and smelling. This last one—the nasal placode—contains the future nasal epithelia and olfactory neurons. To better understand how these placodes form, scientists have focused their attention recently on a family of small, secreted proteins, the so-called chemokines, which were originally identified as controlling immune cell migration.

Using zebrafish, the team led by Nobuhiko Miyasaka from the RIKEN Brain Science Institute in Wako, has now identified the chemokine Cxcl12a and its receptor, Cxcr4b, as key molecules necessary for the correct positioning of the nasal placode[1].

The team showed that in mutant fish lacking either Cxcl12a or Cxcr4b function some cells failed to join this placode. They further showed that in both types of mutant fish the olfactory neurons developed in the placode, though in most instances they subsequently failed to project axons to the olfactory bulb, a region in the brain some distance from the placode that transmit a sense of smell to higher olfactory centers (Fig. 1).

The researchers confirmed these findings by showing that experimentally-induced mis-expression of Cxcl12a also perturbed the placode assembly, but unlike loss of its expression (or that of Cxcr4b), it did not affect olfactory axon outgrowth towards the olfactory bulb. Importantly, this suggests that Cxcl12a is not acting as a guidance factor for olfactory axons because ubiquitous mis-expression would have 'confused' the axons if it was acting in this way. Rather, Cxcl12a is acting as a 'permissive factor' that allows these axons to navigate the local environment.

Previous studies have shown that Cxcl12/Cxcr4 signaling regulates retinal axon projections in zebrafish[2] and motor axon projections in mice[3]. Miyasaka therefore says that "Cxcl12/Cxcr4 signaling might be a general, evolutionary conserved molecular tool that allows for and shapes the initial trajectory needed by various growing axons to properly innervate their respective targets." Insight from future studies could illuminate the molecular mechanisms downstream of these chemokines, which one day may be manipulated to regrow axons on demand. ■

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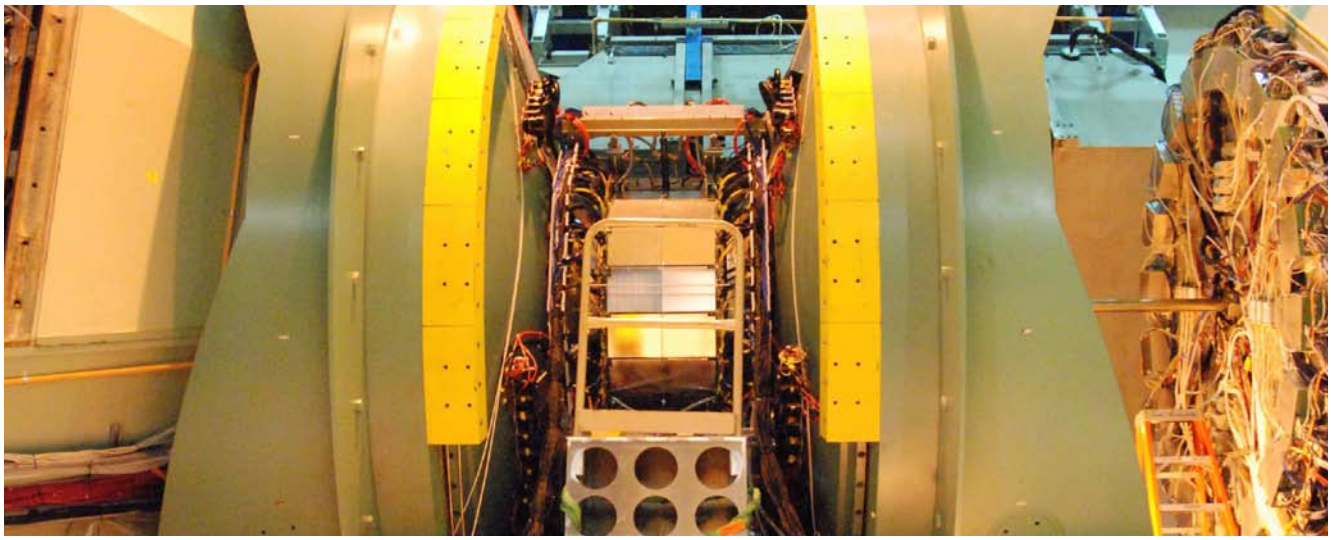
2. Li, Q., Shirabe, K., Thisse, C., Thisse, B., Okamoto, H., Masai, I. & Kuwada J.Y. Chemokine signaling guides axons within the retina in zebrafish. *The Journal of Neuroscience* **25**, 1711–1717 (2005).
3. Lieberam, I., Agalliu, D., Nagasawa, T., Ericson, J. & Jessell, T.M. A Cxcl12-CXCR4 chemokine signaling pathway defines the initial trajectory of mammalian motor axons. *Neuron* **47**, 667–679 (2005).



