

The background of the cover is a large, colorful, abstract image with a grainy, textured appearance. It features a spectrum of colors including blue, green, yellow, orange, and red, arranged in a roughly circular or semi-circular pattern. The colors transition from blue at the top and bottom edges to red in the center, with green and yellow in between. The overall effect is reminiscent of a microscopic view or a data visualization.

**RIKEN 2007-08**  
ANNUAL REPORT

# RIKEN Strives to be Indispensable to Society

By

Making significant advances in science and technology

Contributing to society and being worthy of its trust

Establishing a globally recognized brand image

Why do we pursue science? This is because humans instinctively seek to understand their environment. Knowledge is fundamental to culture, and technology based on scientific knowledge is the foundation of civilized society. In fact, progress in science and technology has pushed the average life expectancy in developed countries from 45 to 80 over the past century. Many people have access to a sufficient food supply, and the world's population has expanded to 6.6 billion despite the hardships some face to make a living. Freed from the need to carry out simple manual tasks, many people today enjoy considerable leisure time in their daily life, and advances in communication technology have made it possible to communicate directly with people on the other side of the earth, or even outside the earth. Modern civilization

has come this far. But it shouldn't run wild to such an extent that it threatens our culture, the foundation of our spirituality. Science and technology should not just satisfy the desire of the present generation, but should contribute more for the betterment of future society.

RIKEN seeks to make itself indispensable to the society of tomorrow. With the RIKEN Spirit—appreciation of nature and a legitimate view of society nurtured by our predecessors at RIKEN over the past 90 years—we intend to work with all our efforts to contribute to society in all its aspects and to meet its expectations.

This *RIKEN Annual Report* summarizes our research results for Fiscal Year 2007. We hope that it will give you an idea of our activities, and we earnestly wish for your ever increasing support for RIKEN.

NOYORI Ryoji (D.Eng.)  
President

March 2008



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# Profile of RIKEN

With a 90-year history of cutting-edge research in the natural sciences, RIKEN is the only fully comprehensive research institute in Japan. RIKEN conducts basic and applied research covering a diverse range of fields including physics, chemistry, engineering, biology, and medical science. Not only does RIKEN participate in research collaborations with universities and corporations and undertake commissioned research projects, it also actively disseminates its scientific and technological findings and facilitates the transfer of technology to industry.

## Mission

RIKEN's mission is to conduct research that extends the boundaries of science and technology. The aim is to produce internationally recognized results and maximize the social benefits of those results, making full use of RIKEN's unique research environment. This includes the pioneering of new research fields reflecting society's needs, and taking the initiative in undertaking research in particularly important areas.

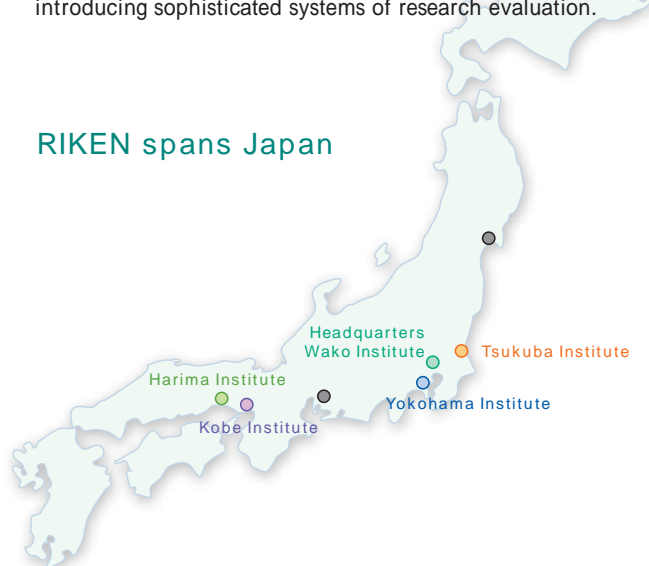
## History

RIKEN was established in Tokyo in 1917 as a private research foundation. After the Second World War, RIKEN was restructured as a private corporation named the Science Research Institute Ltd. (KAKEN), but in 1958, it became a semi-public corporation and was again called RIKEN. In 1967, RIKEN shifted its main headquarters out of Tokyo to its current location in Wako, Saitama. With the continued expansion of RIKEN's research activities, its research facilities are increasing in number and now, in addition to those located across Japan, RIKEN has established research centers in the United Kingdom and the United States. In October 2003, RIKEN underwent another administrative restructuring to become an Independent Administrative Institution (IAI).

## Expectations

RIKEN encourages active research by fostering a competitive environment and further developing its international character through the recruitment of researchers from various parts of the world. RIKEN is expected to maintain a process of constant self-improvement and to take the lead in renovating science and technology systems through collaboration with Japanese and foreign universities, research institutes, and corporations, as well as strengthening ties with local communities, taking active steps toward personnel mobility, actively recruiting young researchers, and introducing sophisticated systems of research evaluation.

## RIKEN spans Japan



## RIKEN's distinguished scientists



**Hantaro Nagaoka**  
Physicist

Nagaoka proposed the Saturnian theory, postulating a planetary model of the atom as a nucleus with orbiting electrons. He was also the architect of Japan's platform for physical sciences and the director of the RIKEN foundation's Physics Division.



**Kotaro Honda**  
Magnetic physicist

Honda pursued the study of metallurgy and magnetism, and raised the level of Japanese research in these fields to international standards with the invention of KS steel, a type of magnetic resistant steel, and an enhanced NKS steel.



**Umetaro Suzuki**  
Agricultural chemist

The founder of vitamin research in Japan, Suzuki successfully isolated vitamin B1 from rice bran, calling it oryzanin. Vitamin B1 proved effective in preventing and treating the vitamin deficiency disease beriberi, which was flourishing at the time. He was also instrumental in inventing and developing other products including "RIKEN Vitamins," which financed much of the RIKEN foundation's activities.

## Organizational structure of RIKEN in fiscal 2007

\*Reorganized in April 2008 (see page 84)

### Headquarters

Research Priority Committee Policy Planning Division Public Relations Office  
 General Affairs Division Personnel Division Finance Division Contract Management Division  
 Facilities and Utilities Division Safety Division Auditing and Compliance Office  
 Internal Communications and Systems Support Office  
 Center for Intellectual Property Strategies Advanced Center for Computing and Communication  
 Next-Generation Supercomputer R&D Center XFEL Project Head Office

### Wako Institute

DRI/FRS Promotion Division Brain Science Promotion Division  
 Discovery Research Institute Frontier Research System  
 Brain Science Institute Nishina Center for Accelerator-Based Science  
 Research and Development Program for Next-Generation Computational Research

### Tsukuba Institute

Tsukuba Research Promotion Division Tsukuba Safety Center  
 BioResource Center

### Harima Institute

Harima Research Promotion Division Harima Safety Center  
 RIKEN SPring-8 Center

### Yokohama Institute

Yokohama Research Promotion Division Yokohama Safety Center  
 Genomic Sciences Center Plant Science Center  
 SNP Research Center Research Center for Allergy and Immunology  
 Center of Research Network for Infectious Diseases

### Kobe Institute

Kobe Research Promotion Division Kobe Safety Center  
 Center for Developmental Biology  
 Molecular Imaging Research Program

Terahertz-Wave Research Program (Sendai)  
 Bio-Mimetic Control Research Center (Nagoya)



**Masatoshi Okochi**  
 Scientist and executive

While promoting original, atypical basic research, Okochi sought ways to nurture emerging research achievements into full-fledged industries, founding the RIKEN Industrial Group (RIKEN Konzern) in the process. He is credited with creating RIKEN's unique environment as a "scientist's paradise" during his term as the RIKEN foundation's third director.



**Yoshio Nishina**  
 Physicist

His Klein-Nishina formula, derived with Oskar Klein, opened the door to a new kind of physics, and his laboratory in RIKEN inspired many scientists with its emphasis on researcher interaction and collaboration. He was president of the Scientific Research Institute Ltd. (KAKEN) after the war.



**Shin-ichiro Tomonaga**  
 Theoretical physicist

Tomonaga's RIKEN career began when he joined Nishina's laboratory in 1932. He shared the Nobel Prize in Physics with Richard Feynman and Julian Schwinger in 1965 for his contribution to quantum electrodynamics theory.



**Hideki Yukawa**  
 Theoretical physicist

Yukawa also joined Nishina's laboratory in 1940 and later became a RIKEN Chief Scientist from 1961 to 1965, working on the properties of elementary particles. His prediction of meson particle existence earned him the Nobel Prize in 1949, making him the first Japanese national thus decorated.

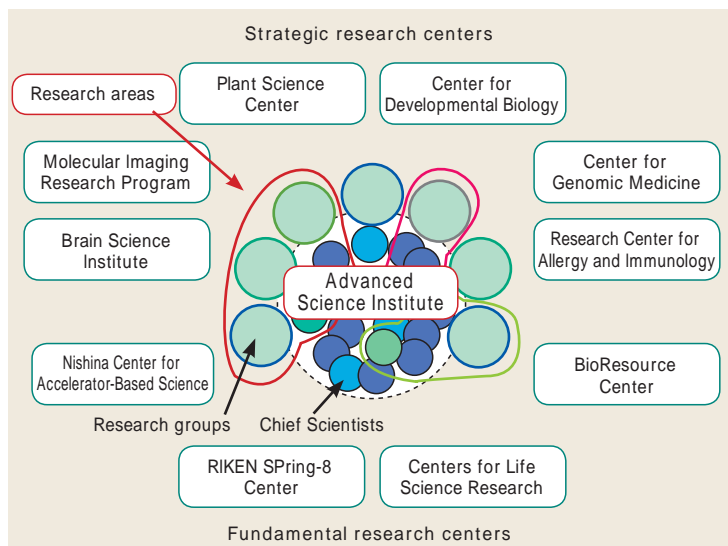
# Reorganization in Fiscal 2008

Wako Institute and Yokohama Institute will begin to take a step toward a new stage on April 1, 2008.

## Wako Institute

Discovery Research Institute (DRI) and Frontier Research System (FRS), at the Wako Institute, will merge into the Advanced Science Institute (ASI) on April 1, 2008. DRI has been making new research fields by conducting a wide range of basic research focused on freewheeling ideas. FRS has developed these research fields into advanced research areas.

ASI will aim to develop research projects, originating from its two forebears, into the world's top-class research schemes, by strategically operating these projects as integrated and time-limited plans in the boundary and multidisciplinary fields. ASI will also try to realize its potential as a dynamic research institute, with researchers from both within and outside Japan exchanging actively by stepping up cooperation with not only RIKEN's strategic research centers, but also other Japanese and foreign institutes.



### Raison d'être of the Advanced Science Institute

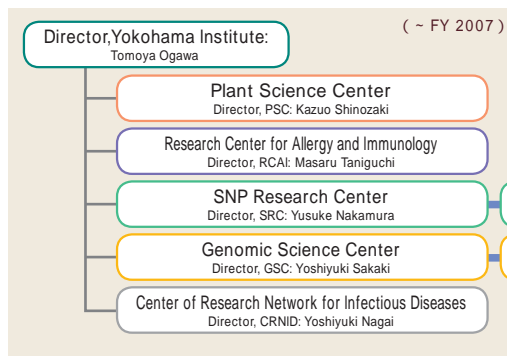
ASI will play the main role in creating new strategic and fundamental research centers, by strengthening its ability to develop new research areas through the fusion of various basic scientific researches. This research will be based on freewheeling ideas (DRI) and research projects aimed at developing new scientific technologies (FRS).

## Yokohama Institute

Genomic Sciences Center (GSC) will be reorganized and developed into three research departments. The purpose of this is to build a common foundation in Japanese life science research and effectively putting such a foundation to use; the reorganization will also apply research results achieved at the center over the past 10 years, since its establishment, and the characteristics of each research group at the center. Its mouse mutagenesis-related operations will be transferred to the Tsukuba Institute and the system biology-related

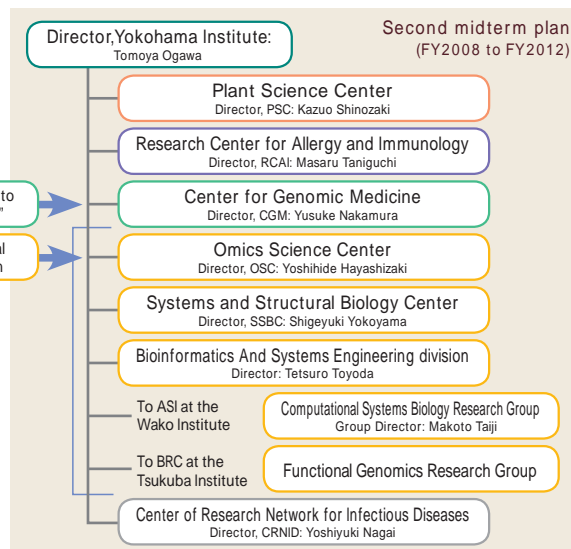
research to ASI, as part of the center's reorganization.

SNP Research Center (SRC) will be renamed Center for Genomic Medicine (CGM) to more accurately reflect SRC's emphasis on medical science and its activities thus far. A pharmacogenomics research group and international collaboration team will be set up at CGM to promote joint research with Japanese and foreign institutes, in order to establish Japan-originated personalized and preventative medicine.



### Chart of reorganization at Yokohama Institute

As a general Center for life science research, Yokohama Institute will contribute to the establishment of a safe and secure society. This will be achieved by using the results of fundamental research, which help us comprehensively understand life phenomena, and the results of a "baton zone" research in medical/welfare fields, such as drug development, personalized medicine, and food production.



Remarkable progresses in the development of  
“key technology of national importance”

“Key technology of national importance”  
... Research or technology that the entire nation must tackle intensively

# World's most advanced XFEL facility under construction

RIKEN is currently building an X-ray Free Electron Laser (XFEL) facility in Harima Science Garden City, near Osaka, jointly with the Japan Synchrotron Radiation Research Institute (JASRI). Lasers with wavelengths in the X-ray band can help researchers clarify the three-dimensional structure of even a single protein molecule. A joint project group of RIKEN and JASRI succeeded in making a prototype laser generate EUV (Extreme Ultra Violet) laser light in 2006, amid fierce competition with rival groups around the world. The group's XFEL facility is scheduled to start in 2010 generating 'dream light' X-ray lasers, which are expected to help develop entirely new scientific fields.

## Acquiring 'dream light'

Just as the invention of telescopes helped people understand the universe more deeply, microscopes have helped clarify the world of micro-scale substances that make up various materials. Clearly, scientific instruments for observing objects of various sizes are indispensable for making technological progress. Very soon, a new type of light source, XFEL, is expected to make a significant contribution to scientific technology by giving scientists the ability to instantaneously capture atomic-scale events.

X-rays, with their very short wavelengths, have more than 1,000 times more energy than visible light. With X-rays, we can see the internal structures of various objects. X-rays can also be used to differentiate atoms. The SPring-8 (Super Photon Ring 8Gev) synchrotron radiation facility next to the XFEL facility construction site is used for examining the structures and properties of materials at the atomic/molecular level using extremely bright X-rays.

