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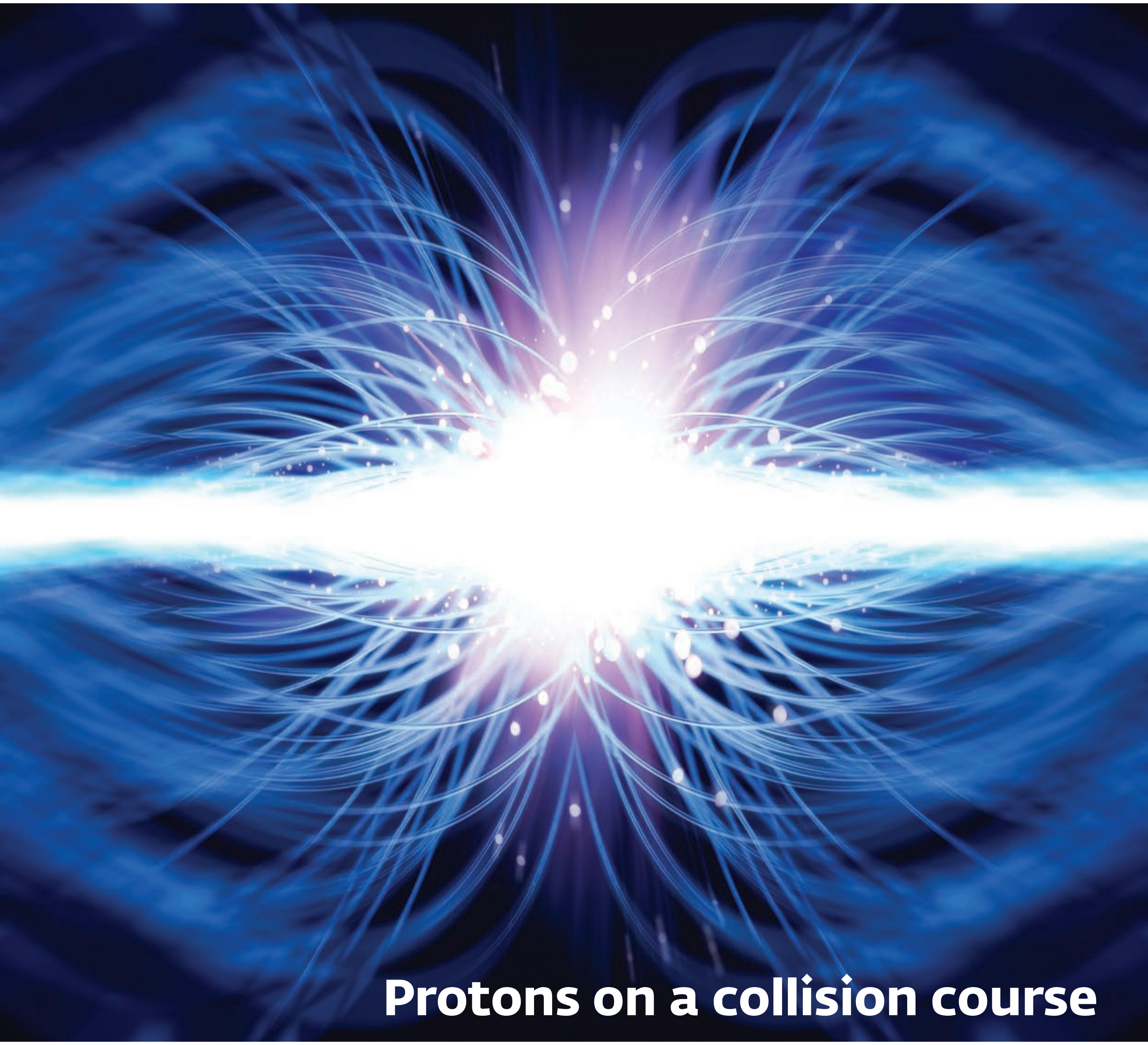


Protons on a collision course

HIGHLIGHT OF THE MONTH

Biology: At the edge of awareness

RIKEN

Biology

At the edge of awareness

Imaging data suggest that conscious perception has little to do with the primary visual cortex—the region where visual information enters the brain

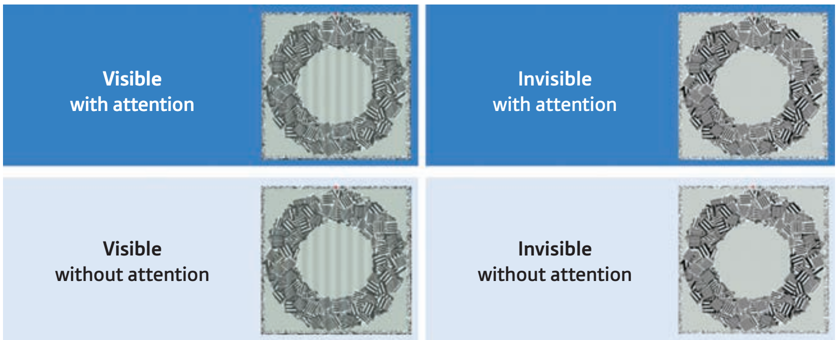


Figure 1: When the rings of dynamic patterns are presented to the same eye (left column), the subject is able to consciously perceive the target pattern–the stripes in the center of the ring. When the two are presented to different eyes (right column), the dynamic pattern suppresses perception of the target pattern. Under both conditions, participants were asked to perform a task that focused attention on the target (top row) or on letters presented outside the target area (bottom row).

From a purely intuitive point of view, it is easy to believe that our ability to actively pay attention to a target is inextricably connected with our capacity to consciously perceive it. However, this proposition remains the subject of extensive debate in the research community, and surprising new findings from a team of scientists in Japan and Europe promise to fuel the debate.

Resolving how these aspects of perception are managed requires a detailed understanding of how the visual centers in our brain process information. A region known as V1 has been investigated as it represents the first portion of the visual cortex to receive and process signals transmitted from the retina.

Many researchers favor a model in which functions pertaining consciousness are widely spread among the whole visual system, including V1. The classical model, which assumes that the neural mechanism of consciousness is integrated into a narrow subset of brain structures, referred to as a homunculus, or 'little human', is almost defunct. However, a modern version of this model is under debate. It proposes that the neural mechanism of consciousness is a privileged set of cortical areas, a subpopulation of neurons, or certain neural dynamics (e.g. oscillations); while there are also visual systems that have nothing to do with conscious vision, explains Masataka Watanabe a researcher investigating brain function at the University of Tokyo, Japan.

Watanabe cites studies proposing that visual attention as processed within V1 may be only minimally impacted by conscious perception; but, the experimental data have been contradictory. For example, studies using a technique called functional magnetic resonance imaging (fMRI) to map brain activity have indicated that V1 contributes to both attention and awareness in humans. However, invasive electrophysiological studies in non-human primates yielded different results. "You would find only 10 to 15% of neurons in V1 that are barely modulated by awareness, and 85% or so that are not modulated at all," says Watanabe. To resolve this ambiguity, he, Kang Cheng from the RIKEN Brain Science Institute, Wako, and their colleagues designed an experiment that examined both processes independently. Surprisingly, their results may lend support the modern homunculus model[1].

Blind-siding awareness

The difficulty in separately testing awareness and attention in an experimental setting is a likely cause for these contradictory results. "I believe previous studies were most likely 'contaminated by attention'," says Watanabe.

Watanabe, Cheng and their colleagues used a technique known as continuous flash suppression (CFS) to address the issue of awareness. The concept is based on 'binocular rivalry': when each eye is presented with a distinct image, perception rapidly shifts between the two images rather than melding them together. However, by making one of these stimuli extremely 'busy' and dynamic, it becomes possible to entirely suppress conscious perception of the other, thereby selectively eliminating awareness.

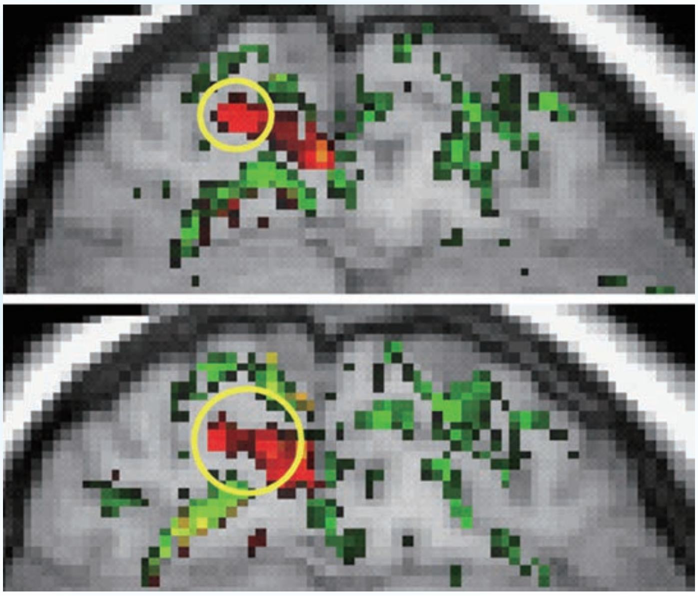


Figure 2: fMRI imaging reveals changes in neuronal activity within V1. The red regions within the yellow circle denote sections of V1 that respond to the target region within the dynamic pattern, whereas the green regions are being activated by the ring-shape that either overlaps or suppresses visibility of the target.

In their study, the researchers used a patterned ring as the visual target. They displayed this to subjects along with an equally sized ring consisting of multiple patches of dynamically shifting patterns. When both target and ring were projected in an alternating pattern to the same eye, the subjects could consciously perceive both the ring and the target at its center. When the two were transmitted to different eyes, however, the dynamic ring suppressed perception of the target (Fig. 1).