RIKEN Brookhaven National Laboratory Research Center

RIKEN Nishina Center for Accelerator-Based Science – Part 2
RIKEN BNL Research Center

An international group of scientists at RIKEN Brookhaven National Laboratory (BNL) Research Center (RBRC) on Long Island, near New York City, is trying to replicate conditions during the first few microseconds after the Big Bang. Using the unique capabilities of the laboratory's Relativistic Heavy Ion Collider (RHIC), many of which were developed at RBRC, researchers can manipulate and observe quarks and gluons, the constituents of protons, with unprecedented clarity.

The history of RBRC began in the early 1990s, when the RHIC was being built, with a proposal from RIKEN researchers to modify the collider. "At BNL they had a gold-on-gold ion collider to create a high-temperature state of matter called a quark–gluon plasma," recalls Hideto En'yo, Group Leader of the Experimental Group at RBRC. "Our proposal was to modify the accelerator to give it the capability to make a polarized proton beam."

So in 1995 RIKEN and BNL agreed that Japan would supply funds to add this capability. RBRC was established in 1997 with Nobel Prize winner in physics Tsung-Dao Lee as its driving force and first director.

With a polarized beam, researchers could control the spin of the particles they were colliding, and that, it was thought, would give powerful new insights into the nature and behavior of quarks and gluons. "Ordinarily, proton spins are random, so you need a trick to get them all in a line," says En'yo.

The main 'trick' at RBRC is the Siberian Snakes, a set of polarizing magnets that were developed by RBRC to align and maintain the spin direction of the protons in the beam being accelerated in the RHIC rings. This makes RHIC the only polarized proton accelerator in the world and permits a level of precision in measurements of quark and gluon spins previously unheard of.

Hideto En'yo

Larry Maclerran

Nicholas Samios

RBRC also has an important theoretical side. "The theory end of things is focused on three major efforts," explains Larry McLerran, Group Leader of the Theoretical Physics Group. "One is trying to understand the nature of protons and neutrons—where their spin comes from and how they are composed of quarks and gluons. Another is related to strong interactions, emphasizing lattice gauge and CKM (Cabibbo–Kobayashi–Maskawa) matrix theory—an attempt to understand the strong and electroweak interactions."

The third area is the properties of matter at extreme energy densities, such as quark–gluon plasma like in the early universe.

These theories can be put to the test thanks to the remarkable versatility of the RHIC. "We can collide deuterons on gold, gold on gold, copper on gold, copper on copper…" says Nicholas Samios, Director of RBRC.

Researchers at RBRC work on the huge PHENIX (Pioneering High Energy Nuclear Interaction Experiment) detector. It is packed with sensors to provide precision measurements of a variety of phenomena arising from the heavy ion and proton collisions.

This was all a bit of a gamble for the creators of the RHIC, according to Samios. "No one knew when we were building the RHIC what the characteristics of this inquiry would be. It could have turned out to be a dud, with little to show for all our efforts."

Fortunately, RHIC turned out to be very exciting, and researchers there quickly discovered something unanticipated. "The quark–gluon

plasma had been thought to be a sort of dilute, weakly interacting gas," recalls Samios. "But we discovered that it was more like a liquid, which is very, very exciting."