Before X-ray examination at SPring-8, the objects to be observed must be crystallized to freeze the element positions of structures for long exposure of the light, because of the intensity of a coherent X-ray component picked up from various wavelengths is low. But the XFEL's light is intensive and its wave phases are aligned. Thus, Noritaka Kumagai,

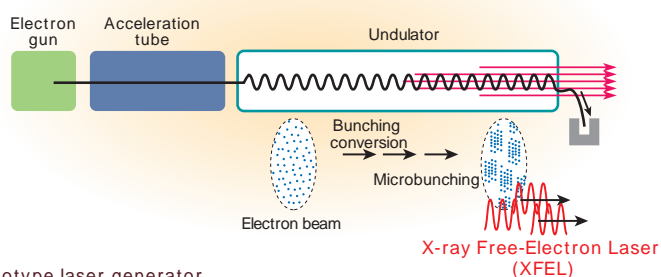
deputy director of the XFEL project, stresses that there is no need for crystallization of the objects, due to the coherence of XFEL X-rays.

Moreover, the XFEL will be 1 billion times brighter than the X-rays generated by SPring-8, so objects will be able to be observed for a short time, because of its peak intensity, and with much more precision, because of its coherency. Most membrane proteins, which are key *in vivo* substances, for instance, are hardly crystallized. With XFEL, it will be possible to observe the three-dimensional structure of even a single molecule of membrane protein in the *in vivo* environment. XFEL light will also help researchers observe objects for 100 femtoseconds (1 femtosecond = 1,000 trillionth of a second). This will make it possible to observe ongoing chemical reactions in cells or materials like watching a film frame by frame.

## Elaborate building of XFEL facility

XFEL is based on three key technologies: the 'monocrystal cerium boride (CeB<sub>6</sub>) thermionic electron gun,' the 'C-band accelerator' and the 'in-vacuum undulator.' Project members call these technologies the 'three sacred treasures,' after the three main Imperial regalia of the Japanese emperor.

## Principles of the X-ray Free Electron Laser



An electron beam is accelerated to near the speed of light, and passes through undulators, a series of permanent magnets with alternating polarity. These sinusoidally deflect the electrons' path with their magnetic fields, causing the interaction between the electrons and generated light. This light and the electron beam repeat their interaction in the undulator many times, generating a free electron laser.

Photo of the prototype laser generator



Thermoelectron gun



C-band acceleration tube



In-vacuum undulator



Aerial photo of the construction site

The XFEL facility (the area surrounded by red lines) is being built next to the SPring-8 Storage Ring (the circular facility). SPring-8, completed in 1997, is the world's premier synchrotron radiation facility, and is capable of generating extremely bright X-rays. SPring-8 has been used for research in a wide range of fields such as life science and materials science, in addition to a variety of applications to various industrial activities.

To stably emit laser light, the performance of the electron gun must be high. Monocrystal cerium boride ( $\text{CeB}_6$ ) was used as the material for the gun's 3mm-wide muzzle, because  $\text{CeB}_6$  can keep its surface evenly and a high brightness electron beam can be emitted from the muzzle of the gun. In addition, the path of the beam must be as straight as possible. "Lasers are not generated unless an electron beam of  $30\mu\text{m}$  in diameter travels straight with an error of up to  $4\mu\text{m}$  per 70 meters of the undulator section. So, correcting the beam's orbit precisely is necessary along the accelerator after the beam is emitted from the gun, and especially required for the undulator section," said Yuji Otake, team leader of the Beam Diagnosis Team and the Timing and Low-level RF System Team. Such correction should be done within several tens of micrometers. Furthermore, the pulse width of the beam is several femtoseconds, therefore, the measurements related to the pulse width must also be made with the same time resolution, Otake is developing a clock even more precise than the highly accurate atomic clocks currently in use.

The project group has sharply reduced the project's construction costs by miniaturizing various types of high-performance equipment without compromising their performance. In the case of the C-band accelerators, the team has halved the length of their acceleration areas by doubling the frequency used for acceleration. Permanent magnets, which are usually put outside the undulators, are now contained inside the in-vacuum undulators. As a result, the gap (beam aperture) necessary for generating lasers inside the undulators has become narrow and they can generate a strong magnetic field.

Kumagai metaphorically describes the current stage of building the facility as the harvest time after his group grew its project into a large tree with firm roots. Completion of the XFEL facility will cap their long-term efforts to challenge limitations.

### Construction with millimeter accuracy

It would not make sense if the facility were built on an unstable foundation, even if equipment at the site had an accuracy of several tens of femtoseconds and a few  $\mu\text{m}$ . At



XFEL facility under construction

the construction site, where the ground is soft, 52-meter-long piles were driven down to bedrock to secure a stable foundation. Kazuo Ohshima, team leader of the Facilities Construction Team, explained that the facility has to be constructed with an accuracy of millimeters. In the buildings and foundation of the facility, even the slightest expansion or shrinkage in the concrete is unacceptable.

Thanks to the group's extensive preproduction planning and high level of technical expertise, construction of the 700-meter-long facility has advanced steadily. Researchers are now considering linking the facility to SPring-8 to improve the quality of the beams generated there. RIKEN also plans to connect the new facility with the Next-Generation Supercomputer to be set up in Kobe (see page 16) to speedily process the huge volumes of data generated at the facility.

XFEL light will soon be produced with the support of RIKEN's rich resources. And new scientific technologies to be created thanks to the XFEL facility are just around the corner.



( from right )

**Noritaka Kumagai** Deputy Director  
XFEL Project Head Office

**Yuji Otake** Team Leader, Beam Diagnosis Team  
Timing and Low-level RF System Team(conc.)

**Kazuo Ohshima** Team Leader  
Facilities Construction Team

# World's fastest computation power — Supporting Japan's scientific research and industry

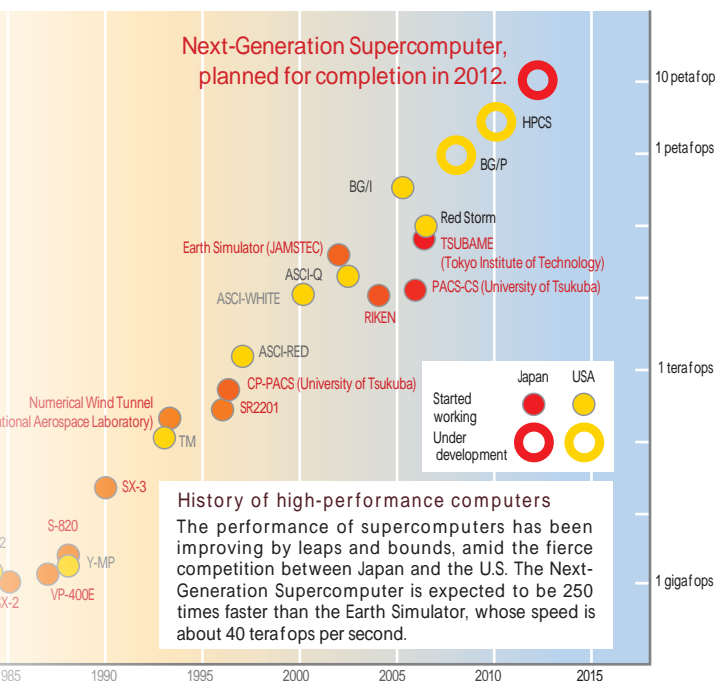
**R**IKEN Next-Generation Supercomputer R&D Center (NSC) is developing the world's fastest Next-Generation Supercomputer for computational scientific applications. After completion of this multipurpose supercomputer, with a calculation speed of 10 petaflops ( $10^{16}$  floating-point operations per second) in 2012, it is expected to not only help develop Japan's computer technology but also be a powerful tool for researchers and engineers in many scientific and industrial fields, including medicine, life sciences, manufacturing, nanotechnology and materials science. RIKEN plans to install the machine at a research facility on Kobe Port Island, Hyogo Prefecture, near Osaka.

## The challenge: to develop a faster and more widely applicable next-generation supercomputer

As scientific technology gets more advanced and complicated, researchers demand more and more accurate prediction and verification of objects that are hard to experiment with and observe. Computer simulations, which are numerical experiments carried out by computer, are crucial for satisfying such needs. Like developing theories and conducting experiments, simulations are a key research method, and the Next-Generation Supercomputer will be a powerful R&D tool in this regard, capable of processing large volumes of data with the world's fastest number-crunching power.

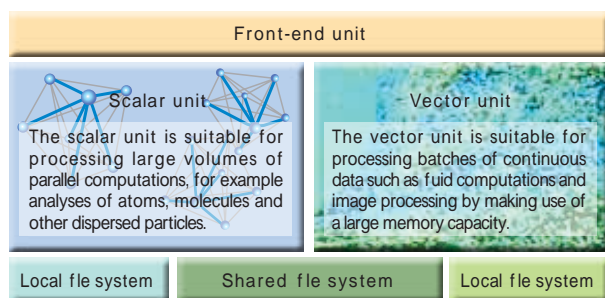
High-speed calculation is not the only reason for the new computer being called a "next-generation" supercomputer. Tadashi Watanabe, project leader of the NSC, is a specialist in high-speed calculations, and was involved in the development of the Earth Simulator,\* the world's fastest supercomputer at the time it was built. "Unlike the Earth Simulator, which was developed exclusively for geophysical computations, our next-generation machine is being developed as a general purpose computer," Watanabe said. "And while the new machine will be able to handle a wide range of scientific calculations, its performance will be continually improved." The Next-Generation Supercomputer will be

\* The Earth Simulator, developed by Japan's NEC Corp., was the world's fastest computer from 2002 to 2004.



**History of high-performance computers**  
The performance of supercomputers has been improving by leaps and bounds, amid the fierce competition between Japan and the U.S. The Next-Generation Supercomputer is expected to be 250 times faster than the Earth Simulator, whose speed is about 40 teraflops per second.

able to support diverse applications because of its novel system configuration combining two types of processors. The combination of vector and scalar processors will make it possible to efficiently carry out any type of computation.



### System configuration

While the processors share calculation data, each processor performs computations that are suitable for it. This parallel processing configuration makes it possible to realize a faster and more widely applicable machine.

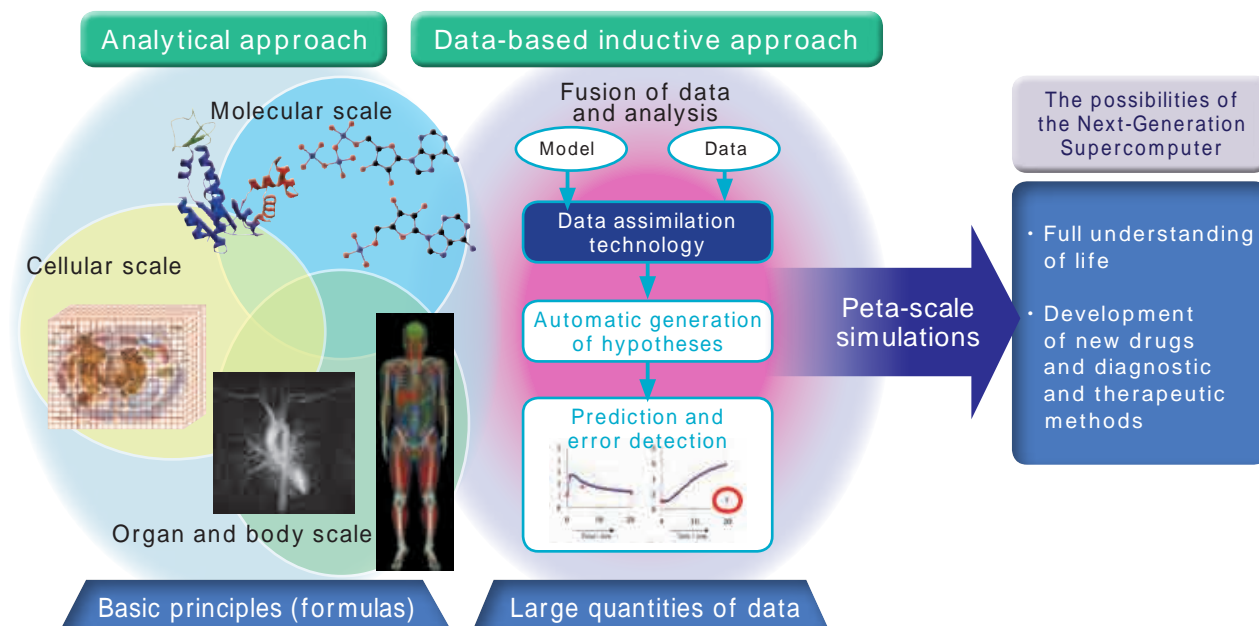
### Application software to address diverse needs

RIKEN's next-generation machine will be capable of simulating blood circulation in an entire body, collision analysis of a whole car and other phenomena in their entirety, making the most of its high speed and multipurpose calculation power. The development team also aims to apply the computer to systematic understanding of life by integrating different levels of simulations, such as those of proteins, cells and organs.

As a major life science research institute in Japan, RIKEN is also developing application software to run on the new

## Role of Next-Generation Supercomputer in life sciences

The new supercomputer will help researchers systematically understand *in vivo* phenomena at various scale levels through simulations from two approaches – basic principles (formulas and models) and analysis of experimental data. Another role of the machine in life sciences will be in developing application software, which will apply systematic methods to medical diagnoses, drug development and health sciences



machine, with emphasis on applying the machine to scientific results and industrial activities. Researchers have high expectations for the software's contributions in the medical and pharmaceutical fields. Selecting chemical compounds for pharmaceutical use involves an enormous volume of calculations, which include analyses of the structures of various proteins and chemical interactions between compounds and proteins. The new supercomputer will be able to process such computations extremely accurately. At the Institute for Molecular Science, atomic- and molecular-level simulations, including calculations of electron orbits, are instrumental in developing new materials and catalysts in nanotechnology.

### Technology and people necessary for developing the world's fastest supercomputer

The new machine's performance per unit of power consumed will be more than 50 times more efficient than the Earth Simulator, according to the development team's plan. Given the power and space constraints, the key to developing such a high-performance machine is technological innovation in microprocessors — the heart of arithmetical processing — and data communications. The finer the circuit lines of a semiconductor become, the less power is consumed and the more powerful the semiconductor becomes. But technological challenges such as difficulty in creating such fine lines and preventing of current leaks must be overcome. RIKEN will try to reduce the circuit linewidths from the current 65 nm to 45 nm by overcoming these challenges.

Moreover, data communications between the various parts of the supercomputer system will be made faster by adopting optical interconnections. These will also make the wiring of the system shorter and simpler. Watanabe said: "Optical interconnections do not affect other electronic devices, as optical signals are not susceptible to noise. In

addition, having less wiring will help save energy." These technological innovations, developed through the supercomputer project, will be applicable to other areas as well.

Improvement of hardware alone is not enough to make the new supercomputer perform at its true capabilities — new software custom-made for its system configuration will also be required. The basic software for running the machine must first be developed, and then tuning of the application software will be needed to efficiently run such software on the high-speed machine.