For both visible and invisible target conditions, the subjects participated in two kinds of trials. In one, they were asked to pay attention to and report the visibility of the target. In the other, they were asked to shift attention away from the target region so they could follow a rapidly changing series of letters appearing within the surrounding ring pattern. Using fMRI, the researchers could specifically track changes in neuronal activity in each subject's V1 that were induced by different combinations of attention and visual awareness under all four conditions.

Attentive, but unaware

The results proved striking: for all seven subjects, the shift of attention toward or away from the target had a dramatic effect on brain activity in the region of V1 corresponding to the visual target (Fig. 2). However, the ability to consciously perceive the target proved surprisingly unimportant, and shifts in target awareness had no clear or consistent effect on the activity of this subset of neurons. "I was quite surprised that there was zero modulation of awareness in V1," says Watanabe. "Even in monkey studies where the [animals] showed only 10% of their neurons being modulated, [those researchers] were nevertheless observing modulation." By comparison, no such awareness effect was observed in the human subjects.

Watanabe and colleagues' findings indicate that awareness is not a major factor in the earliest stages of visual perception, even though it is clearly a core component of the overall process. Further investigation will be required to determine how consciousness becomes integrated with other visual data. "Scientists are pretty sure that the terminal areas of the visual system, such as the regions that process shape and color or motion, are likely to be heavily modulated by awareness," says Watanabe. "But where exactly this modulation starts is still an open question."

Future studies from this research team will seek out the brain structures involved in awareness processing. For now, these data offer surprising support for a still-contested model of visual perception and consciousness. "To tell the truth, three years ago I would not have believed this result," says Watanabe. "I don't think the 'Battle of V1' is fully settled, but these data could imply that the modern homunculus model may be true."

1. Watanabe, M., Cheng, K., Murayama, Y., Ueno, K., Asamizuya, T., Tanaka, K. & Logothetis, N. Attention but not awareness modulates the BOLD signal in the human V1 during binocular suppression. *Science* **334**, 829–831 (2011).

ABOUT THE RESEARCHER

Masataka Watanabe was born in Funabashi, Japan, in 1970. He graduated from the School of Engineering at the University of Tokyo in 1993 and obtained his PhD in 1998 from the same university. After a year of postdoctoral training in the laboratory of Hiroaki Aihara in the School of Engineering at the University of Tokyo, he was made research assistant in 1999 and then associate professor at the University of Tokyo in 2002. Until this time his specialism had been theoretical neuroscience. Following a sabbatical year at Caltech in the laboratory of Shinsuke Shimojo, and collaboration with numerous scientists including Kang Cheng (RIKEN BSI), Keiji Tanaka (RIKEN BSI), Masamichi Sakagami (Tamagawa University), Ichiro Fujita (Osaka University) and Nikos Logothetis (Max Planck Institute [MPI]), he added psychophysics, single unit data analysis and functional MRI to his repertoire. Watanabe currently holds a visiting researcher position in RIKEN BSI and a visiting scholar position at the MPI. His research focuses on conscious perception.

Manipulating the texture of magnetism

Derivation of equations that describe the dynamics of complex magnetic quasi-particles may aid the design of novel electronic devices

Knowing how to control the combined magnetic properties of interacting electrons will provide the basis to develop an important tool for advancing spintronics: a technology that aims to harness these properties for computation and communication. As a crucial first step, Naoto Nagaosa from the RIKEN Advanced Science Institute, Wako, and his colleagues have derived the equations that govern the motion of these magnetic quasi-particles[1].

The magnetic behavior of a material is the result of a phenomenon known as spin. This can be thought of as the rotation of electrons and is usually visualized as an arrow pointing along the rotation axis. In some crystalline solids, neighboring electron spins can interact with each other such that the arrows form vortex-like patterns (Fig. 1). This spin 'texture' is robust and remains intact despite outside influences; it can also move through the material crystal, even though the atoms themselves remain stationary. Because of these properties, physicists often think of such spin vortices as particles in their own right; they call them skyrmions. The work of Nagaosa, with researchers from China, the Netherlands and Korea, provides a theoretical framework that describes skyrmion dynamics.

Skyrmions, and the ability to control them, have the potential to increase the packing density of magnetic recording media; as such, skyrmion-based devices are likely to be more efficient than conventional memories. "Skyrmions can be moved with a current density as much as a million times smaller than those needed to control magnetic structures, thus far," explains Nagaosa.

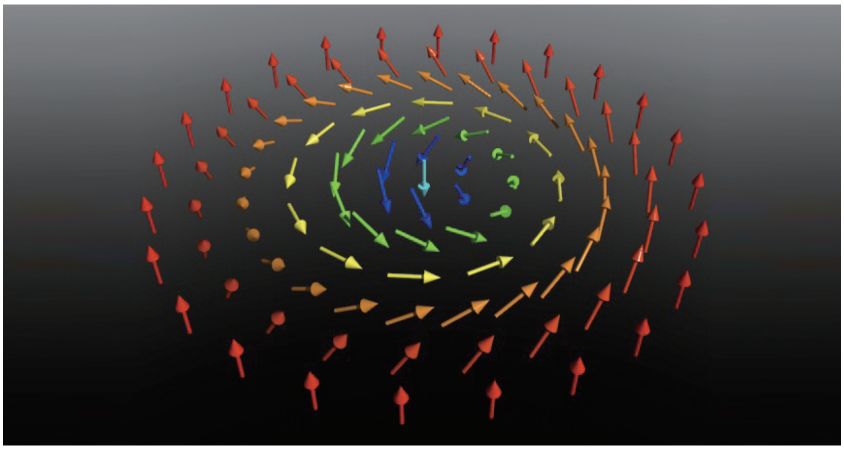


Figure 1: A skyrmion is a vortex-like arrangement of spins, depicted here as arrows. Knowing how to control their motion could lead to a new class of electronic memory.

The researchers theoretically investigated skyrmion crystals—ordered arrays of many skyrmions—that are supported by thin metallic films. Nagaosa and his collaborators[2] had suggested previously that skyrmion crystals are more stable in thin films than they are in thicker 'bulk' materials, making films more amenable to practical applications. The equations of motion derived by Nagaosa and colleagues also showed: how the electrons are influenced by skyrmions; that skyrmions can become pinned to impurities in the film; and that the skyrmion trajectory bends away from the direction of an electrical current. The researchers called this phenomenon the skyrmion Hall effect because of its similarity to the sideways force that is exerted on an electron as it moves through a conductor in a magnetic field, which was discovered by Edwin Hall in 1879.

"Next we intend to study the effect of thermal fluctuations of the skyrmion structure and the optical manipulation of skyrmions," says Nagaosa. "These are the important issues on the road towards applications." ■

1. Zang, J., Mostovoy, M., Han, J.H. & Nagaosa, N. Dynamics of skyrmion crystals in metallic thin films. *Physical Review Letters* **107**, 136804 (2011).
2. Yi, S.D., Onoda, S., Nagaosa, N. & Han, J.H. Skyrmions and anomalous Hall effect in a Dzyaloshinskii-Moriya spiral magnet. *Physical Review B* **80**, 054416 (2009).

Taking a closer look at molecular electronics

Fluorescence-yield x-ray spectroscopy provides a view into how organic transistors work at the molecular scale

Molecules and polymers have unique electronic and optical properties suitable for use in electronic devices. These properties, however, are complex and not well understood. Charge transport, for example, is affected by molecule shape, which can change during device operation and is difficult to measure. Now, a new technique is available to characterize the electronic states of molecules, thanks to research by Hiroyuki Kato from the RIKEN Advanced Science Institute and his colleagues in Japan[1].

The key characteristic of the team's technique—called fluorescence yield x-ray absorption spectroscopy—is its ability to probe molecules that are buried underneath other molecules, as well as under metallic electrodes (Fig. 1). First, x-ray photons illuminate a device of interest, causing core electrons inside a particular atom to be promoted to higher energy levels. When these electrons relax, they release their energy either to other electrons, or to photons, Kato explains. Finally, these energetic electrons or photons are emitted from the device, and the researchers can measure their energy. Then, they can determine the properties of the emitting molecule. The ability to select the type of atom that is excited—for example, carbon—aids the analysis.

Other researchers had previously monitored electron relaxation by observing emitted electrons. However, they were limited to observing molecules near the device surface since electrons have difficulty passing through other molecules and metals. Kato and colleagues therefore monitored the relaxation of excited electrons via emitted photons since they exit the device easily.

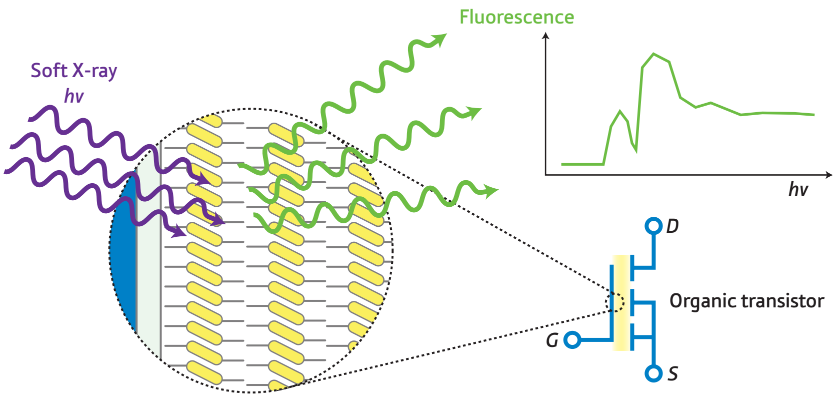


Figure 1: A schematic of fluorescence yield x-ray absorption spectroscopy. X-rays (left) fall onto active molecules inside an organic transistor (bottom right), causing fluorescent emission. The intensity of the emission as a function of incident energy reveals information about the state of the emitting molecules (top right).