"We're really looking at high energy density, hot stuff. The energy and intensity of this machine is such that we've got it all—we can study quark–gluon plasma, color glass condensate, color superconductivity and glasma." A glasma is a pre-equilibrium state of matter formed in heavy ion collisions before a quark-gluon plasma forms.

"The original concept was that Brookhaven provides the infrastructure—offices, assistants, lab space—and RIKEN pays salaries and travel expenses for 20 to 25 physicists doing research that is relevant to physics and to the lab," says Samios. The visiting scientists are granted five-year RBRC fellowships so that they get the experience of working with the RHIC machine, and RBRC gets a steady flow of eager young minds.

The system has worked well. All of the RBRC fellows have gone on to tenured positions at major universities. "The productivity—the number of publications—has been exceptional," says Samios. "We're extremely happy. And the relationship between RIKEN and the lab has been fantastic…It's so nice to have enlightened management higher up."

McLerran concurs. "When the Japanese guys have an idea and see that the physics is good, they just do it. There are very few bureaucratic hurdles. Very senior people come here, and after work go out for beers with the young people and talk things out."

One of the Siberian Snakes magnets at BNL.

Despite its success, the team is about as big as it's likely to get. "We're at a steady state now," says Samios. "This is a good level we have—15 theorists, 8 experimentalists—big enough that you can do good things, but small enough so people can easily talk to each other."

He adds: "This is a constantly changing field, and to stay on top, you need young people constantly thinking about these problems. And that is something RBRC has really enhanced."

Abhay Deshpande—Getting the spin on spin

Abhay Deshpande, a RIKEN RBRC fellow and professor at the State University of New York at Stony Brook, has spent his career trying to determine where the proton's spin comes from.

"Every nucleon has spin; it's one of their fundamental properties," he says. Since nucleons have a spatial structure, the contributions to the total nucleon spin are measured from the nucleon's constituents, the quarks and antiquarks. However, he adds, "Experiments performed at CERN in the late 1980s revealed, to our surprise, that the quarks and antiquarks together carry only about 25% of the nucleon's spin."

So where does the remaining spin come from? It's a vexing problem. Theories proposed that much of the spin might be attributable to particles called gluons, which bind the quarks together inside the nucleon. Most of these reside deep inside the proton, and to measure their spin, much higher energy was needed. So Deshpande joined RBRC. "RBRC made the crucial contribution of the Siberian Snake magnets. Without them there's no way of measuring the gluon's spin."

Deshpande describes how in the experiments, the two accelerator rings of the RHIC are filled with protons of known spin, in predetermined patterns, and these protons are accelerated. "Then we pass the beams through each other, and collisions occur, essentially at the speed of light. At such high energies the results are clear and unambiguous."

Early results indicate that gluons may not contribute much to the nucleon's spin, which is exciting, but needs to be confirmed. "If the results hold, we must consider other contributions, such as the orbital motion of quarks and gluons."

A native of Mumbai, India, Deshpande came to RBRC in 2000 as a RIKEN fellow after earning his PhD at Yale University. "The experience at RBRC has been fantastic. I've had tremendous freedom to pursue my science, and it's a privilege to work with the best scientists in accelerator technology and particle and nuclear physics."

RIKEN Genomic Sciences Center holds 10th Anniversary Symposium

The RIKEN Genomic Sciences Center (GSC) held a symposium to commemorate its 10th anniversary—A Decade of GSC and 'New Challenges' of Genome Science—on September 26 at Keidanren Kaikan in Tokyo. The event attracted more than 400 attendees.

Akiyoshi Wada, the former director of the Center who now serves as Special Adviser, led off the proceedings with a speech in which he traced the history of genomic science until the present time, outlined the current challenges of the GSC, and speculated on its future directions.

"Our ultimate goal," he said, "is not only to be satisfied by describing the structure of life and how it works. It is to explain and clarify our understanding of how life has survived for four billion years, and to trace a path for our continued survival in the future. To achieve this, we need a well-balanced research strategy."