Watanabe emphasizes the need for involving experts from a wide range of fields in developing computer technology. "I think developing the Next-Generation Supercomputer is very important," he said. "The development processes are also crucial, as technology and human resources are developed through the participation of experts from various fields in creating something new." He plans to promote sharing of the new machine with researchers in a variety of areas, and will carry out the development project by deepening collaboration with universities, research institutes and local communities, in hopes that the new supercomputer center will become a key research and educational facility for computational science.



## Tadashi Watanabe

Project Leader  
Next-Generation Supercomputer R&D Center

## The search for a novel type of light — Pioneer a new field in science with an X-ray Free Electron Laser —

An X-ray Free Electron Laser (XFEL) is a laser beam with an X-ray wavelength. This is an ultimate beam, which no one else has achieved. The XFEL at SPring-8, a large scale radiation light facility, is one billion times brighter than a synchrotron radiation X-ray. The XFEL is increasingly expected to become the world's top performance research infrastructure, allowing instant calculation of ultrafine structures at the atomic level, as well as ultrafast changes in chemical reactions.

The importance of developing the XFEL was recognized by the Government of Japan. In the Third Science and Technology Basic Plan, the XFEL project was appointed as a "Key Technology of National Importance", to be dealt with in the long-term national strategy. In addition to Japan, this scientific field is also being developed in the US and Germany; hence, realizing XFEL has become a global competition.

RIKEN collaborates with JASRI in organizing the SPring-8 Joint Project for XFEL, and is promoting its development with the aim of commencing the shared operation of the facility in fiscal 2011. This unprecedented X-ray laser can be used in elucidating the structure and function of membrane

proteins that are important in drug discoveries, developing new materials that can adsorb gases, and developing micro-fabrication technology with ultra-precision at the nano-level. Through this project, RIKEN expects to pioneer new research areas in various scientific fields, such as life sciences, nano-technology, and materials, and derive findings ahead of other competing countries.

Number of full-time personnel: 27 (as of March 31, 2008)



The Third XFEL Symposium on January 16, 2008.  
"The power and future of the unprecedented XFEL"

## Targeting the world's fastest and highest performance

Computational science and technology, along with theory and experimentation, have established strong positions as approaches to take in modern scientific technology. A Next-Generation Supercomputer is something that can contribute to the further development of computational science and technology. Similarly to XFEL, the Next-Generation Supercomputer is positioned as a "Key Technology of National Importance," to be dealt with in the long-term national strategy.

"The Next-Generation Supercomputer project" was introduced by the Ministry of Education, Culture, Sports, Science and Technology (MEXT) in fiscal 2006. Through developing computational science and technology and

providing an infrastructure that allows extensive use across a broad range of fields in scientific technology/academic research and industry, the project's goals include enhancing the competitiveness of Japan, producing research results that will contribute to society in various ways such as developing new materials and medicine, and maintaining and strengthening the technical capabilities that will support the development of supercomputers in Japan.

Specific goals include

- development and improvement of the world's fastest high performance Next-Generation Supercomputer\*;

- \*10 petaflops class

- development and distribution of software (also referred to as Grand Challenge Applications) that can make the most of the Next-Generation Supercomputer;

- establishment of the world's highest standard supercomputing research and education facility, based around the Next-Generation Supercomputer;

Under the MEXT initiative, these goals will be promoted by RIKEN (the developer), taking the lead in collaboration with industry, academia, and government. The targeted completion of the Next-Generation Supercomputer is in 2012.

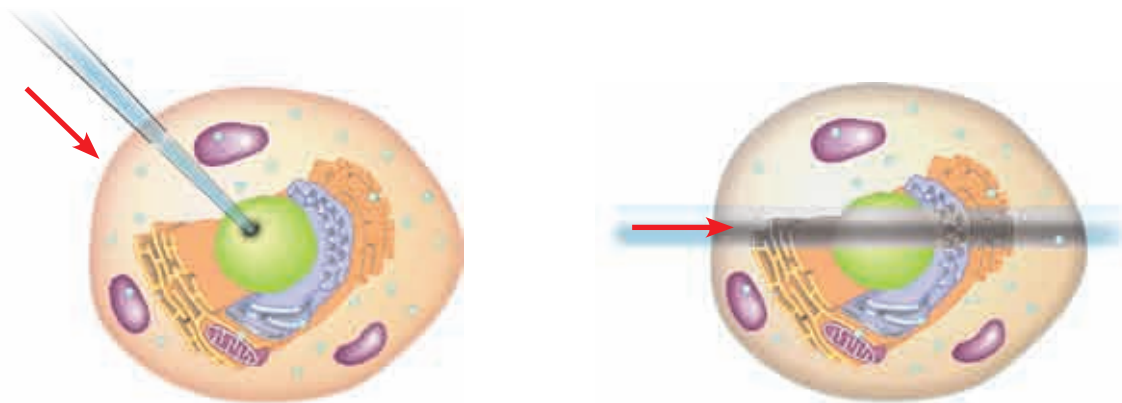
Number of full-time personnel: 28 (as of March 31, 2008)



Kobe's Port Island where the Next-Generation Supercomputer facility will be built

Fourteen outstanding scientific achievements





### Illustration of beam irradiating cell

Using conventional technology (right), a high-energy beam passes through the cell and damages it along the beam's track. But the combination of the tapered glass capillary and a relatively low-energy beam allows precise bombardment and causes pinpoint damage in the cell (left).

through it. The team considered applying this technology to biological research. Even if the capillary is inserted into a cell, no contents of the cell will flow into it when the lid caps the capillary. Such a direct irradiation of a beam in a cell has not been realized so far. "One of the advantages of working at RIKEN is having researchers in various fields around you," Yamazaki noted. "Such an environment prompted us to consider applying this technology to biology. We are basic physics researchers and we happen to have biologists next door. So we came up with the idea of applying our new method to biological research."

To advance this research, Yamazaki's team cooperated with the Discovery Research Institute's Imamoto Cellular Dynamics Laboratory and Beam Application Team, as well as the Iwasaki Advanced Meson Science Laboratory at the Nishina Center for Accelerator-Based Science.

Using ion beams on cells actually has a long history. Researchers have been studying the functions of various parts of a cell through either destroying or changing the parts with ion beams and observing what happens after irradiation. But with conventional technology, only a high-energy beam of ions can be focused to a sufficiently fine beam suitable for cell irradiation. Such high-energy beams pass through the cell and cause damage along the beam's track. Moreover, with the conventional method, the beam's focus deteriorates and the point of the beam that hits the target becomes less accurate because the beam is extracted from the vacuum capillary via a relatively thick window in air and then shoots into a cell in a liquid.

### Beam accurately irradiates target inside cell

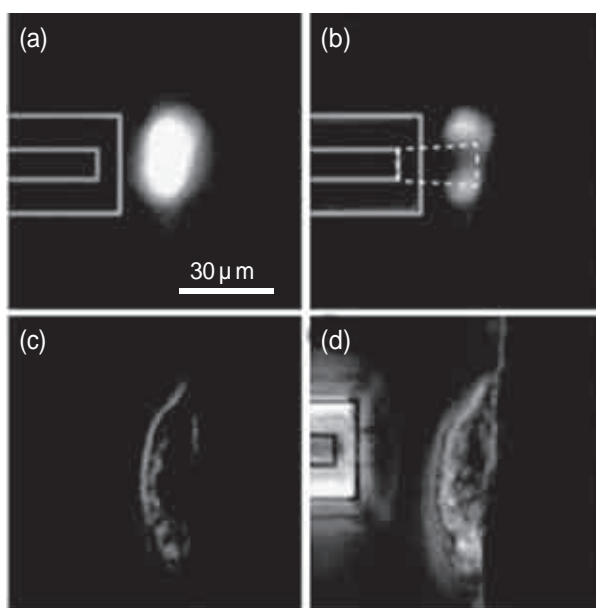
In the glass capillary-based method, the ion beam can irradiate inside a cell directly, so the beam size is kept focused at the target point. In addition, the beam can be accurately positioned to the targeted spot as the tip of the capillary can be seen through an optical microscope. As a typical animal cell is about 50 $\mu\text{m}$  in diameter and the sizes of the cell organelles range from 100nm to 1 $\mu\text{m}$ , the tip of the glass capillary can be accurately aimed at the organelles.

The new technology can also effectively converge a beam even if its energy is about one-100th that of beams now

used in biological research. This is important, because a low-energy beam does collateral damage to other parts of a cell much less than a high-energy one. "We can control the range of the beam, the distance it travels from the lid of the glass capillary, by changing its energy," Yamazaki said. Conventional methods involve the use of an ion beam that damages cell structures along its track inside the cell, while the new technology can precisely induce damage only to the targeted spot.

The team has observed that when an ion beam was irradiated from a glass capillary to the nucleus of a HeLa cell (a human cancer cell) that was labeled by a fluorescent molecule, the irradiated volume was optically inactivated after irradiation. This shows that the beam irradiated a very limited area of the nucleus.

### Test results of beam irradiation of HeLa cell



Before (a) and after (b) ion beam irradiation

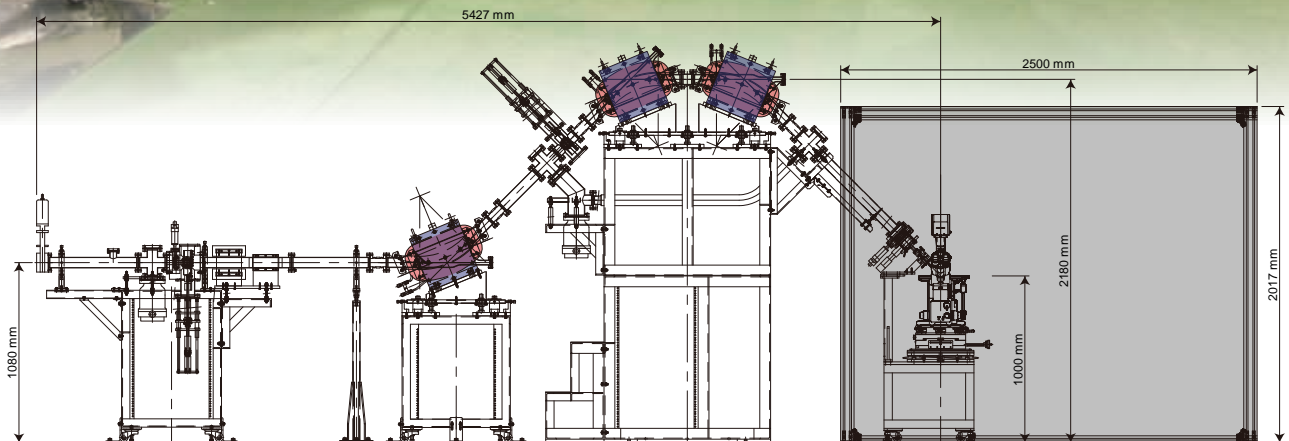
A 4MeV helium ion beam was injected in a HeLa cell from a capillary with an inside diameter of 9.6 $\mu\text{m}$  at the tip and a 7.3 $\mu\text{m}$ -thick lid.

At first glance, there appears to be no change to the cell's surface before irradiation (c) and after (d), suggesting that only a limited area was damaged.

## Newly developed equipment for cell surgery



An ion beam moving from the left through the vacuum pipe is lifted up and down with three magnets in the blue boxes and irradiated diagonally toward the microscope stage at right.



### Promoting applications of the new technology

New equipment dedicated to cell surgery was completed in April 2008 for conducting full-scale research. A beam provided by ordinary irradiation equipment travels horizontally, but it is very difficult to use such a horizontal beam to irradiate a cell in a liquid medium. The new beam equipment at RIKEN has a unique beam line. A series of magnets bend the beam first upward and then downward so that the focused beam from the tapered capillary irradiates a cell placed on a microscope from an angle of 45 degrees. The team plans to study how much damage is induced by such

a beam to each internal organelle by changing the beam's energy and the duration of its radiation. With the damage data, the team will optimize irradiation conditions for cell research.

According to a simulation, a glass capillary with an outlet diameter of 100nm and a 100nm-thick lid can irradiate a volume of about  $100\text{nm}^3$  inside the cell with an ion beam having energy about one-100th the present one. Just a compact beam acceleration system is enough to generate such a low energy beam. The team plans to miniaturize the equipment to the desktop level so that it can be widely used at universities and research laboratories.

## Discovery Research Institute (DRI)

### Japan's Greatest Integrated Basic Science Institute - The Heart of RIKEN -

One of the greatest features of Discovery Research Institute (DRI) is the "chief scientist system"—the unparalleled research system introduced to promote the development of unique research. This system introduced in 1922 by RIKEN's third president, Masatoshi Okouchi, in 1922 offers a flexible research environment by granting total authority—the setting of the research theme, budget planning, member selection, etc.—to a certain number of research leaders (so-called "chief scientists") who have displayed excellent research capabilities. A number of inventions and discoveries have been achieved through this innovative system, which has also produced a number of outstanding human resources, including, among others, Shin-ichiro Tomonaga from Nishina Laboratory and Katsumi Takahashi from Umetaro Suzuki's research team.

Since DRI was organized in 2002, it has adopted various research systems, including the "associate research scientist system," in order to promote a dynamic new research environment. In DRI, chief scientists from various fields actively exchange

opinions while mutually selected representatives intervene in its administration under the supervision of the director. The policy of not drawing any boundaries between different research fields triggers constraint-free research cooperation, and thereby nourishes the germination of new research projects.

DRI is Japan's greatest integrated basic science institute and has the reputation of being "the Heart of RIKEN." For over 90 years, DRI has been contributing to the development of national industries and to the improvement of our daily lives. DRI will become an Advanced Science Institute from the next fiscal year and will continue to operate as the core of RIKEN. We are determined to increase our efforts and assume a leadership role as the front-runner in a wide range of natural science and engineering fields, and also become a global base for creating new scientific fields.

Number of full-time personnel: 414 (as of March 31, 2008)



### Director's Message

#### Unique achievements gained through an interdisciplinary research system

Koji Kaya, Director, Discovery Research Institute

#### Q. Which project did you particularly focus on in fiscal 2007?

A. An alliance agreement was concluded with the Research Institute for Electronic Science, Hokkaido University, in demonstrating the first model of an "alliance laboratory." This alliance will be used as a driving force in enhancing the alliance laboratory division, and will be aimed at further development for university, industrial, and international collaboration. To this end, the Alliance Laboratory of the Research Institute for Electronic Science, Hokkaido University, was established in DRI in order to conduct collaborative research on molecular-informational life science.

#### Q. What are some of the noteworthy achievements of fiscal 2007?

A. Aurelia aurita and Nemopplema nomurai are types of jellyfish that float on tidal currents. The mass-emergence of these jellyfish near the Japanese coast can cause serious damage. We, however, turned the potential disaster into an advantage and developed a useful resource from studying jellyfish.

Kiminori Ushida, the research unit leader of RIKEN's Eco-Soft Material Research Unit, and his colleagues discovered a new type of mucin—a glycoprotein—in the jellyfish. This new mucin has a similar structure to the human mucin, which is a major component of human gastric fluid. This finding is expected to contribute to the development of medicines, cosmetics, and food additives.