The researchers applied their photon-based technique to an organic thin-film transistor made with the molecule DH6T, which is a small polymer called an oligomer. As they operated the transistor by varying the voltage applied to the gate electrode, Kato and colleagues saw the emitted photon spectrum shift in real time. The dependence of this shift on wavelength and voltage showed that, contrary to expectations, the emitted photons were unaffected by charges induced by the gate voltage. Instead, their spectrum was determined entirely by the internal state of the probed molecules, even under an applied electric field.

Further analysis showed that this electric field was not distributed evenly across the oligomer; rather, it fell disproportionately across one of the chemical groups making up the oligomer. This conclusion represents a first look into the electric field distribution in molecular devices at the scale of individual molecules. Kato says he expects the technique will prove to be a valuable characterization tool for the building blocks of future electronic and optical devices. ■

1. Kato, H.S., Yamane, H., Kosugi, N. & Kawai, M. Characterization of an organic field-effect thin-film transistor in operation using fluorescence-yield x-ray absorption spectroscopy. *Physical Review Letters* **107**, 147401 (2011).

Emerging from the vortex

A theory that accurately describes the properties of relativistic electron vortex beams will impact applications such as electron microscopy

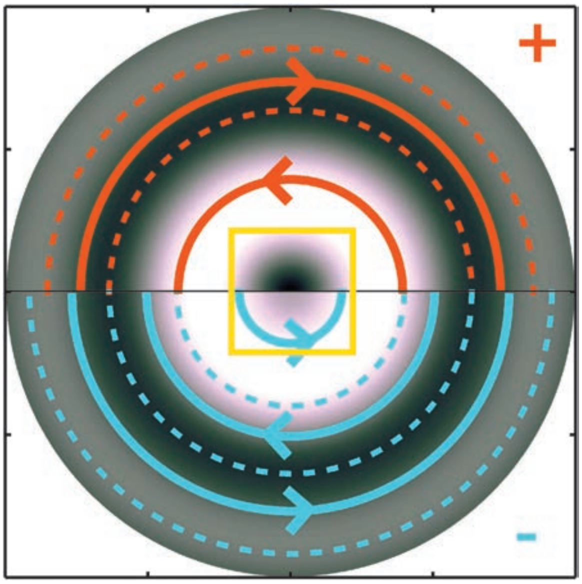


Figure 1: A comparison of electron beams with parallel (top) and antiparallel (bottom) spin and vortex orientation. The plot shows the density (grey) and current distributions (arrows) for electrons in the x and y direction, with either 'up' (+) or 'down' (–) spin, respectively. For electrons in the center of the beam, the distribution is predicted to be different for both cases.

Whether a car or a ball, the forces acting on a body moving in a straight line are very different to those acting on one moving in tight curves. This maxim also holds true at microscopic scales. As such, a beam of electrons that moves forward linearly has different properties to one with vortex-like properties. Since vortex beams show properties in magnetic fields that could lead to novel applications, a RIKEN-led research team has developed a theory that provides an understanding of these properties[1].

"Ours is the first comprehensive theory of relativistic electron vortex beams and adds significantly to their understanding," comments team member Konstantin Bliokh from the RIKEN Advanced Science Institute (ASI).

Like any particle, electrons can exhibit wave-like characteristics; and, understanding this behavior is critical to understanding the behavior of vortex beams so they can be harnessed in future applications. Unlike the broad front of an ocean wave hitting a beach, however, the oscillations of electron waves are out of sync along the beam: the slight shifts in their timing gives the waves a corkscrew character.

A vortex beam shows unique and potentially exploitable quantum effects arising from the interplay between the so-called 'orbital angular momentum' of its electrons and their intrinsic property called spin. The potential of these beams became apparent only recently, when they were demonstrated for the first time by Masaya Uchida and Akira Tonomura from ASI[2].

The complex mixture of electron spin, beam vortex properties and the relativistic properties of the electrons has complicated the theoretical understanding of the beams, says team leader Franco Nori also from ASI. He explains that their fundamental theoretical description was possible only through the combined consideration of quantum and relativistic properties of the electrons in the beam. This provided new insights into the interaction between the electrons' spin and the vortex property of the beam. In particular, the researchers found that this so-called spin-orbit interaction results in a different behavior for vortex beams made of electrons with spins pointing up or down, respectively—an effect that should be observable (Fig. 1).

Beyond providing these fundamental insights, the new theory also has sound practical implications, as the beams are very sensitive to magnetic fields, according to Nori. "The theoretical understanding that we have reached will eventually contribute to the development of enhanced electron microscopes that can image magnetic materials with atomic resolution," he says. ■

1. Bliokh, K.Y., Dennis, M.R. & Nori, F. Relativistic electron vortex beams: angular momentum and spin-orbit interaction. *Physical Review Letters* **107**, 174802 (2011).
2. Uchida, M. & Tonomura, A. Generation of electron beams carrying orbital angular momentum. *Nature* **464**, 737–739 (2010).

When particles collide

Development of a theoretical framework for interpreting the results of subatomic-particle collisions could provide insight into proton composition

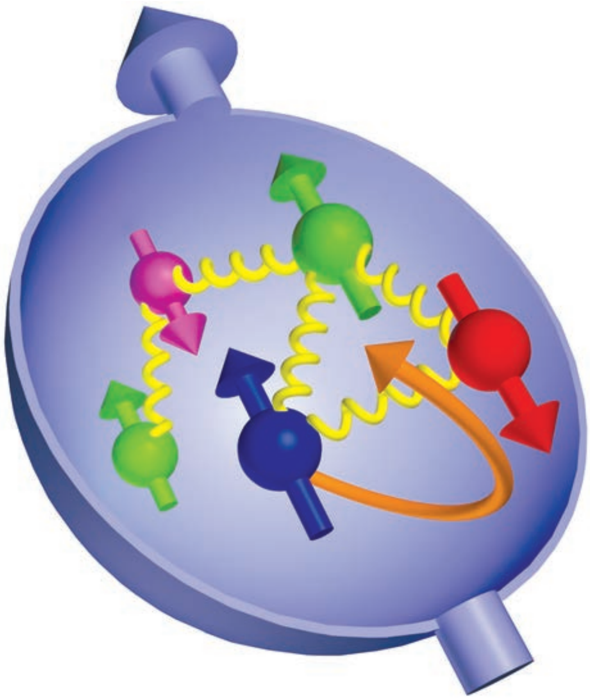


Figure 1: A proton (large, purple sphere) is made up of quarks (colored spheres) held together by gluons (yellow spirals). The arrows represent the axes about which the particles are spinning.

Accelerating subatomic particles to almost the speed of light and then crashing them together reveals much about the nature of the matter. Nuclear physicists need to fully understand these complex collisions if they are to make sense of the large volume of experimental data the world's particle accelerators generate every year. RIKEN scientists Zhong-Bo Kang and Feng Yuan, and their colleague Bo-Wen Xiao from Pennsylvania State University, USA, have presented a new theoretical framework that should accurately model one important type of interaction in particular: proton collisions[1].

The protons and neutrons at the heart of every atom are made up of fundamental entities known as quarks and antiquarks that are held together by a strong nuclear force mediated by so-called gluons (Fig. 1). "One of the most important goals in nuclear physics is to explore the structure of the protons and neutrons in terms of their internal constituent partons—the collective name for quarks and gluons," explains Kang from the RIKEN BNL Research Center, USA.

When physicists smash two high-energy beams of protons together, they decay to create new particles that shoot off in all directions. Measuring how the momentum of colliding particles is distributed among the collision remnants is a crucial tool for investigating the distribution of the quarks within a proton.

The latest theoretical framework, a development led by Yuan from the RIKEN BNL Research Center, considers collisions in which the protons in one beam are spin polarized; that is, the axis about which each proton rotates is perpendicular to the beam's propagation direction. The outcome of the collision is dependent on the direction of spin—a phenomenon known as single-spin asymmetry. "In the past few decades, we have learnt a lot about the 'longitudinal' motion of partons in the proton. But we don't know much about their 'transverse' motion," explains Kang. "It turns out that single-spin asymmetry is a sensitive and direct probe of the partons' transverse motion."

Previous numerical predictions of single-spin asymmetries have only gone as far as first order calculations. Yuan, Kang and colleagues work extends the model to the next level, providing more reliable predictions. "We have developed a theoretical formalism such that we can precisely extract information about the transverse motion of the partons from the experimental data," says Kang. "Knowing about both the longitudinal and the transverse motion of partons will enable us to construct three-dimensional images of a proton for the first time." ■

1. Kang, Z.-B., Xiao, B.-W. & Yuan, F. QCD resummation for single spin asymmetries. *Physical Review Letters* **107**, 152002 (2011).

What lies beneath: mapping hidden nanostructures

A new method to map nanostructures within materials may lead to biological imaging of the internal organization of cells

The ability to diagnose and predict the properties of materials is vital, particularly in the expanding field of nanotechnology. Electron and atom-probe microscopy can categorize atoms in thin sheets of material, and in small areas of thicker samples, but it has proven far more difficult to map the constituents of nanostructures inside large, thick objects. X-rays—the most common imaging tool for hard biological materials such as bones—have a limited focal-spot size, so they cannot focus on nanoscale objects.

Now, Yukio Takahashi and colleagues at Osaka University, together with researchers at Nagoya University and the RIKEN SPring-8 Center in Harima, have succeeded for the first time in producing two-dimensional images of nanostructures encased in thick materials on a large scale[1]. Their work was possible because they designed a new x-ray diffraction microscopy system that does not require a lens.

"The main challenges in this work were to realize x-ray diffraction microscopy with a high resolution and a large field of view, then extend it to element-specific imaging," Takahashi explains. "We achieved this by establishing a scanning x-ray diffraction imaging technique called x-ray ptychography."

Ptychography involves taking images of an object that overlap with one another on a series of coinciding lattice points. The researchers combined this technique with x-rays, and included a system to compensate for the drifting of optics during imaging. Takahashi and his colleagues focused the x-rays using so-called 'Kirkpatrick–Baez mirrors' that allowed them to collect high-quality diffraction data.