The Center's current director, Yoshiyuki Sakaki, started his talk with the history of the GSC before describing its triumph in announcing the successful sequencing of the 21st human chromosome, and the entire human genome, which raised the Center's international reputation. He then went into detail about the leading roles of GSC in post-sequence genomics at the global level, including the Genome Network Project.

Later in the day, six group directors at the Center gave lectures on their research work and future plans.

Kazuo Shinozaki, the former project director of the Plant Functional Genomics Research Group, spoke of the Center's success in developing practical applications for its findings in plant genomics, and its successful cooperation with private companies.

Yoshihide Hayashizaki of the Genetic Structure Functional Research Group gave a talk on the 'Adventure of the Genome Network on the RNA Continent'. He pointed out that the techniques of precise physical measurement and mathematical analysis of life have achieved rapid progress. But a holistic approach is called for; analyzing organisms from the standpoint of only one part of the 'Omic' continuum is not sufficient.

Shigeyuki Yokoyama of the Protein Research Group talked about the research activities in his group over the past 10 years, which ranged from figuring out the structural function of proteins to clarifying the workings of life systems through structural proteomics using nuclear magnetic resonance imaging and X-ray crystallography.

In addition, Toshiyuki Shiroishi, Akihiko Konagaya and Makoto Taiji from RIKEN gave very interesting and impressive lectures on functional genomics and systems biology. Special guests Yoshiki Hotta of Research Organization of Information and Systems and Hideaki Sena of Tohoku University expressed their hopes concerning the future expectations in the field of genomics and the GSC. ■

Cheiron2007—The first Asia-Oceania Forum for Synchrotron Radiation Research summer school

The Asia-Oceania Forum for Synchrotron Radiation Research (AOFSRR) held its first summer school in September, at the SPring-8 synchrotron facility at the Harima Institute. Fifty young scientists and engineers from seven countries attended the summer school, which turned out to be 10 days of edifying talent-nurturing interchange.

The school was co-sponsored by RIKEN, JASRI (the Japan Synchrotron Radiation Research Institute, which is responsible for operating SPring-8), KEK (Japan's High Energy Accelerator Research Organization), and AOFSRR. The curriculum included lectures on synchrotron radiation science and technology, covering everything from synchrotron operation to industrial applications. The sessions finished off with a talk on future directions in synchrotron science.

The participants also had an opportunity to experience real experiments on SPring-8 beamlines, during the two one-day practice courses.

The 'Meet the Expert' sessions—round-table discussions for 5–10 students—were a good opportunity for students to meet experienced scientists and ask practical, specific questions about their research.

The name of the summer school is derived from ancient Greek mythology. Cheiron was an immortal god, intelligent, civilized and kind, as well as a teacher who would impart his knowledge only to those mortals most worthy of it. This matches the purpose of the summer school, which seeks to nurture the best and brightest young minds in science from around the world. ■

RIKEN Brain Science Institute and Harvard University get together for a neuroscience summer school

The RIKEN Brain Science Institute (BSI) and Harvard University in the USA collaborated to hold a joint summer school in neuroscience for 10 weeks from June 10 to August 19 this year.

The four participating students gained invaluable experience working alongside Japanese researchers and technicians on cutting-edge brain research in BSI's labs.

The students were able to choose from among all the BSI labs, to work on independent research projects according to their own interests and background. The four BSI facilities participating were the Okamoto, Hashimoto, Miyawaki and Aruga labs. In addition, they attended lectures based on an international lecture series hosted by the RIKEN BSI. The lectures addressed a variety of topics relevant to the institute's four main research themes—understanding, protecting, creating, and nurturing the brain. During the summer school the students were required to write two papers based on the lectures and lab work, and at the end of the course they each gave a presentation.

In addition to the lab work, the students took Japanese language classes and gained experience in using their Japanese during excursions to Meiji Shrine, Harajuku, and Omotesando in Tokyo where classical and contemporary Japan coexist.

The students received credit toward their degrees—both research and elective neurobiology course credits—and costs for the 10-week course were covered by scholarships from the Reischauer Institute of Japanese Studies at Harvard University and the Harvard Summer School.