#### Q. What are your future prospects?

A. DRI will be integrated with FRS to form an Advanced Science Institute (ASI), and will be germinating new research fields based on basic science research supported by the free-thinking of researchers. These new research fields will then be strategically developed into viable research areas, with the institute being their core research base. In order to achieve these roles, we are determined to go beyond any specific field, organization, and country.



Jellyfish (Nemopplema nomurai)  
The body can grow up to two meters long.

# Controlling the coupling between quantum bits: a crucial step in developing quantum computers

Researchers at the RIKEN Frontier Research System (FRS) have demonstrated that the coupling of quantum bits, or qubits, which are the basic data-processing units of quantum computers, can be controlled. This is a significant step for realizing quantum computers — dream machines that might be able to solve problems in under a minute that would take existing supercomputers many years. If they can be developed, quantum computers could play a significant role in cryptography technologies, retrieving information from databases and simulating various phenomena to solve problems.

*In April 2008, the FRS was reorganized into the Advanced Science Institute (ASI)*

## The power of quantum computers

The basic units used by conventional computers are bits, which can be in either a '0' or a '1' state. Such computers convert information into binary digits for processing. The basic units of quantum computers are qubits, which can also be in either the '0' or '1' state — or both simultaneously, in what is called a superposition state. Moreover, if two qubits in a superposition state are put into an entangled state, in which their quantum states are linked together so that one qubit cannot be described without its counterpart — even though the individual qubits may be spatially separated, quantum computers will be able to compute four combinations of calculations simultaneously. With N qubits, such a machine will be able to calculate combinations of the Nth power of 2 in parallel at the same time. Quantum computers are expected to be much more powerful than existing supercomputers in solving certain problems involving calculations of huge numbers of combinations.

The word 'quantum' originally meant the smallest unit of a material that has the properties of both wave and particle. Typical quanta include electrons and photons. One of the quantum's properties is that its energy levels sometimes take discrete values. Electrons in atoms move around their nuclei at very high speeds. As there are gaps in energy levels between orbits, electrons in one orbit do not jump to the next. But if energy corresponding to an energy gap between two orbits is added, electrons can move back and forth between these two energy levels. These oscillations create quantum superposition and quantum entanglement.

## Difficulties trying to couple quantum bits

Franco Nori, laboratory head of the Digital Materials Laboratory, has been proposing various ideas about circuit designs for quantum computers. Recently, he came up with a new idea to generate quantum entanglement by using microwaves. Such entanglement involves mutual interactions of two coupled qubits.

Quantum computers will perform calculations by combining two types of operations — independent manipulation of the state of a single qubit and making two coupled qubits interact — in accordance with quantum algorithms. In these operations, the interactions between two coupled



**Franco Nori** Laboratory Head  
Digital Materials Laboratory



**Jaw-Shen Tsai** Laboratory Head  
Macroscopic Quantum Coherence Laboratory

qubits must be controlled. However, Nori says, "Controlling the coupling between qubits is difficult."

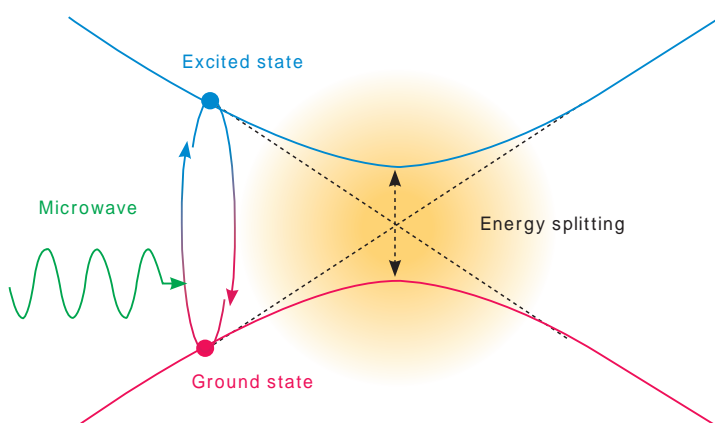
Nori's research team studies superconducting qubits based on Josephson devices. These can be used for controlling quantum states using applied electrical and magnetic fields, including microwaves. The wave properties of quanta usually appear at a microscopic scale. Some relatively large structures that can be designed and manipulated possess such properties. Josephson devices are such structures.

Nori's team has pioneered several research results in superconducting qubits including: coupling qubits to a quantized electromagnetic field inside a cavity, the first study of quantum tomography in solid state systems, quantum thermodynamics, cooling qubits, photon-generation on demand, qubit-based micro-masers, coupling with mechanical qubits, quantum transducers, and how to best couple qubits.

### Using microwaves with different frequencies

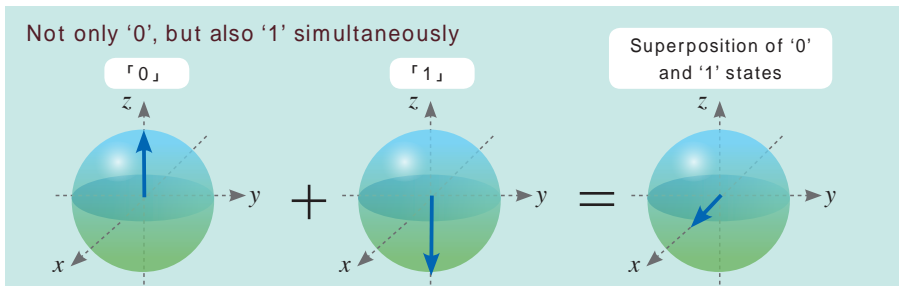
Josephson devices are circuit components made of superconducting materials containing Josephson junctions, in which two superconductors are linked by a non-conducting

### Controlling quantum states by using microwaves

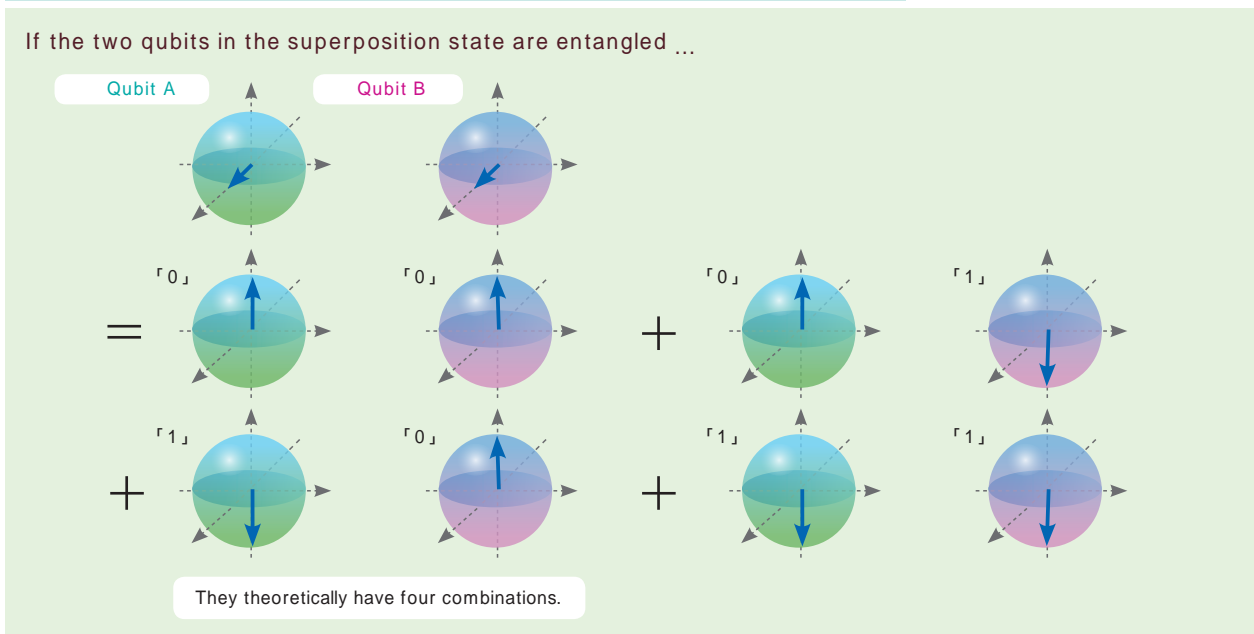


Microwaves have energies corresponding to their frequencies. Microwaves with an energy corresponding to the gap between the two specific states of a particle can induce oscillations between these two states.

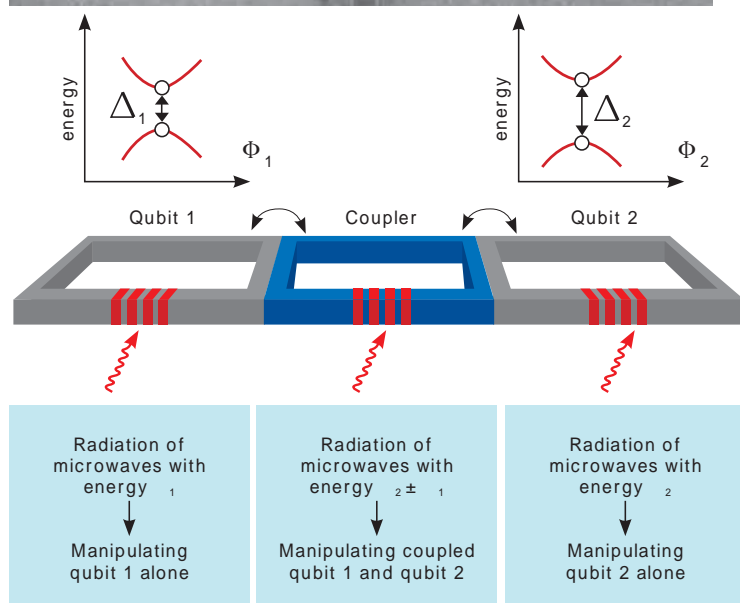
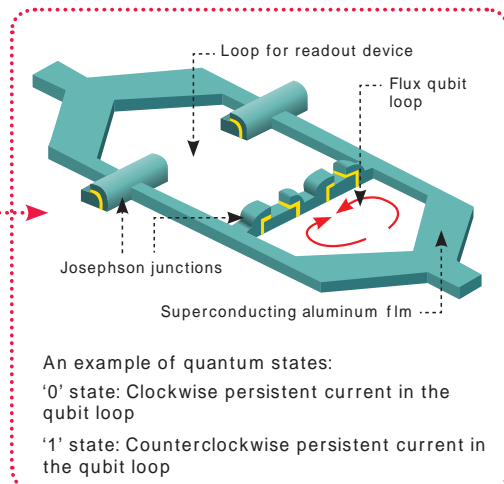
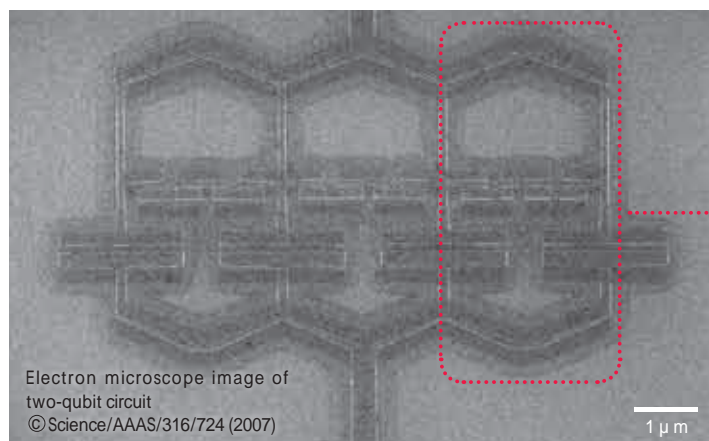
barrier. As Jaw-Shen Tsai, laboratory head of the Macroscopic Quantum Coherence Laboratory, says, "These circuit components have many electrons, which move freely under normal circumstances. But when they are cooled to very low temperatures, they become superconductive and their electrons fall into a macroscopic quantum state in which they behave like a single wave." As Josephson device specialists, Tsai's team has been making significant contributions toward



The state of a qubit can be expressed with an arrow pointing to a certain point on a spherical surface. If the north pole is '0' and the south pole is '1', a qubit could take any point on the surface, depending on the degree of the superposition of the '0' and '1' states. If the superposition with the probability of the '0' state is 50% and the '1' is 50%, the arrow indicates a point on the equator.



## Two-qubit circuit with tunable coupling



1 and 2 are qubits and the coupler is at the center. There are two methods to create a quantum superposition of superconducting qubits; one is by charge qubits and the other by (magnetic) flux qubits. Superconducting flux qubits are used in this device.

realizing quantum computers. As shown schematically in the above figures, electrons in the macroscopic quantum state flow in the loops clockwise or anticlockwise as a resistance-free persistent current. The clockwise current can be used as '0' and the other current as '1' because the energy states of these two types of currents are different.

Tsai's team has designed and produced a quantum computer circuit using three Josephson devices. In the figure above, the loops on the right and the left are qubits, while the central loop is a coupler to magnetically connect the two qubits. Each qubit can be operated independently by irradiating it with microwave frequencies corresponding to the energy of the selected or target qubit. The circuit is designed so that each qubit has a different energy level. Tsai's team has also demonstrated for the first time anywhere that the two qubits can be coupled and made to interact when the central circuit is irradiated with microwaves with frequencies corresponding either to the sum or the difference of the energy gap of the two qubits. The coupling of two superconducting qubits can be controlled by changing the frequencies of the microwaves and the length of time they are applied.

## For realizing future quantum computers

Tsai's quantum computer circuit might be suitable for producing large-scale circuits by connecting many qubits because its qubits and the coupler have the same structure. Tsai's team has also succeeded in maintaining the quantum superposition and entanglement states for a world-record-long 10 microseconds. This period is thought to be almost long enough for operating a quantum computer. "We radiated microwaves three times in our experiments," Tsai says, "We think that quantum algorithms will be executed by radiating about 10 times. If the algorithms are carried out, we will have developed a prototype quantum computer consisting of two qubits. That is our next goal."

Nori's team has already started examining other ideas and approaches. He says, "Since the study of quantum computers has just started, it's too early to tell whether the superconductive circuits we're studying will be more fruitful for this task in the long run. Several possibilities are still open. Therefore, at this point this is a very exciting area of research." Researchers at RIKEN are searching for a way to develop quantum computers through close cooperation between the theoretical and experimental teams.

## Frontier Research System (FRS)

### - The Fountainhead of RIKEN's Vitality -

Frontier Research System (FRS) was established in October 1986, initially as the Frontier Research Program. Using clear targets, excellent researchers were then recruited from various fields, under the fixed-term system. This novel research system, with limited term research projects, had an impact on the Japanese research system, which had traditionally been staffed by fully-tenured research personnel. In 1997, Brain Science Institute was established through this research system, and since then, other research organizations, both within RIKEN and externally, have followed suit, establishing research organizations using FRS as a model. This indicates the height to which this research system has been evaluated and has attracted interest.

Out of the many other limited-term RIKEN research organizations, FRS is the only existing organization with no specific research field in its appellation. This characterizes FRS's mobility,

flexibility, and the expectations it bears to serve as an incubator for new interdisciplinary projects and to test new research system operations.