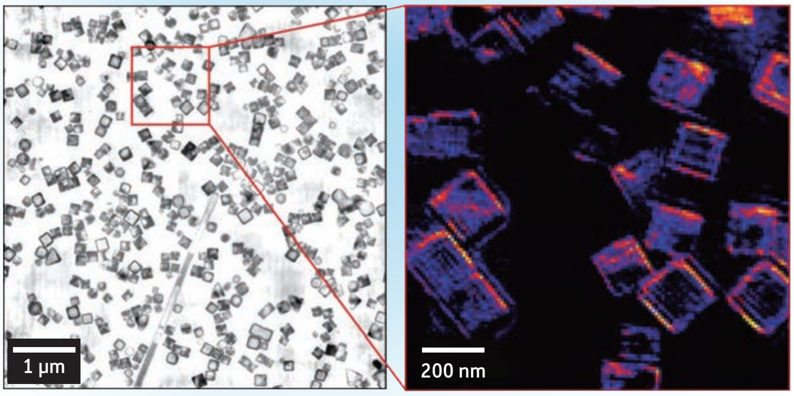


Figure 1: Images of gold/silver nanoparticles, acquired using a combined method of x-ray ptychography and anomalous x-ray diffraction.

Their system monitors the changes in the diffraction of x-rays at two different energies. The degree of phase difference between the two x-ray energies changes significantly at the absorption edge of the target element. This is related to the atomic number of the element, meaning that the elements present in the material can be identified. To verify that their system works, the researchers deposited gold/silver nanoparticles around 200 nanometers in size on a silicon nitride membrane, and produced high-resolution and large-scale images of the particles. The resolutions were better than 10 nanometers (Fig. 1).

"One of the practical applications of this technique in future is the possible observation of cells," explains Takahashi. "The shape of a whole cell and the spatial distribution of its organelles could be three-dimensionally visualized at 10 nanometer resolution—to provide key insights into the organization inside cells. We hope to see this technique being used in biological and materials science in future." ■

1. Takahashi, Y., Suzuki, A., Zettsu, N., Kohmura, Y., Yamauchi, K. & Ishikawa, T. Multiscale element mapping of buried structures by ptychographic x-ray diffraction microscopy using anomalous scattering. *Applied Physics Letters* **99**, 131905 (2011).

Cells on film

Development of polymer film loaded with antibodies that can capture tumor cells shows promise as a diagnostic tool

Cancer cells that break free from a tumor and circulate through the bloodstream spread cancer to other parts of the body. But this process, called metastasis, is extremely difficult to monitor because the circulating tumor cells (CTCs) can account for as few as one in every billion blood cells.

Research led by scientists at the RIKEN Advanced Science Institute in Wako, in collaboration with colleagues at the University of California, Los Angeles, and the Institute of Chemistry at the Chinese Academy of Sciences, Beijing, has produced a polymer film that can capture specific CTCs[1]. With further development, the system could help doctors to diagnose an advancing cancer and assess the effectiveness of treatments.

The researchers used a small electrical voltage to help deposit a conducting polymer film of poly(3,4-ethylenedioxythiophene) (PEDOT) bearing carboxylic acid groups on to a 2-centimeter-square glass base (Fig. 1). The polymer formed nanodots, tiny bumps that measure 100 to 300 nanometers across, depending on the voltage used (1–1.4 V).

Adding a chemical linker to the film allowed it to bind a protein called streptavidin; this protein then joined to an antibody. In turn, the antibody could latch on to an antigen called epithelial cell adhesion molecule (EpCAM), which is produced by most tumor cells. In this way, the film could grab tumor cells from just a few milliliters of a blood sample.

The team tested several types of tumor cells on films with various sizes and densities of nanodots, and used a microscope to observe how well they captured the cells. The most effective film, with nanodots measuring about 230 nanometers across and containing about 8 dots per square micrometer, captured roughly 240 breast-cancer cells per square millimeter of film. In contrast, it caught fewer than 30 cervical cancer cells that do not express EpCAM, proving that the antibody used on the film is highly selective. A smooth PEDOT-carboxylic acid film with the same antibody captured only 50 or so breast cancer cells.

The film's efficiency depends on the size and spacing of the nanodots, and the presence of the capturing antibody. Since these can be easily modified, the same method could be used to make films that sense other types of cells.

The next step is to "further optimize the nanostructures of the conducting polymers and understand in more detail the cell-capturing mechanism," says RIKEN unit leader Hsiao-hua Yu. "We are also currently working on a direct electrical readout of the captured cells, without needing to use a microscope." ■

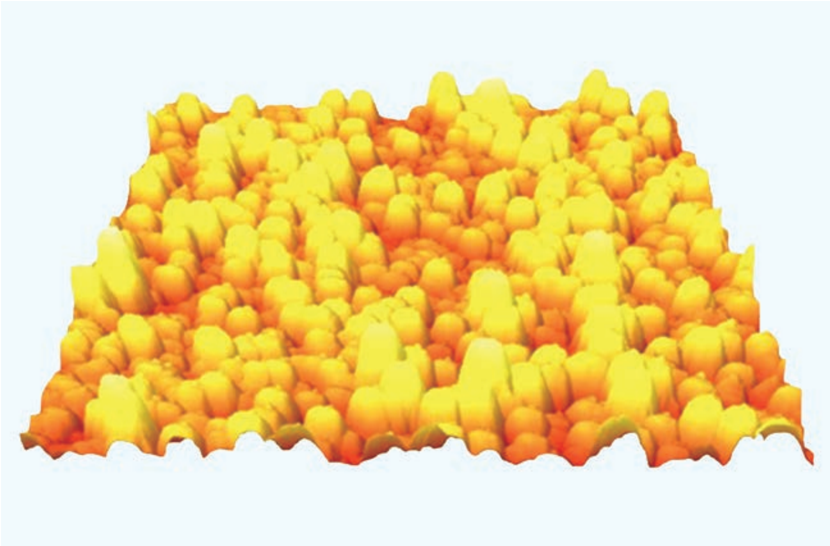


Figure 1: The polymer film forms nanodots: tiny bumps that can be functionalized with antibodies to grab passing cancer cells.

1. Sekine, J., Luo, S.-C., Wang, S., Zhu, B., Tseng, H.-R. & Yu, H.-H. Functionalized conducting polymer nanodots for enhanced cell capturing: the synergistic effect of capture agents and nanostructures. *Advanced Materials* **23**, 4788–4792 (2011).

Unpicking HIV's invisibility cloak

Revelation of how certain compounds adhere so strongly to HIV's coat points to a fresh therapeutic approach

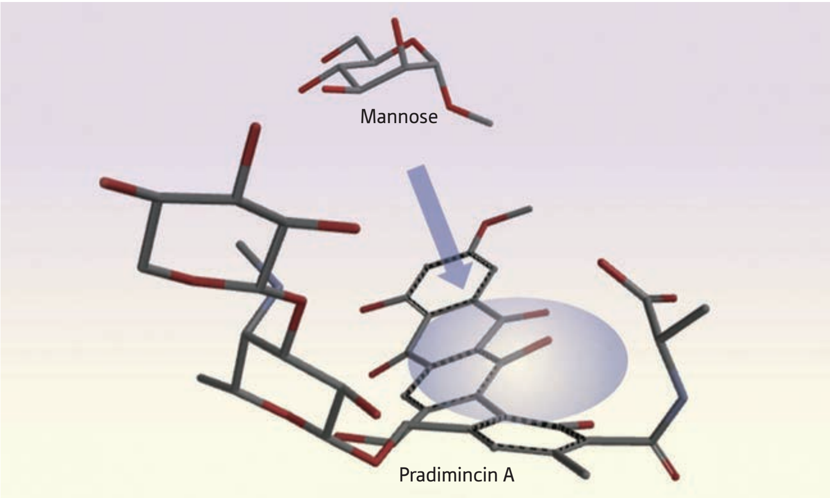


Figure 1: The compound pradimicin A disrupts the human immunodeficiency virus (HIV) by clinging to its mannose-rich coat. The mannose sits within a cavity in the pradimicin A structure (purple shading).

Drug researchers hunting for alternative ways to treat human immunodeficiency virus (HIV) infections may soon have a novel target—its camouflage coat. HIV hides inside a cloak unusually rich in a sugar called mannose, which it uses to slip past the immune system before infecting its host's cells. Recently, however, biochemists discovered a family of chemical compounds that stick strongly to mannose. Understanding how this mechanism works could reveal a way to make drugs adhere to and kill HIV. Yu Nakagawa and Yukishige Ito at the RIKEN Advanced Science Institute in Wako and their colleagues from several research institutes in Japan are leading the effort: they have mapped the binding site of the mannose-binding compound pradimicin A[1].

Mannose-binding compounds are particularly attractive to drug researchers thanks to their double-action anti-HIV effect. By sticking to mannose in the virus's coat, pradimicin A first freezes HIV's molecular machinery for entering and infecting its host's healthy cells. The virus responds by reducing the mannose in its coat thereby revealing itself to the immune system, which can then attack.

Unraveling just how pradimicin A recognizes mannose, however, has proven surprisingly difficult. In solution, the two components stick together in variously sized small clusters, confounding conventional analytical techniques such as solution-based nuclear magnetic resonance (NMR) and x-ray crystallography. Nakagawa, Ito and their colleagues side-stepped the clumping problem by using solid-state NMR, which allowed them analyze the compounds as solids, rather than in solution.

The research team's approach involved inserting carbon-13, a chemical label, into particular parts of the pradimicin A structure. Carbon-13 boosts the NMR signal wherever it is inserted, so the team could 'walk' around the compound and detect where it interacts most strongly with mannose.

The results revealed that pradimicin A curls up to form a cavity, within which the mannose structure sits (Fig. 1). "Our study highlights the benefit of solid-state NMR methodology to investigate this interaction," says Nakagawa. "Solid-state NMR is, at present, the only technique to analyze such a complicated system." Flagging the potential utility of the technique, Nakagawa adds that: "Our analytical strategy might be applicable to other systems that similarly suffer from aggregation in solution."