The school was made possible through the efforts of Takao Hensch, professor of molecular and cellular biology at Harvard and BSI.

RIKEN BSI is widely considered to be the premier neuroscience research center in Asia, with modern, well-equipped labs located at the main RIKEN campus in the city of Wako. ■

Benefiting from external advice

RIKEN's system to seek management advice from international research authorities was a first in Japan

Researchers are, by and large, subject to external evaluation through peer review of their work, but additional measures are needed to evaluate their management. By 1990, chief researchers at RIKEN were required to have their laboratories' activities evaluated by external reviewers every seven years. Projects of the RIKEN Frontier Research System have also been reviewed mid-term since its establishment in 1986. This system brings greater transparency to the management of research activities.

But that was not enough for RIKEN's executives. One lunch time in 1990 after a management meeting, some board members casually suggested the president's management policies also be subjected to an external review. The suggestion was welcomed, reflecting RIKEN's open culture and willingness to try an unprecedented approach.

The driving force behind the move was RIKEN's sixth president, Minoru Oda. The astrophysicist had an aptitude for drawing, and often illustrated RIKEN in cartoons as an insect-like amoeba because it keeps changing its shape by constantly developing research activities in a variety of fields. Oda asked George W. Clark, then professor of physics (currently professor emeritus) at the Massachusetts Institute of Technology, to conduct the first preliminary review. After a week-long inspection in November 1990, Clark suggested RIKEN establish a visiting committee that gives advice to the president and management board.

Following Clark's proposal, RIKEN set up in 1991 a committee to prepare for establishing the 'RIKEN Advisory Council' (RAC). Some executives also went on a study tour to various institutes in Europe. They then compiled a basic outline in early 1992, and drew up the 'White Paper on RIKEN,' an overview and a roadmap of its research activities in English. RIKEN invited 15 research authorities with different backgrounds from the US, Europe and Japan to become RAC members. Heinz A. Staab, then director of Max Planck Institute for Medical Research, was appointed as chairman.

The first RAC met for four days in June 1993 (Fig. 1). The RAC made several recommendations that RIKEN adopted by the next meeting in 1995. For example, as it was recommended that researchers keep training at least until their mid-30s, RIKEN raised the minimum age for hiring tenure scientists from 32 to 35.

RIKEN later introduced the advisory council system to the Brain Science Institute and each of five other life-science research centers established after 2000. The RAC has not only guided RIKEN to further improve its management quality, but also influenced Japan's policy to evaluate research institutes on the whole. In 1997, the government decided to annually review, in turn, one of Japan's five public research institutes.

Figure 1: The first RIKEN Advisory Council, consisting of 15 of the world's top scientists, met in 1993 to provide management advice to RIKEN.

So far, RIKEN has held six RAC meetings. At each meeting, the RAC praised RIKEN's high-quality and vigorous research activities, and acknowledged its sincere attitude in adopting recommendations, even though some of them were tough. At the fifth meeting, the RAC issued seven main recommendations, such as strengthening scientific governance, improving the decision-making process and increasing the quality of post-doctoral researchers and students. At the latest meeting[1] held in 2006, RIKEN reported its implementation of many new measures, including the establishment of the Career Support Office, and the Science Council, which allows researchers at all levels to offer opinions to management.

Currently, RIKEN is working to incorporate the RAC's latest recommendations into its management policies. The council advised strengthening science and technology by carefully balancing investments in large infrastructure projects with small, but valuable, basic research. RIKEN is also in the process of further strengthening scientific governance, increasing its visibility and international standing, and enhancing interactions with the society, including Asia. ■

1. Interview, RIKEN's place in the world. *RIKEN Research* **1(1)**, 1-2 (2006).

For more information, please visit:

http://www.riken.jp/engn/r-world/info/report/rac/index.html

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RIKEN, Japan's flagship research institute, conducts basic and applied experimental research in a wide range of science and technology fields including physics, chemistry, medical science, biology and engineering. Initially established as a private research foundation in Tokyo in 1917, RIKEN became an independent administrative institution in 2003.

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