FRS has played a pivotal role in germinating new research fields, in line with the future planning of RIKEN. At present, we are integrating with Discovery Research Institute (DRI), which promotes creativity-based, free-thinking basic research in a variety of fields; we are also taking a new step forward as Advanced Science Institute (ASI), from fiscal 2008. By taking advantage of our comprehensive research institute, we will do our best to fulfill our role as an Advanced Science Institute that promotes advanced cross-disciplinary research in extensive fields, through a flexible and borderless research system.

Number of full-time personnel: 172 (as of March 31, 2008)



### Director's Message

### - The Fountainhead of RIKEN's Vitality -

Kohei Tamao, Director, Frontier Research System

#### Q. Which projects did you particularly focus on in fiscal 2007?

A. Studies on the supra-biomolecular system and spatio-temporal function materials, both of which commenced in October 1999, were successfully concluded with a number of notable achievements. Reports from the Spatio-Temporal Function Materials Research Group and the Supra-Biomolecular System Research Group were heard on September 14 and September 20, respectively, and were well attended by many concerned parties. In October 2007, the Cross-Correlated Materials Research Group, the Responsive Matter Chemistry & Engineering Research Group, and the Systems Glycobiology Research Group were launched and began their research.

Based on RI-MAN, a lifestyle-support robot developed by the Bio-Mimetic Control Research Center, the RIKEN-TRI Collaboration Center for Human-Interactive Robot Research was established in August in order to realize the practical use of human interactive robots, which can be trusted and relied upon when they are used at care facilities.

#### Q. What are some of the noteworthy achievements of fiscal 2007?

A. The Single Quantum Dynamics Research Group, which commenced its studies in October 2001, obtained a number of findings in 2007 and held four press conferences. Specifically, and worthy of special mention, the Macroscopic Quantum Coherence Team successfully demonstrated the world's first controllable coupling between quantum bits. On December 12, Akira

Tonomura, group director of Single Quantum Dynamics Research Group, was appointed as a member of the Japan Academy, due to his remarkable academic achievements.

#### Q. Where there any movements in the research system in fiscal 2007?

A. Some of the achievements of the Supra-Biomolecular System Research Group have been succeeded by the Systems Glycobiology Research Group for further development. Using the high-performance nano membrane technology — developed by the Topochemical Design Laboratory (Toyoki Kunitake, director and laboratory head) in the Spatio-Temporal Function Materials Research Group — as a business foundation, NanoMembrane Technologies, Inc. was established on September 14, 2007, and conducts R&D as a RIKEN venture company.

#### Q. What are your future prospects?

A. In the Advanced Science Institute, which will be launched in fiscal 2008, researchers from various fields will work together on creative and leading research projects under the flexible and borderless research system. ASI will play a critical role in the research process, which circulates from germinating new research to strategically nurturing research fields and developing a core research base.

We believe that this process will result in great scientific and technological progress, and contribute to the development of human society.

# Discovery of genetic defect linked to autism

## RIKEN researchers unlock the mechanism of cerebellar development

Autism is a developmental disorder whose cause is unknown, though researchers have long suspected that it may be genetic. Researchers at RIKEN Brain Science Institute (BSI) have discovered genetic abnormalities that are expected to help clarify how autism develops, and have started examining the possibility of applying their discovery to early diagnosis of the disorder. Autism specialists expect RIKEN's new finding to lead to the development of medications and other treatments for the disorder. Functional analysis of the abnormal gene suggests that autism may be caused by improper formation of neural circuits.

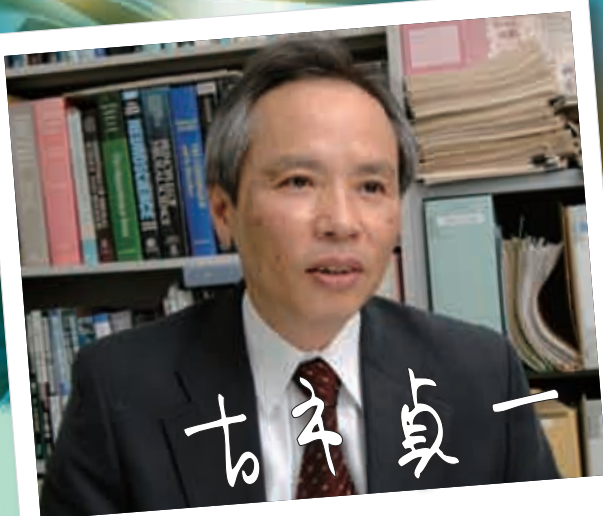
### Clue may clarify autism's development mechanism

Autism is a disorder characterized by unique behavioral patterns among its sufferers, including serious problems with social interaction and communication with other people, and repetitive behavior. The disorder is relatively common, occurring at a rate of one in 1,000 people during infancy. There is great variation in the severity of these features. Studies indicate that if broader diagnostic criteria are applied (autism spectrum disorder, ASD), the rate of ASD could be as high as 6 in 1,000. But the underlying cause of autism has not been found, and no cure has been developed. Some autistic patients' aberrant behavior and function improve to some extent through special training and treatment early in life. But identifying the root cause and establishing a basic therapy are urgent tasks in light of the relatively high occurrence of the disorder and the impact on patients' families.

In recent years, researchers have suspected the involvement of genes that could be a clue to clarifying the autism development mechanism. When an identical twin has autism, the probability of the other twin also suffering it is 60-92%. In the case of fraternal twins, whose genetic information is different, the rate falls to 0-10%. Researchers have identified potentially important candidate genes that they believe are linked to autism, but they lack conclusive evidence. The genes in question were found in less than 1% of all cases and model mice with most genes did not develop autism-like phenotypes. Now the RIKEN researchers are investigating the possibility that the Ca<sup>2+</sup>-dependent activator protein for secretion 2 (CADPS2) gene may be involved in causing the disorder. CADPS2-deficient mice have shown behavioral patterns similar to those of autistic patients. In addition, aberrant splicing of CADPS2 transcript has been identified in four of 16 autistic patients and seven single nucleotide variations in CADPS2 gene have been identified by analyzing genomes of 252 patients.

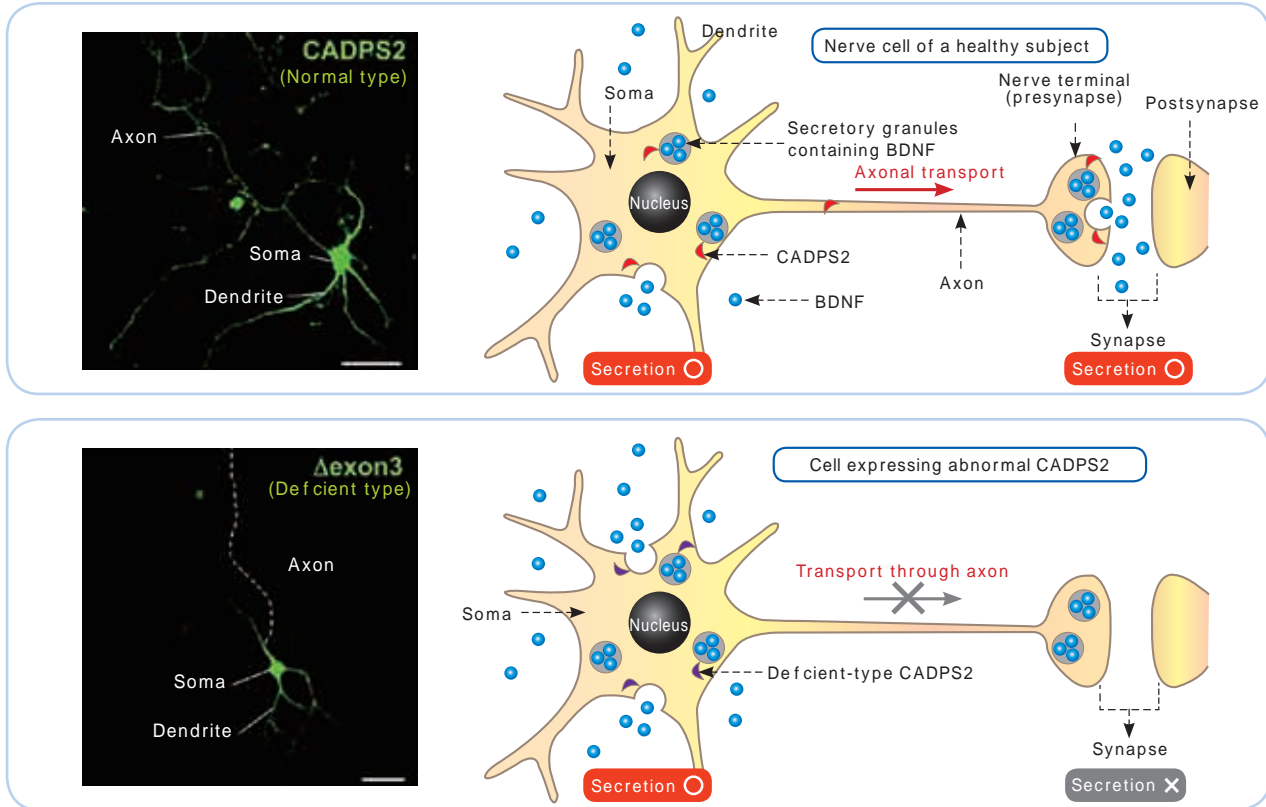
### Hypothesis formulated through testing on knockout mice

Neural circuits in the cerebellum usually develop as the individual grows. But Teiichi Furuichi, laboratory head of



**Teiichi Furuichi** Laboratory Head  
Laboratory for Molecular Neurogenesis

## CADPS2 protein and BDNF release



**Axonal localization of CADPS2 protein**  
(Top) While normal CADPS2 is distributed from the dendrite and soma to the tip of the axon (synapse), the deficient-type CADPS2 is not transported to the axon (dotted line) and is localized only around the dendrite and soma (below).

The CADPS2 protein promotes the release of BDNF, which regulates the formation of neural circuits and memory and learning functions. The normal CADPS2 protein is transported to the axon and BDNF is released from the presynaptic terminal. But CADPS2 lacking exon3, which is produced due to aberrant alternative splicing, is not transported to the axon. As a result, BDNF is not secreted from the presynaptic terminal.

the Laboratory for Molecular Neurogenesis, studying the genetic process of cerebellar development, and Tetsushi Sadakata, a member of his team, have found that when the CADPS2 gene has abnormalities, these circuits are not properly formed. “We created CADPS2-deficient knockout mice, and found that the release of the brain-derived neurotrophic factor (BDNF) was reduced in comparison with that of their wild-type littermates. As a result, we concluded that the CADPS2 protein is involved in BDNF secretion,” Furuichi said. BDNF, which promotes neuronal differentiation and survival, regulates functions crucial for synaptic plasticity and connectivity. The brain develops by wiring and rewiring of neural circuits through the individual’s learning and experience. A BDNF shortage may cause developmental deficits in neural circuit underpinning social behaviors, Furuichi said, adding, “Through detailed examination of the knockout mice, we found that they displayed aberrant cellular and behavioral phenotypes that were reminiscent of the features that characterize autistic patients.”

Autistic patients are sometimes found to have underdevelopment (hypoplasia) in a particular region of their cerebella. The team found that their knockout mice had hypoplasia in the same region of the cerebellum as autistic patients do. The number of specific neuron types in the cerebrum and hippocampus as well as the cerebellum is decreased. But the cell numbers can be recovered if BDNF is administered, demonstrating that a BDNF deficit causes such reduction of neuron number. The knockout mice were normal in

basic visual, olfactory and auditory functions, but showed problems with social interaction and response to unfamiliar environments and exhibited hyperactivity. These behavioral problems appear to be autistic-like symptoms, Furuichi said. “We hypothesized that autism may be caused by improper development of neural circuits during infancy, a very critical brain development stage. Such improper wiring may prevent the brain from working properly.”

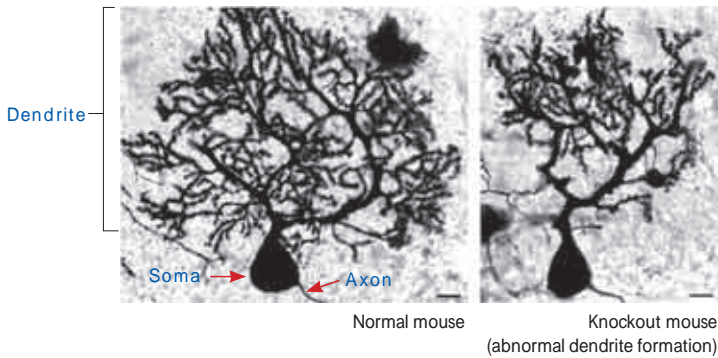
### Genetic abnormality also identified in humans

The human CADPS2 gene exists within the chromosomal region that is thought to be associated with autism susceptibility. Furuichi said his team decided to find out whether CADPS2 gene in autistic patients has abnormalities. The team found a shorter transcript (mRNA) encoding the deficient type of the CADPS2 protein in the blood of four of 16 autistic patients. This type of protein is not identified in the blood of healthy people. Sequencing the short mRNA also showed that when the CADPS2 gene is transcribed, the third exon (exon3) of all 28 exons\* is skipped. Moreover, the team clarified the importance of the exon3 in its interaction with a protein involved in transporting CADPS2 through axons. Furuichi noted: “The exon3-deficient CADPS2 is not transported from soma (cell body) to the tips of axons (the synapses). As a result, I think that the synapses may not

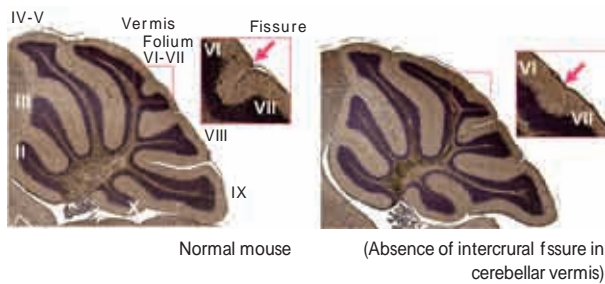
\*Exon ... protein-encoding sequence

## Aberrant cerebellar development and abnormal behaviors of the CADPS2 knockout mouse

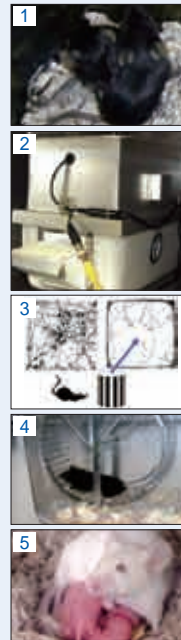
Comparison of dendrite morphology in cerebellar Purkinje cells



Comparison of formation of intercrural fissures in cerebella



Behavioral tests of normal and knockout mice



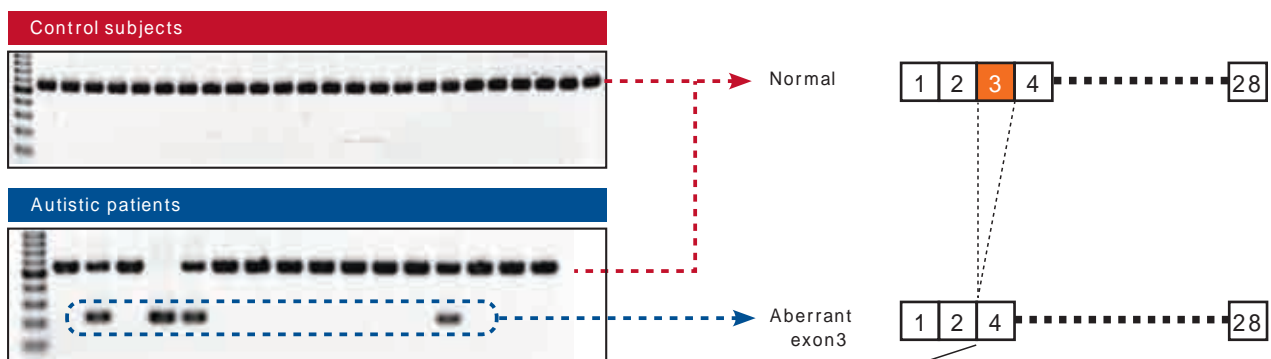
- 1. Social interaction:** A pair of mice was placed in a neutral cage to observe their social interactions such as physical contact and grooming. The wild-type (normal) mice often made contact, while the knockout mice did so much less frequently.
- 2. Home-cage activity:** The horizontal movements of mice in their home cage were measured by counting how many times an infrared beam was interrupted. The test found that the knockout mice moved actively (hyperactivity), an autistic symptom, was observed.
- 3. Response to unfamiliar environment:** The knockout mice tended to avoid unfamiliar objects placed in an open field (novel environment). Low adaptation and/or increased anxiety to the unfamiliar environment were observed.
- 4. Intrinsic sleep-wake regulation (circadian rhythm):** The wild-type mice behaved in accordance with their intrinsic biological clocks in a dark environment all day long. But such cycles of their knockout counterparts was impaired.
- 5. Maternal behavior:** The ratio of mothers who did not raise their offspring was higher among knockout mice than among their wild-type littermates.

release BDNF and that neural circuits may not be formed properly, due to a lack of local BDNF action at synapses.”