Meanwhile, solid-state NMR can offer even more in probing mannose–pradimicin A binding, Nakagawa says. Having determined how and where pradimicin A grabs mannose, the team's next step will be to use the technique to identify the specific molecular interactions that bind the pradmicin A to this potential Achilles' heel of HIV. ■

1. Nakagawa, Y., Doi, T., Masuda, Y., Takegoshi, K., Igarashi, Y. & Ito, Y. Mapping of the primary mannose binding site of pradimicin A. *Journal of the American Chemical Society* **133**, 17485–17493 (2011).

Bird brains follow the beat

By training birds to 'get rhythm', scientists uncover evidence that our capacity to move in time with music may be connected with our ability to learn speech

Even though typical dance-floor activity might suggest otherwise, humans generally demonstrate a remarkable capacity to synchronize their body movements in response to auditory stimuli. But is this ability to move in time to musical rhythm a uniquely human trait?

Some animals are capable of vocal learning, changing the sounds they make in response to those they hear from other members of their species. Scientists have hypothesized that such behavior may be associated with the capacity for so-called 'rhythmic synchronization'. "Motor control of vocal organs is naturally important in vocal learning," says Yoshimasa Seki of the RIKEN Brain Science Institute in Wako. "Once auditory–motor coordination in the vocal control system has been established, a similar auditory–motor transformation system for other body parts might be derived from that."

Studies in vocal-learning species have largely focused on case studies of individual animals, but Seki and colleagues conducted larger-scale experiments and found that budgerigars (Fig. 1) may have an inherent capacity for rhythmic synchronization[1]. The researchers tested their hypothesis by training eight budgerigars to peck a button in response to the rhythm of an external metronome, which could be adjusted to present the birds with audio–visual stimuli at varying intervals.

In all 46 experiments, the birds were able to consistently respond to rhythmic beats within a certain time-frame, demonstrating successful entrainment. However, the accuracy of their timing was dependent on the tempo. Only one out of seven birds was successfully able to match the onset of each beat when the stimuli were generated at 450 millisecond intervals, while all animals achieved this feat when that interval was lengthened to 1,500 or 1,800 milliseconds.

Figure 1: The budgerigar, *Melopsittacus undulates*, is one of several vocal-learning species of parrot, well known for its capacity to mimic human language.

To confirm that actual synchronization was taking place, the researchers used computer simulations of other bird behavior scenarios, such as random pecking or responding directly to individual stimuli rather than the rhythm itself. However, none of these alternative models was sufficient to explain the observed activity. "Our results showed that budgerigars can show rhythmic movements synchronized with external stimuli, which means they potentially have this capability of auditory–motor entrainment as a species," says Seki.

As such, this species may offer a useful model for future investigations of the neurological mechanisms that potentially connect vocal learning with rhythmic synchronization in both birds and humans. "Such studies should contribute to discussions of specific characteristics of the human speech system and its similarity to the vocal learning systems found in other animal species," explains Seki. ■

1. Hasegawa, A., Okanoya, K., Hasegawa, T. & Seki, Y. Rhythmic synchronization tapping to an audio–visual metronome in budgerigars. *Scientific Reports* **1**, 120 (2011).

Plant enzymes reveal complex secrets

Biologists are uncovering intricate pathways underlying the chemical modification of a functionally important class of plant molecules

The enzymes needed for producing and chemically modifying functionally important plant molecules called anthocyanins have been identified by a research team led by Kazuki Saito of the RIKEN Plant Science Center, Yokohama[1].

Anthocyanins belong to a class of organic compounds called flavonoids, which are naturally produced by plants. Defined as secondary metabolites, which have various functions, they are not required directly for development, growth or reproduction. As pigments, they produce some of the colors that flowers need to attract insect pollinators. Others protect against damaging ultraviolet light or defend against plant diseases. The flavonoids secreted from the roots of legumes, such as peas, facilitate interactions with soil microbes that are ultimately beneficial for plant growth. Many of the flavonoids ingested by humans promote good health, or even protect against cancer.

"The biosynthetic pathways that give rise to flavonoids are complex, involving multiple enzymes," says Saito. "These enzymes are encoded by multi-gene families, making it difficult to elucidate their precise physiological functions."

Saito's team set out to identify genes involved in flavonoid biosynthesis in *Arabidopsis thaliana*, a species often used as an experimental model in plant genetics (Fig. 1). The availability of the complete genome sequence of *Arabidopsis* has allowed the development of 'omics'-based databases and bio-resources. "Just as the genome contains information about all of the plant's genes, the proteome and transcriptome contain information about protein and gene expression, respectively, whereas the metabolome signifies metabolites, including secondary metabolites such as flavonoids," explains Saito.

Figure 1: A wild-type *Arabidopsis thaliana* (thale cress) plant (left) and a mutant plant accumulating anthocyanins (right).

Taking advantage of this information, and using sophisticated genetic and analytical techniques, Saito and colleagues found that the genes *UGT79B1* and *UGT84A2*, which encode enzymes called UDP-dependent glycosyltransferases (UGTs), clustered with other genes involved in producing anthocyanins. When they deleted the *UGT79B1* gene in *Arabidopsis* plants, they found it drastically reduced anthocyanin production. Further experiments, using genetically engineered UGT79B1, allowed them to uncover the precise biochemical function of the UGT79B1 enzyme, including its substrate specificity.

The *UGT84A2* gene was already known to encode an enzyme that attaches glucose to a molecule called sinapic acid—a building block of anthocyanin sinapoylation, which is a chemically modified type of the anthocyanin molecule. Saito and colleagues experiments revealed that the level of sinapoylated anthocyanin was greatly reduced in mutants lacking the *UGT84A2* gene.

The researchers were also able to study the evolutionary relationships of the UGT enzymes in various plant species. "Our work provides a 'roadmap' for anthocyanin modification routes in *Arabidopsis* and other plants," says Saito. ■

1. Yonekura-Sakakibara, K., Fukushima, A., Nakabayashi, R., Hanada, K., Matsuda, F., Sugawara, S., Inoue, E., Kuromori, T., Ito, T., Shinozaki, K., *et al*. Two glycosyltransferases involved in anthocyanin modification delineated by transcriptome independent component analysis in *Arabidopsis thaliana*. *The Plant Journal* **69**, 154–167 (2012).

Finding a tumor suppressor's groove

By piecing together the interactions between a pair of proteins involved in colorectal cancer, researchers may have identified suitable targets for drug development

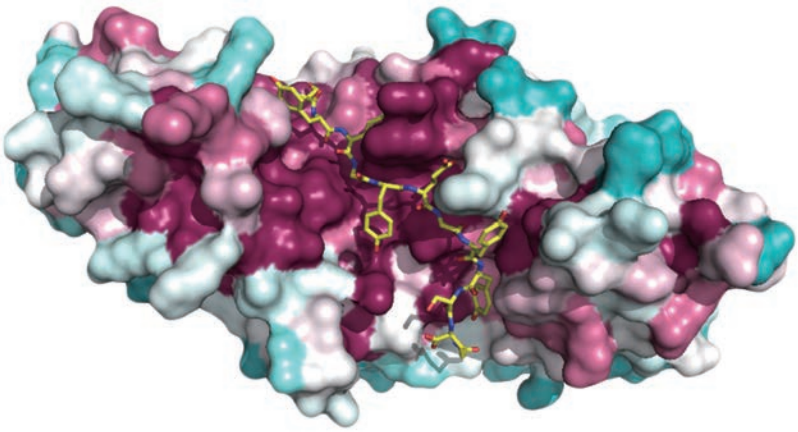


Figure 1: Crystal structure of the complex of the Arm domain of APC and Sam68. The groove on the Arm domain of APC contains highly conserved residues (magenta) that form numerous specific interactions with Sam68 residues (yellow).

The tumor suppressor protein called adenomatous polyposis coli (APC) is a central genetic risk factor for colorectal cancer. In fact, mutations that potentially alter the structure or function of this protein are found in an estimated 85% of human colorectal tumors, which are currently the third highest-ranked cause of cancer-related death worldwide.

Unfortunately, APC is a very large protein with numerous interacting partners, making it a challenge to determine the direct impact of a given mutation. "The mechanisms by which these mutations lead to cancer is still poorly understood," says Shigeyuki Yokoyama, Director of the RIKEN Systems and Structural Biology Center in Yokohama.