It is crucial to start providing proper training and treatment for autistic patients as early as possible. Early diagnosis could lead to the formation of educational and treatment programs for autistic infants. Furuichi and his team have already obtained a patent on deficient-type CADPS2-based early autism diagnosis. “Although combined action of multiple interacting genes is implicated in autism, identifying what genes are involved and studying their functions could lead to the development of drugs and treatments. We want to collect more data about CADPS2 gene from patients,” he said. He is enthusiastic about applying his team’s discovery to future drugs and therapies for autistic patients.

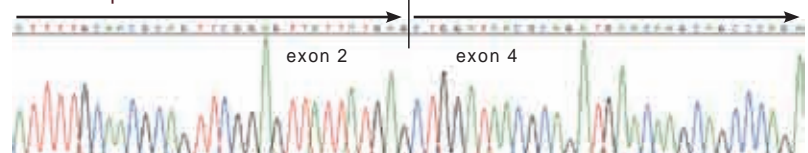
## Results derived from study on ‘genetic design of cerebellum’

Furuichi and his team have created a database that could be called a “genetic design of the cerebellum,” by investigating when and how certain genes are expressed in developing mouse cerebella. He and his team have already mapped about 9,000 such genes, which they posted on the Internet. Furuichi stressed that basic research has led to a clue to clarifying the development mechanism of autism, and stressed that he and his team do not focus on studying autism alone. Further research on gene functions may lead to the discovery of the involvement of other genes in the development of other disorders and diseases. The team’s research is expected to greatly contribute not only to understanding of the human brain but also treatment of a variety of medical problems.



CADPS2 mRNA expressed in the blood of autistic patients

The expression of the mRNA that encodes the deficient-type CADPS2 protein was confirmed in the blood of some autistic patients. This deficient type is not found among healthy people. Sequencing the CADPS2 mRNA revealed that when the CADPS2 gene containing a total of 28 exons is transcribed, its third exon is skipped.



## Brain Science Institute (BSI)

### Aiming at a new height

Ten years have passed since Brain Science Institute (BSI) was first established in October 1997, as a core national brain science research organization. In order to study the brain, researchers and engineers from various fields, including medical science, biology, physics, engineering, information science, mathematical science, and psychology, have assembled; the intention of this collaboration is to carry out extensive theoretical and experimental research in an integrated manner. Thanks to a number of research achievements and the contribution of human resource development, today, BSI has gained worldwide fame and trust.

Over the past 12 months, even more remarkable research achievements have come to light: the elucidation of the high order mechanism of the brain that learns through conceptualizing right and wrong, etc.; the development of genetic technology that breaks and recovers specific neural circuits; the elucidation of the pathogenic mechanisms involved in ALS, schizophrenia,

Alzheimer's disease, etc.; the establishment of a tool-using rodent model; the development of real-time observation technology for use in DNA replication and cell division; and many others.

In fiscal 2007, we also actively addressed collaborations with industry and increased communication with the public; we have also enhanced the development of human resources, in the field of brain science research, through activities such as internationalization, collaborations with research institutes at home and abroad, conducting summer programs, and holding a series of tutorials. As expectations and demands on brain science and its responsibility to society increase, the role of BSI becomes ever more important. We will continue to create new comprehensive human sciences and streams of knowledge so that brain science can meaningfully contribute to society.

Number of full-time personnel: 495 (as of March 31, 2008)



### Director's Message

#### Aiming to jump higher

Shun-ichi Amari, Director, Brain Science Institute

**Q. Which project did you particularly focus your attention on in fiscal 2007?**

A. Ever since BSI was established in 1997, it has been assuming a leading role in the development of brain science research in Japan with a long-term perspective in mind. In fiscal 2007, our 10th anniversary, I believe that we reached a major turning point.

One of the reasons for this turning point is that a brain science committee, which discusses national brain science strategies, was established at the Ministry of education culture sports science and technology (MEXT) despite the fact that brain science research budgets are being cut back. This event has shown just how important brain science is at the national level.

The second reason is that an element of brain science has reached the stage at which it can be put to practical use, and, as a result, it is gradually being tightly bound to society. Another notable achievement was the establishment of two collaboration centers within BSI: the RIKEN BSI-OLYMPUS Collaboration Center and the RIKEN BSI-TOYOTA Collaboration Center. A research project on the brain activity of people playing Shogi also commenced, in cooperation with Fujitsu Limited and the Japan Shogi Association.

The third reason for the turning point is that a 10th anniversary event was held. To enable more people to understand brain science and BSI's activities, we conducted a range of activities, including an event called Brain Science Park and the creation

of a Dreaming Brain Science Map, in cooperation with experts from various fields. These activities resulted in a large influx of feedback from society.

**Q. What are the center's future prospects?**

A. BSI's strongest points are its comprehensive interdisciplinary nature and its challenges in merging cross-cutting researches. From fiscal 2008, we intend to remove the current boundaries between fields and aim at further evolution through reorganization into four core areas of research: Mind and Intelligence Research Core, Neural Circuit Function Research Core, Disease Mechanism Research Core, and Advanced Technology Development Core — all of which will be increasingly important for the future of brain science research.

BSI is also an organization that is very advanced in regard to internationalization. It not only accepts a number of foreign researchers but also actively promotes collaborations with the Massachusetts Institute of Technology, Harvard University, and a number of other universities. We are successfully obtaining the world's leading researchers.

In addition, BSI has developed advanced technologies that can act as a foundation for brain science and is making them available to the rest of the world. It is currently leading the world in the fields of fluorescent proteins, imaging technology, and neuroinformatics technology, and is making significant contributions to the research activities of the national brain science community.

# New radioisotope discovered at RI Beam Factory

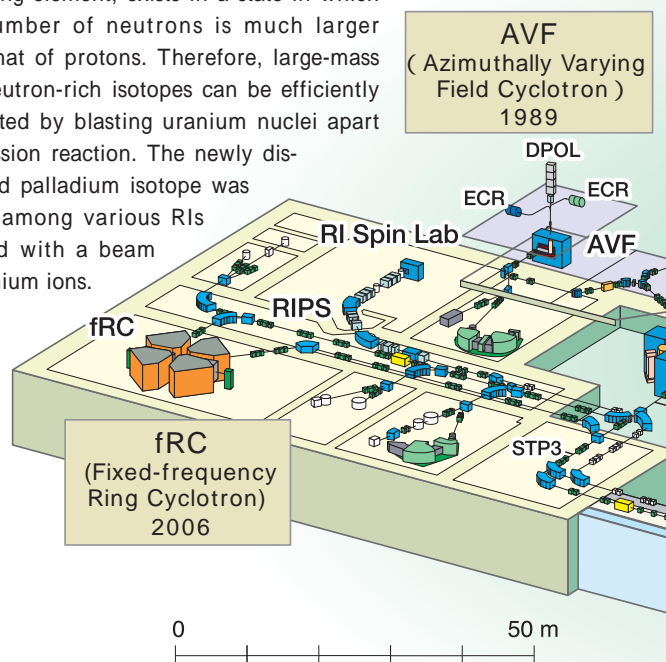
The new RI Beam Factory at the RIKEN Nishina Center for Accelerator-Based Science (RNC) began its working life in style last year — researchers there discovered a new isotope of palladium (Pd 125) in June 2007, shortly after the facility started operations. The achievement clearly demonstrated that the RIBF, which was designed to generate known radioisotopes (RIs) as well as discover new ones, can already deliver the world's most advanced performance of any facility of its type. Various research projects are already being implemented at the as-yet unfinished RIBF, which is targeted for completion in 2012.

## Studying the origins of elements

Scientists understand the basics of how the lighter, naturally occurring elements, from hydrogen to iron, were created after the Big Bang — the birth of the universe — though the process is still being clarified. But how elements heavier than iron formed remains a mystery, and radioisotopes hold the key to resolving this question.

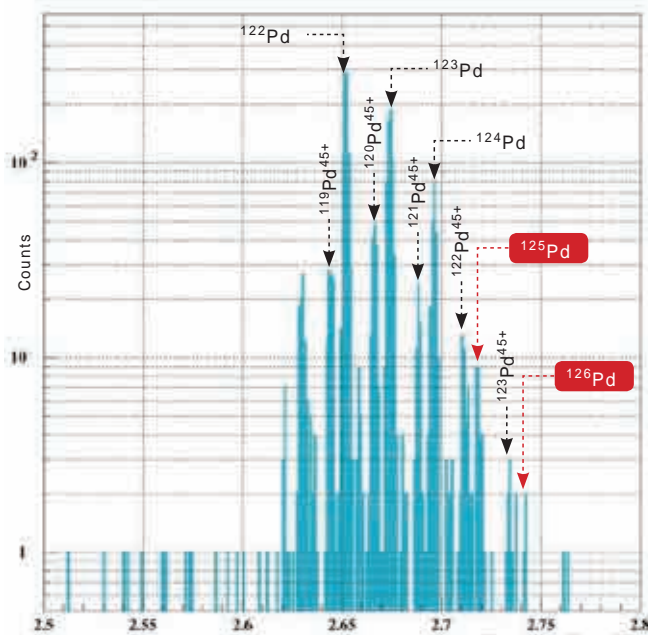
The atomic nuclei of elements that occur naturally are usually stable. Nuclei consist of neutrons and protons, and when the number neutrons becomes excessive or that of protons becomes much smaller, the nuclei become unstable and as a result decay quickly after their creation. These unstable nuclei are called radioisotopes. The generation and observation of RIs that do not occur naturally is indispensable for learning about the origins of heavy elements and clarifying their structures.

RIs are generated as a result of the fragmentation, or fission, of nuclei when they collide at extremely high energies with target nuclei. At the RIBF, the world's first five-stage acceleration system became available in 2006 with the completion of a superconducting ring cyclotron (SRC) with the world's most advanced acceleration performance. The RIBF is capable of accelerating uranium ions to about 70% of the speed of light. Uranium, the heaviest naturally-occurring element, exists in a state in which the number of neutrons is much larger than that of protons. Therefore, large-mass and neutron-rich isotopes can be efficiently generated by blasting uranium nuclei apart in a fission reaction. The newly discovered palladium isotope was found among various RIs created with a beam of uranium ions.



### Discovery of Pd 125, a new RI

Creation and separation of radioisotopes are carried out at the RIKEN in-flight RI beam separator (BigRIPS), completed in February 2007 at the RIBF. Toshiyuki Kubo, group director of the Experimental Installations Operation Group, was in charge of developing BigRIPS and led an experiment to find new radioisotopes. "We carried out full-scale trial experiments from May 16th to June 3rd to



Discovery of a new radioisotope, Pd 125  
Palladium radioisotopes were separated from RIs generated through collisions of uranium and target nuclei. They were then plotted according to the ratios of mass number and charge. Forty-three events of Pd 125 were confirmed. Four events that appeared to be palladium 126 were also observed. Detailed analysis of their data is under way.

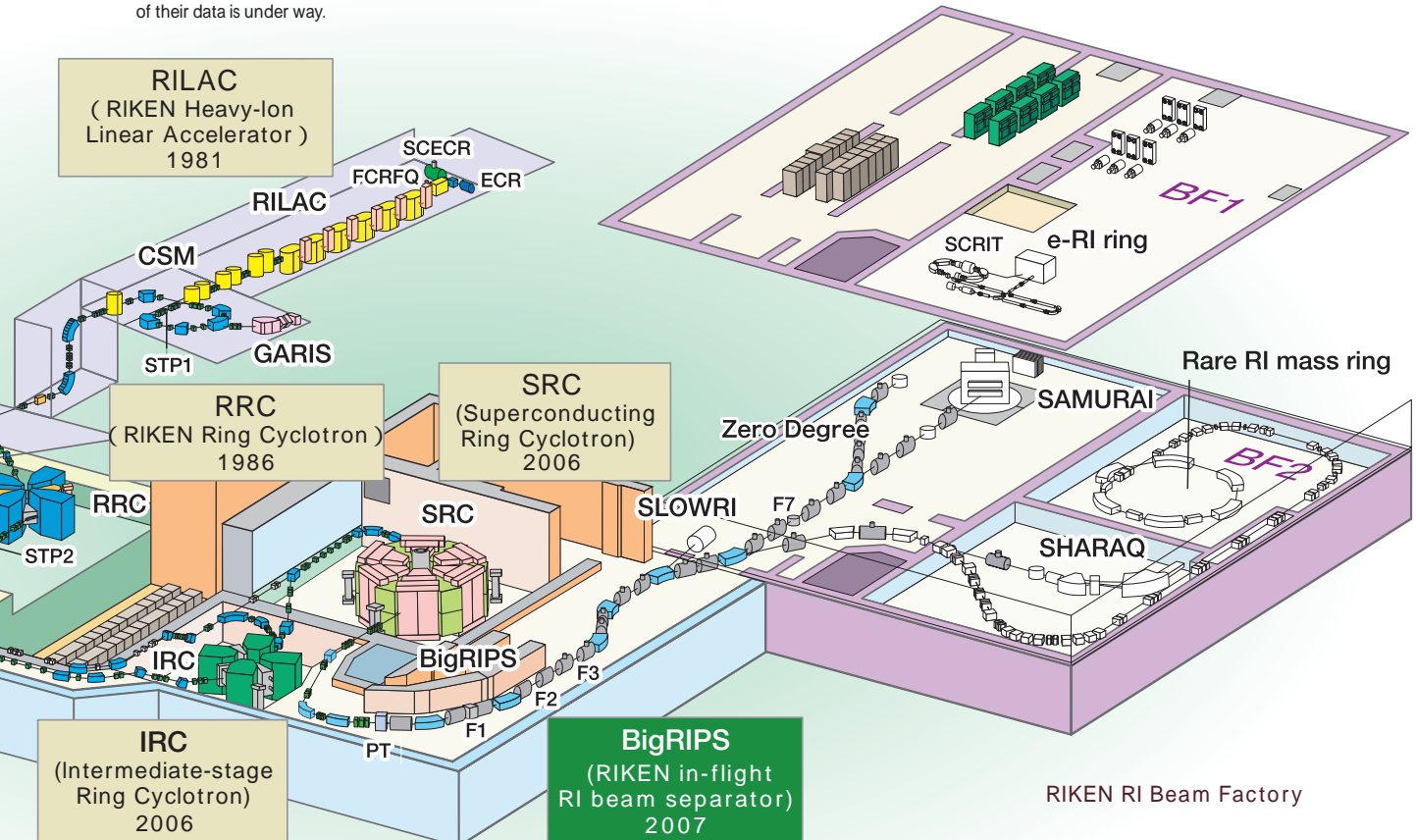
discover new RIs," he said. "In the first half of the project, we conducted tests to confirm BigRIPS's performance and in the second half started experiments for finding new radioisotopes by using a uranium beam."

In the experiment to create RIs, his team bombarded a beryllium target with a beam of uranium ions accelerated to 70% of the speed of light. For the first time, 43 events of palladium 125 were discovered among the RIs obtained in the experiment. Pd 125 is a palladium isotope containing 15 more neutrons than palladium 110, the heaviest naturally-occurring palladium atom.

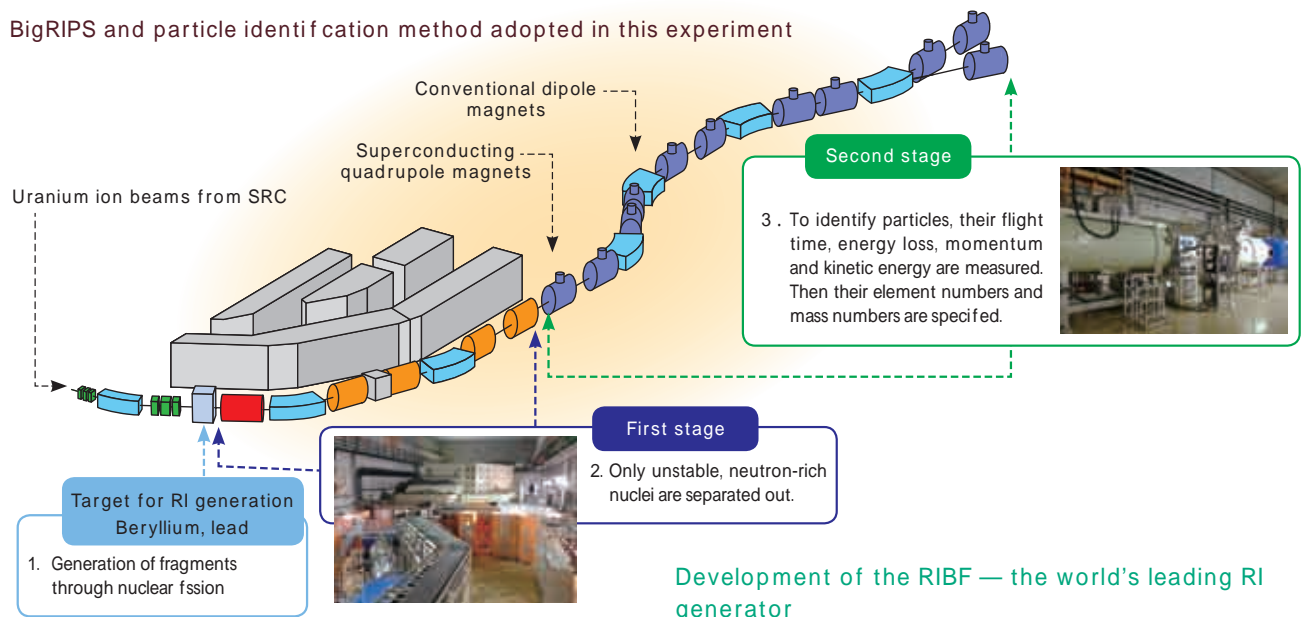
It is widely known that atomic nuclei become especially stable when they contain specific "magic numbers" of protons and neutrons, for example 50 protons and 82 neutrons. Many researchers are paying close attention to the structure of the newly discovered palladium 125, with its 46 protons and 79 neutrons, because these numbers are close to the magic numbers. The discovery was immediately reported at the International Nuclear Physics Conference INPC 2007, on June 6, 2007, and highly praised by nuclear physicists around the world.

### High RI identification and generation capabilities of BigRIPS

The discovery was due to the advanced capabilities of BigRIPS, which was designed specifically to handle uranium ion beams. BigRIPS has a two-stage tandem structure: the first stage is for collecting and separating radioisotopes, and the second is for identifying them. Its high radioisotope identification performance stems from this two-stage structure. As the RIBF can rapidly generate RIs at intervals of



## BigRIPS and particle identification method adopted in this experiment



100 billionth of a second, it is possible to observe them for a relatively long time before they decay. As a result of the smashing of the uranium atoms, nucleus fragments fly off in wide directions. BigRIPS can collect about 50% of all generated RIs not only by widening the diameter of the beam line through which the beams pass, but also by converging the beams with powerful superconducting quadrupole magnets. Some RIs that appear to be close to the target radioisotope are separated out from the collected RIs and sent to a second stage, where the separation criteria include the ions' radius of curvature when they move in a magnetic field, and energy loss when passing through a metal plate.

In the second stage, the RIs are identified by their flight time and energy loss, and their elements and their degree of neutron richness are specified. Kubo explained, "We change the strength of the magnetic field and thickness of the metal plate or adjust the RI detectors, according to the target radioisotope. After a name tag is attached to each separated RI, they are sent to the next facility beyond BigRIPS." In addition to palladium 125, Kubo's team also found four events that appeared to be Pd 126, and they are currently analyzing the data to confirm this.

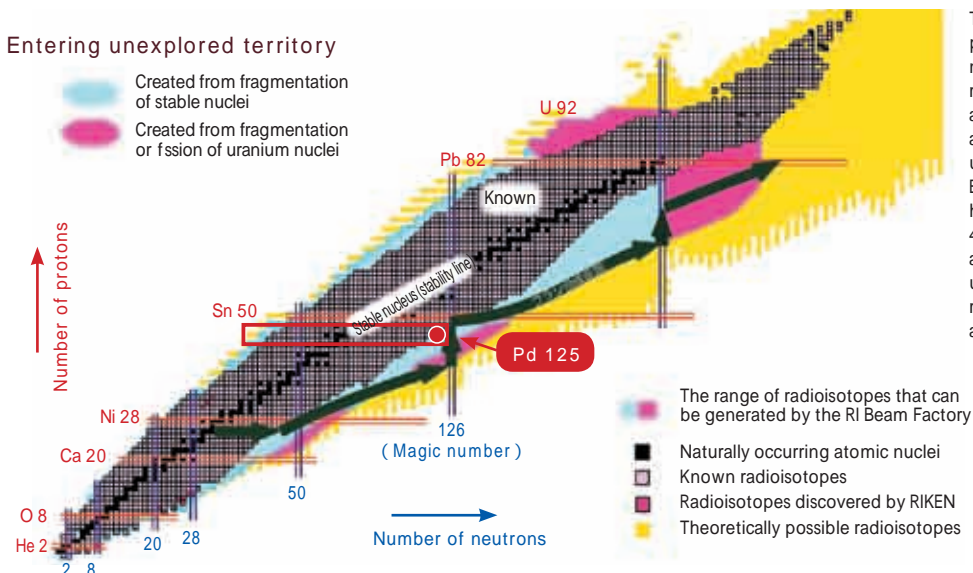
## Development of the RIBF — the world's leading RI generator

The experiment to discover new RIs was carried out in collaboration with other laboratories outside RIKEN, with the participation of American, French and German researchers. Kubo said: "The U.S. and European countries are developing their own large particle accelerators. In that sense, they are our competitors. But international cooperation is crucial to make the most of very high-performance facilities like the RIBF by overcoming various challenges."

The RIBF can generate about 4,000 different kinds of RIs, including about 1,000 never before seen. The facility has already succeeded in creating two kinds of unknown radioisotopes even at 100,000th the beam strength it eventually aims to achieve, demonstrating that the RIBF has the world's highest RI generation capability. RIKEN plans to solicit proposals from researchers around the world for experiments to resolve a host of unsettled issues in nuclear physics.

Construction of new experimental equipment linked with BigRIPS began in April 2008. RIKEN will continue development activities to complete the RIBF in 2012 to keep its lead over its European and U.S. rivals in the competition to develop RI beam generation facilities.

## Entering unexplored territory



The vertical axis is the number of protons and the horizontal axis is the number of neutrons. Each small square represents an atomic nucleus. There are about 270 naturally-occurring stable atomic nuclei. Around these are many unstable nuclei (radioisotopes). The RI Beam Factory can use uranium or other heavy-ion beams to generate about 4,000 kinds of radioisotopes, including about 1,000 that were previously unknown. In this way it enables researchers to find new radioisotopes and study the origin of the elements.

## Nishina Center for Accelerator-Based Science (RNC)

### Leading the world through tradition and innovation

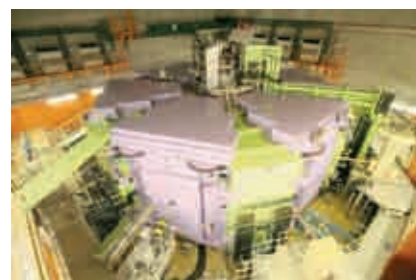
#### - Tradition and innovation -

Approximately 70 years have passed since Japan's first, and the world's second, cyclotron was constructed by Yoshio Nishina, in 1937. Since then, RIKEN has been promoting accelerator science year in and year out, and has maintained its position as a global front-runner.

RIKEN Nishina Center for Accelerator-Based Science (RNC) was established in 2006 in order to comprehensively promote accelerator science at RIKEN, and was named after Yoshio Nishina, "The father of modern Japanese physics." The center has bases at Brookhaven National Laboratory in the United States and Rutherford Appleton Laboratory in the United Kingdom, and has been promoting the development of the RI Beam Factory (RIBF), a next-generation accelerator facility. The mission of the center is to elucidate the mystery of material creation by thoroughly investigating the entity of the atomic nucleus and the elemental particles and to further develop technologies that can use the power of the atomic nucleus in industries such as agriculture and medicine.

The RIBF, currently being developed at the Wako Institute,

is an advanced research facility, equipped with the world's first Superconducting Ring the cyclotron (SRC)—a collection of fundamental accelerator construction technologies.



Superconducting Ring Cyclotron

The construction of the main facility was completed in 2007 and will soon be in full operation and conducting experiments.

By utilizing the RIBF, which was acquired over time using advanced technologies, and overseas research bases that promote international collaborations, RNC will continue to change the face of the new history of accelerator science as a global front-runner.

Number of full-time personnel: 141 (as of March 31, 2008)



### Director's Message

#### The time has come to launch the RIBF, a collection of fundamental accelerator construction technologies

Yasushige Yano, Director, Nishina Center for Accelerator-Based Science

**Q. Which project did you particularly focus your attention on in fiscal 2007?**

A. The development of the main RIBF facility, which has been promoted by the Wako Institute since 1997, was completed in 2007, and an initial experiment has just begun.

In June 2007, the largest international conference in the field of nuclear physics (International Nuclear Physics Conference (INPC)) was held in Japan for the first time in 30 years. On this occasion, we created a report titled "The discovery and creation of a new isotope of palladium 125," based on the first research achievement made in the RIBF; for this, we received praise from nuclear physicists from a variety of countries. Since the development of the main facility was only just completed in March 2007, it was an enormous challenge to have equipment adjusted and conduct experiments in order to gain research achievements within two



months, since the international conference was held in June. However, we did successfully deliver our first research achievements to the world at

the best opportunity to do so, as a result of the concerted effort made by the center researchers.

**Q. What are some of the noteworthy achievements of fiscal 2007?**

A. Makiko Nio, contract researcher (currently a research scientist) from Theoretical Physics Laboratory, as well as her colleagues, successfully calculated the electromagnetic force of a single electron to an accuracy of parts per trillion using RIKEN's RSCC supercomputer. This finding demonstrated a new determination of a fine structure constant to the world's highest accuracy. It will be the foundation for further understanding of the roots of natural phenomena.

**Q. What are your future prospects?**

A. We believe the RIBF, having the world's highest performance, should be international common property that can be used to generate new knowledge. The center is also promoting creative research through organic bidirectional collaborations. As part of the responsibility of being an organization that has been entrusted with a world-leading research facility (similar to the aforementioned), we plan to open the RIBF's doors to the rest of the world and continue to develop a smooth system to accept external research institutes establishing their research bases.

# Highly efficient ultraviolet LEDs being developed through “baton zone” between RIKEN and industry

The High-Power UV-LED Laboratory, a research team within the RIKEN Center for Intellectual Property Strategies (CIPS), has been developing ultraviolet light emitting diodes (UV-LEDs) for commercialization. The team has succeeded in emitting UV light of very short wavelengths through the development of a new mixed crystal technology. UV-LEDs are expected to be used as a new light source to replace fluorescent lamps. They will also be used for medical and environmental purposes. This team was set up as part of the Integrated Collaborative Research Program with Industry—an industry-academia collaboration program run by CIPS. The program is aimed at realizing speedy commercialization of research results through joint research with industry. In this joint research at RIKEN, emphasis is put on corporate leadership.

## Wide range of potential applications of UV-LEDs

The wavelengths of visible light range from 400nm (violet) to 800nm (red). Ultraviolet has shorter wavelengths and higher energy levels than violet, and various applications of UV are under consideration based on its wavelengths and high energy.

If highly efficient ultraviolet LEDs with wavelengths of 260 to 340nm are developed, it will be possible to create various types of light — including types that are gentle on the eyes or that mimic sunlight — through blending of many colors of fluorescent materials. Ultraviolet of 300 to 350nm has high potential for medical applications. Ultraviolet can be used to detect cancer cells and other diseased areas by injecting special pigments into the body and irradiating them with UV light to illuminate those parts. Furthermore, UV of around 265nm can effectively sterilize bacteria.