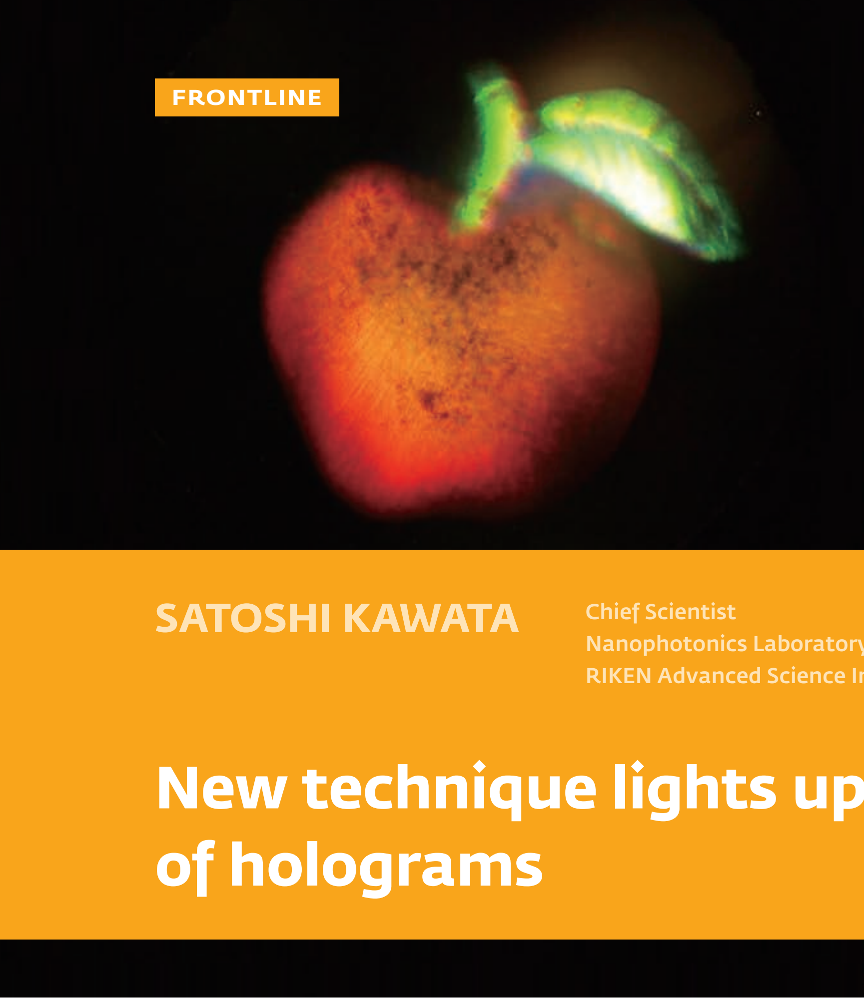
Structural analysis offers helpful insights into protein function, but obtaining these data can be difficult with such massive target proteins. Yokoyama and colleagues therefore decided to focus on one particular segment of APC, known as the armadillo repeat (Arm) domain[1]. In particular, they were interested in understanding how Arm interacts with and inhibits Sam68, an APC-binding protein that is believed to contribute to the activation of genes involved with tumorigenesis.

The researchers determined that the Arm domain forms a helical structure, with an L-shaped groove for the recognition of binding partners. The Arm-interacting domain of Sam68, on the other hand, appears to be relatively disorganized until it binds this groove, an association stabilized by a number of interactions between specific amino acids on the two proteins (Fig. 1). Yokoyama and colleagues were subsequently able to confirm the contributions of these residues by systematically introducing mutations and determining their impact on these proteins' affinity for each other.

With this information in hand, the researchers assessed the potential significance of real-life mutations at these points of interaction. "We were able to map cancer-related APC mutations within this domain and analyze their effects on the structure of APC and on the binding of proteins to APC," says Yokoyama. Indeed, some of the amino acid changes introduced by these mutations appeared to be directly detrimental to complex formation between APC and Sam68.

Arm interacts with several other important proteins, and Yokoyama's group plans to perform equally in-depth analyses to characterize the structural bases for these associations. However, he notes that the present findings—in conjunction with data obtained by co-author Tetsu Akiyama at the University of Tokyo—may already offer direct clinical utility. "We think that targeted disruption of the interaction between mutated APCs and Sam68 might be a good strategy to prevent the development of cancer," says Yokoyama. ■

1. Morishita, E.C., Murayama, K., Kato-Murayama, M., Ishizuka-Katsura, Y., Tomabechi, Y., Hayashi, T., Terada, T., Handa, N., Shirouzu, M., Akiyama, T. & Yokoyama, S. Crystal structures of the armadillo repeat domain of adenomatous polyposis coli and its complex with the tyrosine-rich domain of Sam68. *Structure* **19**, 1496–1508 (2011).



FRONTLINE

SATOSHI KAWATA

Chief Scientist
Nanophotonics Laboratory
RIKEN Advanced Science Institute

New technique lights up the creation of holograms

A red apple with green leaves—it seems real enough to pick up in one's hand, but there is nothing there to actually touch. This is because the apple is a hologram, a three-dimensional image projected by light (Fig. 1). In April 2011, Chief Scientist Satoshi Kawata of RIKEN, the head of the Nanophotonics Laboratory at the Advanced Science Institute in Wako, along with his colleague Miyu Ozaki, a visiting scientist of RIKEN, succeeded in developing a novel holography principle distinct from conventional methods which makes it possible to reconstruct a full-color three-dimensional object. The key to their success resided in superposing a thin silver film on which surface plasmons—collective oscillations of free electrons within a metal—were excited. In recent years, research on surface plasmons has rapidly expanded against a background of remarkable advances in nanotechnology, helping establish the subject as a field of engineering. In addition to holograms, Kawata has also undertaken groundbreaking research on surface plasmon applications in metallic nano-lens technology.

Full-color holograms

Seven years ago during an interview with *RIKEN News* in February 2005, Kawata mentioned, "I want to do two things at RIKEN, one of which is to pioneer the new discipline of plasmonics." Since then, he has authored several landmark publications in plasmonics, including one article which he coauthored with Miyu Ozaki, titled "Surface-Plasmon Holography with White-Light Illumination," which appeared in *Science* (April 2011).

"In recent years, three-dimensional (3D) movies and television sets capable of 3D imaging have been gaining popularity, but the images of the objects we see are for the most part nothing more than pairs of planar images recognized as 3D objects by the brain due to the effect of lateral parallax," Ozaki explains. "Meanwhile, holography has long been available as a classical technique for presenting 3D images. You may have seen a red or blue stereoscopic image floating in the air at an amusement park or science museum. However, it is difficult to create colored holograms because of the principle behind the technique. We have now succeeded in developing full-color holography using a new method. The red apple with green leaves shown in Fig. 1 is one example," says Ozaki. Surface plasmons have enabled Kawata and Ozaki to produce holograms that are distinct from conventional ones.

A hologram is like a photograph that records the light waves scattered from an object, and reconstructs the object in three dimensions when the object is not actually present (Fig. 1). The image that we can see is the result of captured light that has collided with and been scattered by the object. "For recording, a laser beam is used, and is divided into two identical beams. The illumination beam lights up the object, and light reflected by the object is applied to a light-sensitive material, such as photo film.

At the same time, another light source called a reference beam is superposed onto the photo-sensitive material," explains Kawata. "The two beams interfere with each other and produce a pattern of dark and bright bands. This interference fringe contains information from the light scattered by the object, including information about the shape of the object, which is then recorded onto the photo-sensitive material or hologram. To reconstruct the object in three dimensions, ordinary light illuminates the pre-recorded hologram. The illumination is diffracted by the interference fringe pre-recorded in the hologram to regenerate the light wave scattered by the object during the recording. When we see the hologram under illumination, it looks as if the object is actually present."

To obtain an exhaustive interference fringe, a laser that produces light waves with uniform crest-to-crest and trough-to-trough patterns must be used as the reference beam. The color of the diffracted light is influenced by the laser beam used, so the image reconstructed through a conventional hologram is the same color as the laser used. This is why most holograms are monochromatic. "Our newly-developed system employs laser beams for recording the hologram, but does not use any laser beams for the illumination beam that is required for image reconstruction. Instead, we use a beam of white light, which comprises a blend of many different wavelengths. Since the three primary colors of light—red, green and blue (RGB)—can be extracted from white light, stereoscopic images are reconstructed from holograms in the respective colors, and the three stereo images are superposed to obtain a combined full-color image," Kawata says.

Ozaki graduated from the Faculty of Engineering at Tokyo Denki University in 2002. He obtained his PhD in 2009 from the same university, where he is now assistant professor in Mechanical Engineering.