The High-Power UV-LED Laboratory has been conducting joint research with Matsushita Electric Works Ltd. as part of the Integrated Collaborative Research Program with Industry of the Center for Intellectual Property Strategies (CIPS) at RIKEN. The research has been implemented in combinations of RIKEN's crystal growth and device processing technologies with Matsushita's excellent device-mounting technology. Hideki Hirayama, deputy team leader of the Integrated Collaborative Research Program with Industry High-Power UV-LED Laboratory, summarized his team's goal in developing the new LEDs: “Our team has been trying to develop semiconductors for emitting UV light, which has more energy than blue light.”

## High efficiency from quaternary mixed crystals

When voltage is applied to semiconductor layers, electrons inside move from their original layer to a layer at a lower energy level. As a result, light corresponding to the energy gap (band gap) between the layers is emitted. This explains how an LED emits light. The larger the band gap, the shorter the emitted light's wavelength becomes. In 1993, Shuji Nakamura developed blue LEDs based on indium gallium nitride (InGaN). At that time, development of blue LEDs was believed to be impossible. Since his successful development, very bright, low-power-consuming blue LEDs have been spreading rapidly in various applications, such as traffic signals and billboards.



## Applications of ultraviolet LEDs

### Semiconductor white light source (long-life fluorescent lamp)

Essential wavelengths 260 ~ 340nm (Absorption of fluorescent band)

Highly efficient: ~ 40%  
Very long-life: several decades

Light source to replace fluorescent lamps

UV-LED array

White fluorescent band

Power source equipment

Highly bright white light

### Laser for high-density optical recording

Wavelengths ~ 250nm

UV-LD

Shorter laser wavelength → higher density

### Medical applications (skin treatments, cell identification with special pigments)

Deep UV light source 300 ~ 350nm

Cell tissue

Cancer cell and others

Capable of identifying diseased areas by using multiple pigments

### High-speed resolution of toxic materials

Titanium oxide (optical catalysis)

Pollutants (polluted water)

Pollutants: dioxin, PCBs, agricultural chemicals, endocrine-disrupting chemicals, organic chlorine compounds, etc.

UV-LED array 260 ~ 400nm

(Purified water)

- Decontaminating lakes, rivers and seas
- Decontaminating soil and air
- Decontaminating industrial effluent
- Applications in other fields

Ultraviolet semiconductor light source

UV-LED      UV-LDs

Miniaturization, higher efficiency, long-life

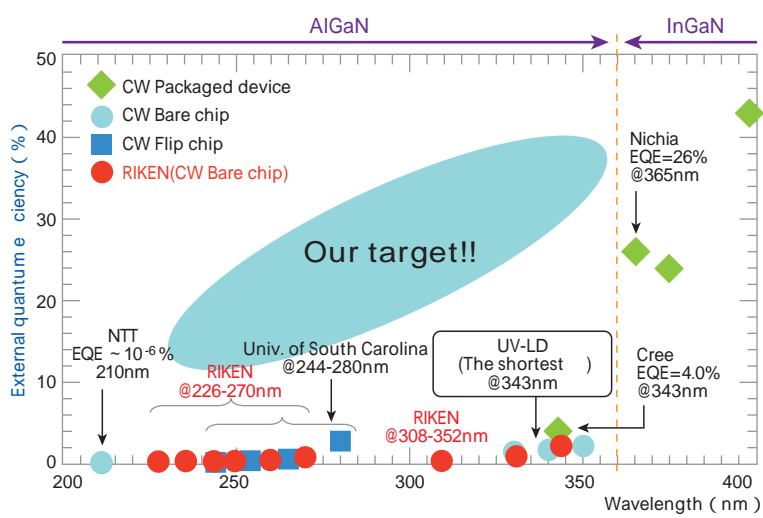
Other application fields: High-speed treatment of vehicle exhaust (pollution-free vehicles)  
Sterilization, home-use air cleaners  
Various types of optical information sensing (fluorescent analysis, surface analysis, UV sensors, etc.)  
Chemical industry, biochemical industry

Development of UV-LEDs, which can emit light with higher energy, began around 1997. Researchers have been using aluminum gallium nitride (AlGaN) as an LED material, but its output is 0.02 microwatts—too small for use in commercial applications, according to published reports. In September 2007, a joint group of the Terahertz Quantum Device team, led by Hirayama at RIKEN, and Saitama University developed a high-power LED that emitted 0.15 milliwatts of light with a wavelength of 227.5nm. The group also developed LEDs capable of emitting 1mW of 253nm light, 1.65mW of 261nm and 3.3mW of 273nm. These wavelengths are in the band where UV is effective in killing germs. Behind the success is the use of new LED materials and improvement in quality of the basic layer (buffer layer).

In 2000, Hirayama developed a material based on quaternary mixed crystal composed of AlGaN and a small volume of indium. His new material can emit light several hundred times stronger than other similar substances. LEDs are produced through the metal organic chemical vapor deposition (MOCVD) method, in which gasified organic materials containing LED elements are used to grow LED crystals on the substrate. It had been difficult to produce such quaternary mixed crystal because the temperature at which indium can be added to AlGaN crystal is 400 degrees lower than that at which stable AlGaN crystal can be developed.

But Hirayama discovered that if the volume of aluminum gas flow is increased during development of LED crystal, indium can be added at a much higher temperature. “After the discovery, through much trial and error, we tried to find a better combination of gas flow volume, temperature and material composition to improve the light output of our LEDs,” he said.

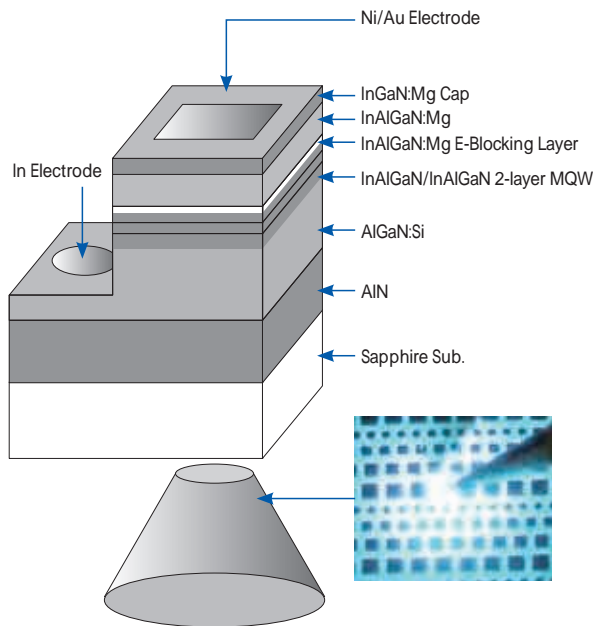
In order to develop clear crystal, a stable foundation is indispensable. The group began to improve the quality of



External quantum efficiency of nitride-based UV-LEDs  
The external quantum efficiency is the ratio of the number of photons emitted from the light-emitting device to the number of electrons injected into the light-emitting layer. In the wavelengths region shorter than 360nm, the external quantum efficiency stands at only several percent overall. The research team aims at improving the efficiency of LEDs in this wavelength band.

### Structure of 340nm-band LED

A buffer layer as the foundation was initially formed on a sapphire substrate. An n-type layer, light emitting layer, p-type layer and others were formed on top of the buffer layer. The light-emitting layer is quaternary mixed crystal. The challenge the team is facing is to find a way to effectively dope the p-type layer with substances.



### 'Baton zone' between RIKEN and companies

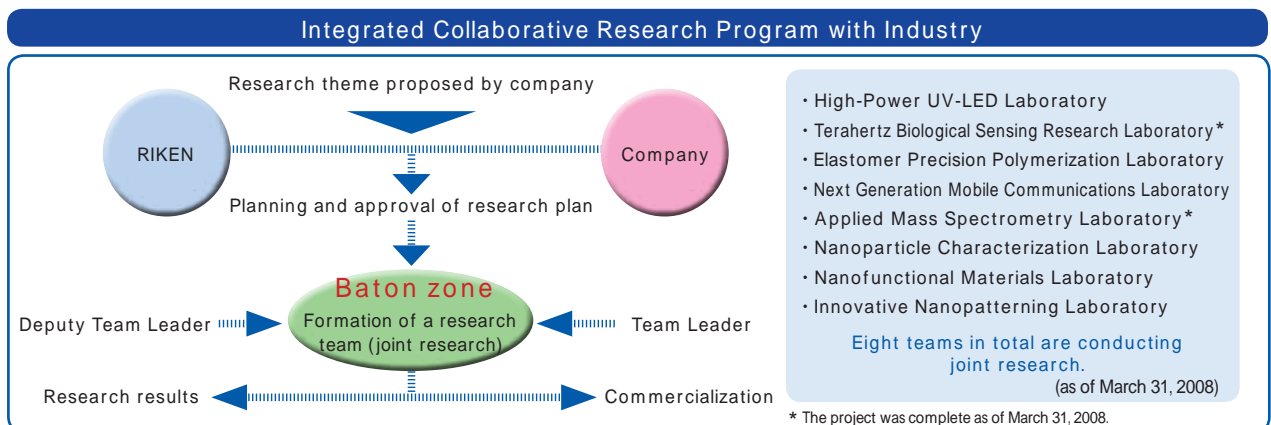
Industry-academia collaboration via existing Technology Licensing Organizations (TLOs) can be quite difficult, not only in the speedy exchange of experienced-based knowledge but also when commercializing scientific results. RIKEN's industry-academia collaboration programs consist of joint research with industry, in which corporate partners take the lead. This is the first time in Japan for companies to take the lead. Introduction of the 'baton zone,' in which research activities and commercialization efforts run in parallel, is aimed at smoothly commercializing research results.

Kenji Tsubaki, team leader of the Integrated Collaborative Research Program with Industry High-Power UV-LED Laboratory, said: "Matsushita Electric Works Ltd. is conducting this joint research to use RIKEN's UV-LED development technology to develop not only the company's lighting equipment business but also new business opportunities. RIKEN is flexible and provides an environment for us to conduct the research without restraints." Hirayama also stressed the merits of the baton zone approach, saying that RIKEN's original technology can be merged with the rich background technology owned by its corporate partner, which helps accelerate research activities.

"Our challenge is to improve the emitting efficiency of the LEDs. Their internal quantum efficiency has reached 50%. But the overall efficiency of the equipment stands at a few percent. The overall rate should be raised to 30-50%," Hirayama said. Tsubaki added: "We aim at commercializing UV-LEDs in the near future. We also want to accumulate more technology necessary for commercial production of LEDs through this project."

RIKEN and its corporate partner will continue tackling these challenges.

the aluminum nitride (AlN) crystal of the buffer layer for that purpose. The group has developed the ammonia pulse-flow multilayer growth method to develop high-quality AlN crystal as the buffer layer on a sapphire substrate. In the new MOCVD-based method, AlN crystal is developed through the continuous supply of aluminum material gas and pulsed supply of ammonia gas. In addition, another layer is developed through the continuous supply of the aluminum material and ammonia gases. The layer formed through the pulsed supply reduces gaps in atom positions between crystal lattices with different inter-atomic distances on the substrate, while the layer made through the continuous supply keeps the flatness of layers in the atomic level. The alternate development of the two types of layers also helps prevent cracks. As a result of these efforts, Hirayama's team has raised the emitting intensity of LEDs by another 50 times.



## Center of Intellectual Property Strategies (CIPS)

### Using a “baton zone” to make RIKEN that is useful to the world

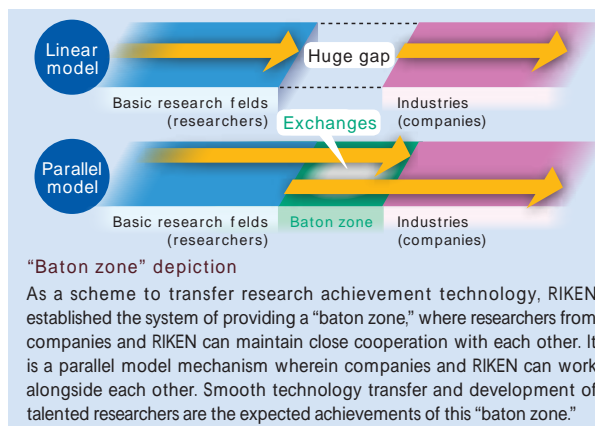
The Center of Intellectual Property Strategies (CIPS) was established in April 2005 in order to implement one of the Noyori Initiative policies, namely that of making “RIKEN that is useful to the world.” The objective of the center is to efficiently create intellectual property from RIKEN's excellent research achievements and effectively feed it back to society in cooperation with industry.

CIPS acts as a gateway between RIKEN and society, and has functions which are significant throughout RIKEN's activities, such as the creation of intellectual property from research achievements, cooperation with industry through licensing and collaborative research, etc., and the acquisition of external and competitive funding. In addition, the center is working on the establishment and implementation of a “baton zone”; this is an even faster and more efficient technology transfer scheme.

As part of the “baton zone” implementation program, “Integrated Collaborative Research Program with Industry” and “Collaboration Centers Program” commenced in 2004 and 2007, respectively.

Both focus on the needs of companies and promote collaborative research in problem solving projects initiated by companies.

Number of full-time personnel: 97 (as of March 31, 2008)



### Director's Message

#### Feedback of research achievements to society, and contributing socially through research

Shigekazu Saitou, Director, Center for Intellectual Property Strategies

#### Q. What are some of the noteworthy achievements of fiscal 2007?

A. Public research organizations, like RIKEN, conduct activities to assert the rights of research achievements as patents, and then offer the use of those patents to companies. These days, universities are also making a strong effort to conduct these kinds of activities. However, a problem arises when thinking about how to use an invention after it has already been created—this delay means it can be too late for the invention's effective use. In order to promote the world's most cutting-edge research and make excellent achievements, it is necessary to overcome this difficulty. Moreover, as research themes and researchers themselves are inseparable, it is probably natural that researchers occasionally put in less effort on a research theme that they are reluctant to investigate. Nevertheless, in order to make research achievements useful to society, I consider it necessary for a research institute to have a policy or a character of targeting research themes that can be useful to society. You could say that it is a type of social contribution through research.

By RIKEN efficiently adopting the research themes and resources of companies, CIPS has been able to focus its energy on facilitating and operating a research system that pleases both RIKEN and companies. This is what the “baton zone” between RIKEN and industries is intended for.

Through the “baton zone,” where companies and RIKEN share

common objectives and move in the same direction to transfer research achievements and technologies in daily research cooperation, remarkable progress was made in 2007 including the following:

1. The establishment of three collaboration centers (Olympus Optical Co., Ltd.; Tokai Rubber Industries, Ltd.; and, Toyota Motor Corporation).
2. The implementation of business that puts RIKEN technologies (such as SNP typing and molecular imaging) into practice in cooperation with companies.
3. The completion of the “RIKEN-WAKO Incubation Plaza.” This facility is located adjacent to RIKEN and is used as a “baton zone” where research ideas for use in RIKEN ventures are made available to RIKEN by companies.
4. The creation of a strong baton (drug patent)—commencing a baton zone development in the field of drug discovery.

#### Q. What are your future prospects?

A. We will continue to provide feedback regarding our excellent research achievements to society based on a trusting relationship with individual researchers. Likewise, using our continued trusting relationship with companies as the cornerstone, we would like to further improve our organizational coordination and social contribution, with a view to developing new industrial areas.