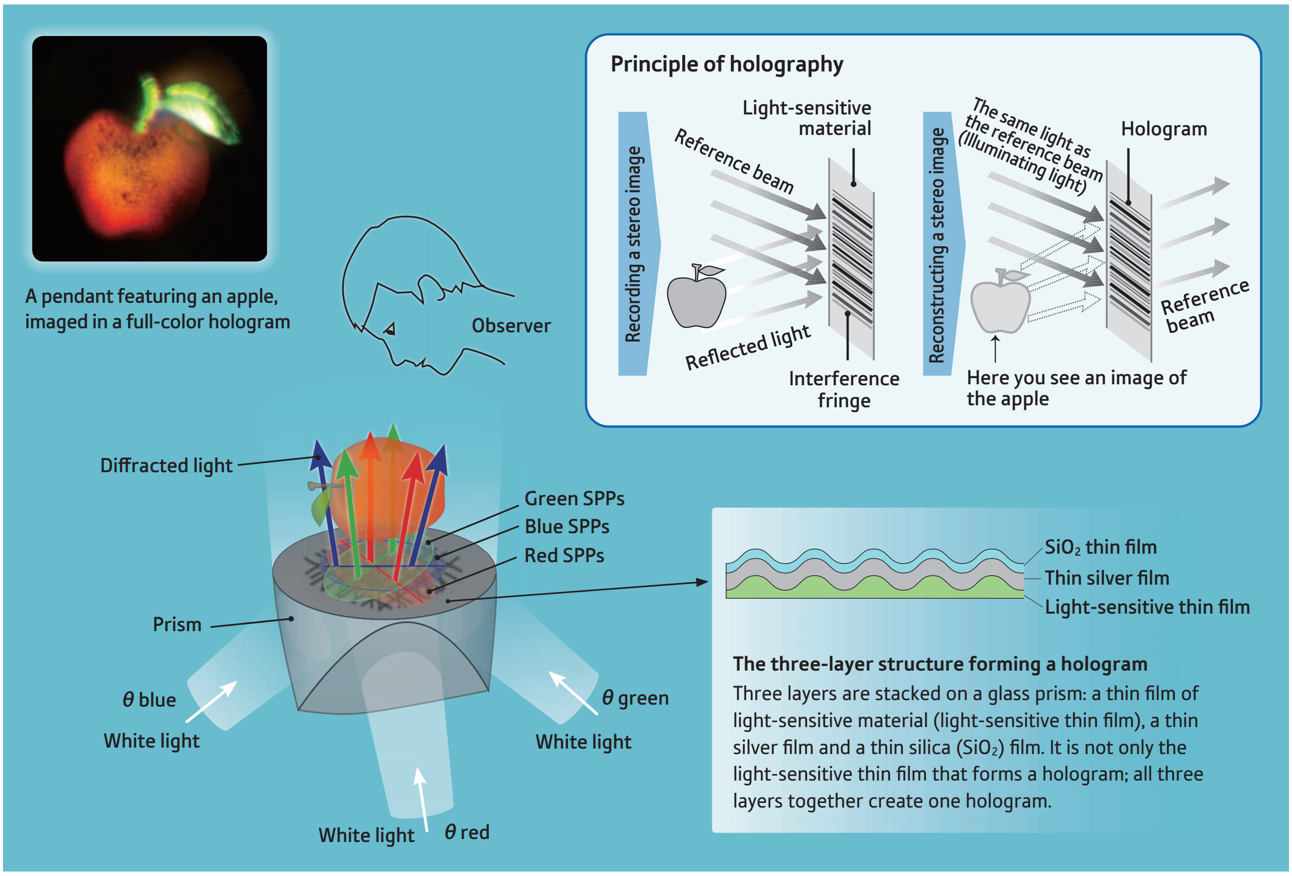


Figure 1: The mechanism of full-color holography

The major difference between the researchers' technique and ordinary holography is the use of a prism to adjust the light beam's angle of incidence in combination with a thin silver film to produce the surface plasmons. When the angle of incidence is controlled appropriately, the silver film is excited to produce surface plasmons, which in turn cause the white light to reach the hologram in the three primary colors of red, green and blue, producing a floating full-color stereoscopic image. Although only still images can be obtained at present, Kawata is planning to improve the current system to enable movie imaging based on the same principle in the future.

Extracting the three primary colors from white light using surface plasmon resonance

"The key to successfully extracting RGB separately from white light resides in superposing a thin silver film onto light-sensitive material. In doing so, surface plasmon polaritons (SPPs) are excited on the thin film," says Ozaki.

A metal contains a great number of free electrons that are oscillating together while simultaneously interacting with each other. The quantum of this collective oscillation of free electrons in a metal is called a plasmon. A plasmon is always accompanied by a photon or electromagnetic field. On metal surfaces, plasmons and photons propagate along the surface, and this combination is called surface plasmon polariton (SPP). Figure 2 illustrates how SPP works.

When a beam of monochromatic light at a particular wavelength is applied to a thin metal film through a prism, it is totally reflected at angles of incidence between the critical angle (ϑ c) and 90 degrees. At the same time, dim light exists close to the boundary face. The resulting evanescent waves excite SPPs along the surface of the thin metal film. Usually, an SPP is not excited by the light incident on the metal film, except only at an angle for resonating SPPs. At a resonant angle, the energy of the incidental light transfers to the SPPs rather than to the reflected light. We use the evanescent light field associating with SPPs to illuminate a hologram.

Surface plasmon resonance is seen at given parameters of film thickness, material, incident angle of light, and wavelength of light. In the case of white light, which is a blend of many different wavelengths, the angle of incidence varies as a function of wavelength for RGB. "We make the best use of this mechanism. By changing the angle of incidence to a value that accommodates RGB, we can extract light beams in the three colors R, G and B separately from the same white light," Ozaki says.

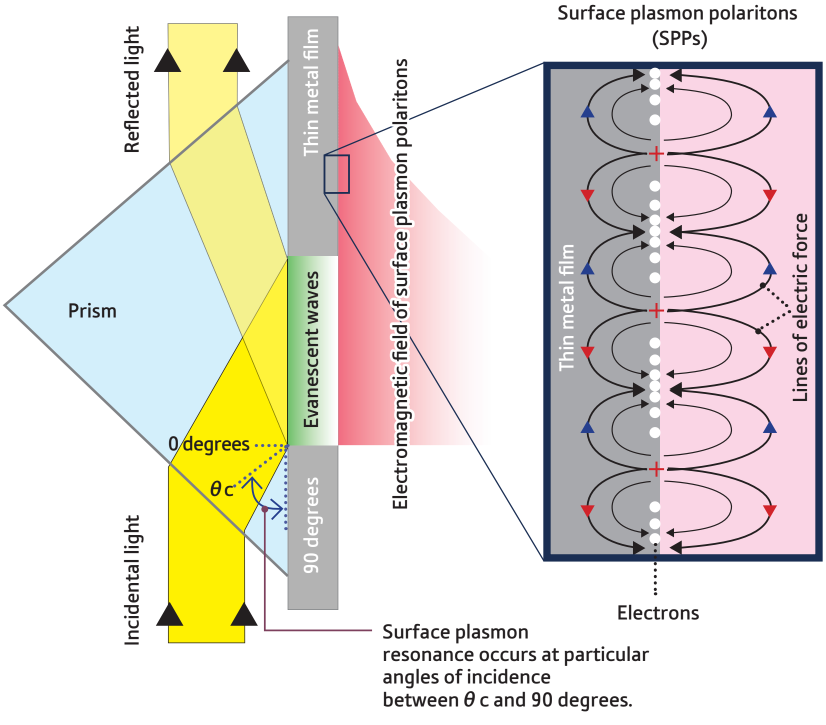


Figure 2: Principle of surface plasmon resonance

When a beam of monochromatic light is directed onto a thin metal film through a prism at angles of incidence between the critical angle θ c and 90 degrees, it is totally reflected. In this process, a form of light known as evanescent waves is produced, and these in turn excite the surface of the thin metal film to produce surface plasmon polaritons (SPPs). At particular angles of incidence between θ c and 90 degrees, the wavelength of the evanescent waves along the boundary face and the wavelength of the SPPs coincide with each other, producing resonance. Most of the energy from the incidental light is transferred to the SPPs and intensified. The panel on the right shows an enlarged view of part of the thin metal film to explain the principle of SPPs. On metal surfaces with a nanoscale structure such as microparticles, thin lines or thin films, surface plasmons are produced as a result of the collective oscillation of electrons (white dots), meeting the boundary conditions. Also, electromagnetic field oscillation is induced near the surface in synchronization with the surface plasmons. The SPPs are quasiparticles resulting from coupling between surface plasmons and electromagnetic waves.

A powerful tool that will enhance communications technology

While the system diagram in Fig. 2 comprises only two components (a prism and a thin metal film), the hologram developed by Kawata and Ozaki (Fig. 1) has three layers. These layers comprise of a thin film of light-sensitive material, a thin silver film and a thin silica (SiO_2) film stacked on a glass prism with undulations that correspond with the interference fringes for the three colors R, G and B on all three layers. A hologram is therefore not produced by the light-sensitive thin film alone, but by all the three layers as a whole. The thin silver film, which serves to facilitate color separation, is 55 nm thick, and the undulations matching the interference fringes are about 25 nm high. The total thickness of the three layers is several hundred nanometers.

"The three angles of incidence of white light (ϑ red, ϑ green, ϑ blue) have been adjusted in advance to allow surface plasmon resonance to occur for each of the R, G and B colors," explains Ozaki. "A beam of white light applied in three directions, as shown in Fig. 1, excites the SPPs in each color, and the resulting electromagnetic fields are holographically diffracted to reconstruct a stereo image. Looking at it from above, the viewer can see a full-color stereo image." The hologram created in this experiment measured 38 mm in length and 26 mm in width, with the subject being a fingertip-sized pendant featuring the image of an apple.

"This achievement will find applications in three-dimensional display devices in the future," says Ozaki. "In the case of holograms generated using surface plasmons, white light alone serves as the incidental light, and beams can be applied from behind, so our system can be utilized in small devices such as smart phones."

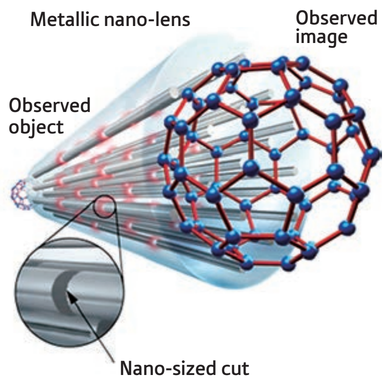


Figure 3: Conceptual diagram of metallic nano-lens

A metallic nano-lens improved to enable enlarged viewing and color representation. Major improvements include bundling extremely thin wires of silver into a fan formation, and cutting individual wires to a shorter size to form gaps between the wires. This device promises innovative applications in a broad range of fields, including medical care.

Ozaki notes that some problems remain to be solved before the system can be brought into practical use. "The system must be improved to allow larger objects to be imaged. In addition, the viewing angles for stereo images are now limited to about 25 degrees both vertically and laterally, so this range must be broadened. However, these engineering problems can be solved. Using our system, we also aim to create moving pictures. By using surface plasmons and holography in combination, numerous approaches are available, and we may later use a technical approach that is totally different from the technique we have just announced," says Ozaki.

Metallic nano-lenses

Prior to developing the full-color holography technique, in 2005 Kawata created a metallic nano-lens based on the principle of surface plasmons. The device is configured with bundles of nano-sized, thin metal wires and arranged in the form of a pin support. When an object is placed on top of the device, the light reflected by the object collides with the tips of the metal wires, producing surface plasmons. These plasmons carry information about the object and travel through the metal wires resulting in the reconstruction of an image on the opposite side. Due to the wires' thinness, greater detail about the object can be transmitted, which produces a higher resolution of the reconstructed image. Theoretically, images can be transmitted at a resolution of 1 nm. However, the device created by Kawata and colleagues was only able to produce fixed-size images, and the colors of transferable images were limited to discrete wavelengths.

Later in 2008, Kawata published a new idea for a metallic nano-lens capable of providing enlarged images of objects at a resolution of several nanometers in *Nature Photonics* (Fig. 3). The new device is currently under fabrication. "The features of bundling many metal wires and transferring surface plasmons through metal wires are the same as those I announced in 2005," says Kawata. Improvements include the capability of enlarging observed images to macroscopically visible sizes by arranging metal wires into a fan formation, and cutting the metal wires at some points to form nano-sized gaps. The gaps help to broaden the waveband, which can be covered. Information on the object is transferred through the wires as surface plasmons, and as light through the wire-to-wire gaps, and the plasmons are eventually released as light to image the object. In the case of gapless wires, the number of oscillations that permit surface plasmon resonance is subject to limitations, and the surface plasmons gradually lose oscillation energy. By providing gaps, the energy attenuation is prevented, and all wavelengths over the entire band of visible light are covered, so the object can be examined in full color. We have demonstrated this through theoretical calculations and computer simulations."

Because the principle predicts that metallic nano-lenses will also work in water, further advances would enable examination of living cells on the nanoscale, offering expectations of applications in bioengineering and nanolithography in the future. "Plasmonics has a wide range of applicable fields, and some researchers are working on developing medical applications. For example, a cancer therapy may be feasible in which microparticles of silver-coated silica are delivered to the affected part of the body, and a beam of near-infrared rays is applied there to attack the cancer cells with plasmons. Because effective near-infrared rays are available in sunlight, sunbathing could possibly serve as a treatment," says Kawata.

Watching single DNA bases using deep ultra-violet ray imaging

Kawata has been expanding his research area to encompass nanophotonics and plasmonics, and he is now focusing on deep ultra-violet ray plasmonics. "In the deep ultra-violet ray zone covering the wavelengths between 220 and 350 nm, gold and silver lose their metallic nature and no longer produce surface plasmons, while aluminum alone produces surface plasmons. If we realize deep ultra-violet ray imaging using an aluminum needle to narrow the surface plasmon resolution to 0.3 nm, we would be able to directly observe the base sequence of the DNA, which can be compared to the basic design of life. While many researchers study the terahertz band, which covers wavelengths of around 300 micrometers, I want to explore things that have not yet been explored by anyone else," says Kawata. ■

ABOUT THE RESEARCHER

Satoshi Kawata received his BSc and PhD in Applied Physics from Osaka University in 1974 and 1979 respectively. After working at the University of California, Irvine as a postdoctoral scientist, he joined Osaka University as a faculty member, where he is now professor in Applied Physics. In 2002 he joined RIKEN as a chief scientist and the head of the Nanophotonics Laboratory. Professor Kawata has received several prestigious awards, including the Purple Ribbon Medal of Honor from the Emperor of Japan, the Japan IBM Science Award, and the Leo Esaki Prize. The "8-micron bull," which was fabricated with Kawata's two-photon technology, was awarded in *The Guinness Book of Records* (2004 edition).

RIKEN PEOPLE

Yoko Endo
Chief
Welfare Section
General Affairs Division

Providing first-rate staff support and services

What do you do at RIKEN?

I work at the Wako Main Campus in Saitama in the Welfare Section. My work includes running child-care facilities at RIKEN, managing the accommodation for RIKEN researchers and overseeing our staff welfare organization, the RIKEN Mutual Benefit Society (RIKEN Kyosaikai).

What attracted you to RIKEN?

At graduate school I majored in plant physiology and metabolism and wrote my thesis on the metabolism of purine alkaloids, such as caffeine and theobromine, contained in tea and cacao plant leaves. I really enjoyed performing experiments and data analysis, as well as engaging in scientific discussion. I was drawn to RIKEN because of its stimulating environment and the broad array of research that is carried out here.

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

One of the most challenging and rewarding projects I have been involved in was the establishment of the RIKEN Mutual Benefit Society. This organization originally catered to a small section of our staff, but in October 2011 it underwent major expansion to cover all 3,500 employees with an increased remit to manage welfare, mutual aid and social activities. The new organization provides a full spectrum of services to our employees by providing guidance on a variety of matters, including wages and insurance; monetary benefits relating to childbirth, marriage, and bereavement; personal development; accommodation; as well as hosting social activities ranging from sports to cultural activities.

The transition was a year in the planning, and involved soliciting opinions and ideas from various groups and establishing a working party comprised of volunteers to devise plans and formulate policy. This information was then communicated to all RIKEN staff through a series of open forums, and staff members approved the changes by ballot. After this it took another six months of hard work by a 25-strong committee to put in place the appropriate management structures and personnel before the changes could be implemented.

I have also recently taken on a new challenge to rebuild the child-care facilities at RIKEN, which were first opened in 2004 with places for 30 children. However, demand for this service increased year-by-year, so the center expanded to cater for a total of 60 places. My own experiences of child-rearing have been extremely valuable in this project in working alongside architects and child-care professionals to create an environment in the new facility that benefits both the children and staff. Provision of child care is one excellent example in which RIKEN are actively facilitating a smooth return to work for parents following maternity and paternity leave, and the center is part of RIKEN's vision to provide a workplace that allows both men and women to realize their full career potential whilst promoting a healthy work-life balance. This kind of support is crucial to RIKEN's goal of attracting and retaining top-class staff from Japan and overseas. In addition to the facility at the Wako Campus, there are also child-care centers at the RIKEN campuses in Yokohama and Kobe.

What is the best thing about working at RIKEN?

I particularly like the fact that everyone, even junior staff, can contribute their ideas and opinions freely, and that these are considered and may be adopted. I also like being able to interact and work with a wide variety of different people. Working in this environment helps to broaden my horizons.

CONTACT INFORMATION

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Stem cell researchers convene in Tokyo for international symposium

The international symposium, "Neural Development: Stem Cell Perspective," was held on 17 and 18 January 2012 in Kitakan Hall at Keio University. Jointly organized by the RIKEN Brain Science Institute and the British Embassy Tokyo, the symposium was sponsored by the program, "Strategic Exploitation of Neuro-Genetics for Emergence of the Mind." This program is headed by Hideyuki Okano, a professor at Keio University School of Medicine and core researcher of the Funding Program for World-Leading Innovative R&D on Science and Technology (FIRST). Co-organized by Hideyuki Okano and Erika Sasaki (Central Institute for Experimental Animals), the symposium included lectures given by 15 distinguished researchers in neuroscience, stem cell biology, and developmental biology. The two main areas addressed were (1) pluripotent stem cells: embryonic stem cells and iPS cells and the production of genetically modified animals; and (2) neural stem cells: outer sub-ventricular zone progenitors contributing to the enlargement of the cerebral cortex. The lectures were followed by lively group discussions on these timely and important topics in biology, and FIRST researchers had the opportunity to discuss their research with the invited speakers and initiate new collaborations. The success of this symposium further advances the progress of FIRST as a leading program in cutting-edge research in Japan.

Top stem cell experts including Professor Hideyuki Okano (front row, fourth from left) convene at Keio University

RIKEN President visits Xi'an Jiaotong University in China

On 21 February 2012, RIKEN President Ryoji Noyori visited the Xi'an Jiaotong University (XJTU) in China to attend the opening ceremony for the RIKEN-XJTU Joint Research Center. RIKEN and XJTU have already been collaborating on joint research in the three areas of environmental fluids, ubiquitous intelligence systems, and biomaterials, and the Joint Research Center aims to further collaborative research between the two institutions.

In his speech at the ceremony, Noyori proclaimed, "As Japan's leading institution for comprehensive scientific research, RIKEN is eager to forge strong ties with the international scientific community, particularly in Asia." Noyori also called for the up-and-coming generations of Asia to take an active role in overcoming the challenges of the 21st century. Through this joint endeavor, RIKEN and XJTU will expand their collaboration to include other research areas that will enhance the globalization of both institutions.

RIKEN President Noyori answers questions from Xi'an Jiaotong University students in a lively exchange following his commemorative lecture.

In the afternoon, Noyori presented a commemorative lecture titled "Science and Technology for Future Generations". Over 400 XJTU students attended the lecture, which was followed by an engaging Q&A session. Noyori thoroughly enjoyed the exchange and tried hard to answer each and every query.

This year marks the 40th anniversary of the normalization of diplomatic relations between Japan and China. It is hoped that the RIKEN-XJTU Joint Research Center will serve as a bridge of cooperation and friendship between the two countries.

RIKEN exhibits at 2012 AAAS Annual Meeting

As one of the most widely recognized global science events, the Annual Meeting of the American Association for the Advancement of Science (AAAS) attracts thousands of the world's leading scientists and engineers every year. RIKEN has once again participated as an exhibitor at the event, and two prominent RIKEN researchers, representing the fields of plant science and nuclear physics, also gave presentations on their research. This year's meeting was held from 16–20 February at the Vancouver Convention Centre.

Based on this year's theme of 'Flattening the World: Building a Global Knowledge Society', over 180 exhibitors presented various approaches to tackle global problems such as climate change, and focused on issues including energy, agriculture, health, water, biodiversity and ecosystems, population growth, and economic development. RIKEN's booth at the 2012 AAAS meeting presented research on the broad themes of Health, Food and the Environment. Together, these three themes covered research ranging from care-giving robots for the elderly to DNA amplification technology for fighting global pandemics, new varieties of salt-resistant and high-yield rice produced using heavy-ion beams, and supercomputer-based global climate prediction.

RIBA-II, a care-giving robot developed by a RIKEN team in August 2011, attracted a great deal of interest from researchers, medical professionals, and members of the general public including families with children. *The Vancouver Sun*, one of Western Canada's largest daily newspapers, covered the story in their health section.

On the Family Science Days held on 18–19 February, RIKEN delegates demonstrated how to make a small paper spectroscope, to the delight of children who were fascinated by the 'rainbow' that appeared in the spectroscopes they had made.

In addition to the exhibit booth, Kazuo Shinozaki, Director of the RIKEN Plant Science Center, gave a talk on some of the latest research being conducted in the area of stress-inducible genes and applications to the development of drought tolerant plants. Nuclear physicist Pieter Doornenbal of the RIKEN Nishina Center for Accelerator-Based Science presented a perspective from Japan on the response to the Fukushima nuclear power plant accident.

RIKEN

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

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