MESSAGE

Full Research as a Growth Medium for Researchers

FEATURE

Health and Science Technology
Predictive Diagnosis and Risk Reduction of Diseases

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Research Hot Line

In Brief
In what way can those who work at the National Institute for Advanced Industrial Science and Technology (AIST) expect to grow?

The people who make up AIST include not only those engaged in research but also those involved in research management. Some of these people will spend their entire careers at AIST, while others will spend only a few months or years with us. Furthermore, both “research” and “research management” cover a lot of ground. Research activity can vary widely in content depending on the field. For this reason, one person’s time here may be very different from the next person’s. But even though their activities may differ, they must somehow stay connected. I believe that every organization must offer something unique in terms of what its members gain from working there and how they grow. I believe AIST offers this unique environment.

For anyone who seeks to join and work within an organization, the potential for growth is usually a deciding factor. Even the motivation for joining seems to be an organization’s social prestige or its efficacy as a stepping stone to other jobs. A more fundamental motive often lies beneath those superficial considerations, and that is the organization’s unique possibilities for personal and professional growth. This is a positive motivation, for it is only when people use this criterion that an organization acquires members truly suited to carrying out its purpose. In other words, this is a necessary condition for any organization to play an effective and uniquely meaningful role in society.

AIST does indeed offer unique growth possibilities, but it is necessary that we elucidate them from time to time to ensure that all of us share the same understanding. It is also vital that every one of us works continuously to further develop these possibilities.
Before examining the special nature of professional growth at AIST, let me first express my personal views on the subject of growth. The first necessary condition for people to grow in their work is that they have an overarching goal, and secondly, that they be provided with an environment conducive to achieving that goal. By overarching, I mean "global" as opposed to "local" — in other words, a goal whose intent is to make a real difference to society. The criteria for such a goal do not include whether it helps one advance to a high position or secure generous research funding. I am not opposed to such aims, but I do not believe they have much effect on a person's growth. For someone involved in research, these are things that may be gained when others recognize the value of one's research management skills or research results; they should be regarded as outcomes, not goals. These superficial dreams will contribute nothing to a person's development. The single biggest factor affecting a researcher's professional growth is whether he or she has a goal formulated with the intent of making a difference to society. By defining the relationship between one's research and society, it requires the researcher to outline the social implications of his or her research topic. And this is the first step to filling a major condition to be met before one can be considered an independent researcher: social responsibility. The second condition, that one be provided with an environment conducive to achieving such a goal, requires no explanation.

Now let us see how all this applies to AIST in general and its researchers in particular. The overarching common goal of the Institute is to generate industrial technology that will contribute to sustainable development. As long as this remains an abstract concept, it will have no special impact on our researchers, and accordingly, it will have no positive effect on the Institute's outcomes. This goal is only meaningful when it has clearly shaped each researcher's selection and pursuit of a research topic as seen in a realistic mechanism for contributing to the goal and a practical research plan. This is not always easy.

What sort of technology is necessary for industries that contribute to sustainable development, i.e., "sustainable industries"? Some examples are technology for environmental monitoring, restoration of degraded environments, renewable energy sources, energy conservation, design of sustainable products, sustainable manufacturing (as well as inverse manufacturing), waste management, life-cycle management, and environmental conservation. As even a cursory look at this list reveals, these are not solutions that can be developed within the confines of a single traditional field of technology; rather, they demand a synthesis spanning multiple fields. This means that each researcher needs to work with researchers in other fields even while remaining grounded in his or her own field. Moreover, the kind of cooperation required is often something with which no one has prior experience, necessitating the development of new models of cooperation and a common language to facilitate dialogue between different fields. In essence, it requires the creation of an ad hoc discipline.

This type of technological research raises another, more fundamental issue, and this concerns the science supporting such interdisciplinary research. In most cases, when one creates an ad hoc discipline, one needs to return to the basic science underlying the disciplines one seeks to merge. However, in the case of technological research for sustainable industry, we sometimes find that, in fact, there is no basic science to return to. Consider, for example, the field of waste-management technology, specifically underground disposal of radioactive waste. The key here is the long-term structural stability of the ground in which the waste is buried. But, we know that it is currently difficult to make reliable predictions concerning ground stability owing to our insufficient understanding of the way the changes in geologic strata and transfer of substances.

What is the current state of scientific knowledge? Research into the microscopic structure of matter has progressed, yielding fairly detailed knowledge regarding even the elementary particles. Yet our macroscopic understanding of things like plate tectonics remains rudimentary. There is a serious reason for this seemingly illogical imbalance. It is widely assumed that scientific knowledge is neutral and balanced because the driving force behind it is the pure intellectual curiosity of scientists. But scientists are human beings and as such are often caught in the spirit of the times in which they live. The fifteenth century, when modern science first began to blossom, was the golden age of navigation — the Age of Exploration, when European civilization, at that time the center of scientific knowledge, was bent on exploring every corner of the earth. Scientific curiosity and the impulse to amass material wealth reinforced one another to create the spirit of the age — the impulse to journey forth as far as possible. And in one form or another, that
spirit has continued even to today. In response, science has ventured not only as far out as possible by means of space travel but also as far into matter as possible by means of microscopic observation. Such exploration was motivated by curiosity to discover what lies beyond, or within, and this curiosity was quickly gratified thanks to the development of the telescope and the microscope as tools. In addition, the knowledge gained through observation was organized into theoretical systems, which in turn gave rise to further knowledge.

Scientific curiosity — the urge to explore the unknown — tends to focus on explaining the nature of things and phenomena that exist in nature, and science has progressively revealed to us the universal and unchanging aspects of existence. As a result, it seems that science has concerned itself only secondarily with the process of change as it affects these existing phenomena. Speaking in terms of the two major theories of the ancients, that matter is made up of atoms and that all things are in flux, we might say that human curiosity has always been heavily biased toward the atomic theory. This predilection overlaps with and has thus been reinforced by the desire to make use of that which exists in nature. The historical changes that such entities have undergone are not as pertinent to the fulfillment of that desire.

The extended Age of Exploration has also been an age of unrestrained development. Today, however, we are entering the age of the environment, in which development must be restrained by the limits of sustainability. The central ideal of the new era is protection of the global environment. Thus, the key object of intellectual curiosity must shift to how that which exists in the present will change over time, a question corresponding to the ancient notion that all things are in flux. Increasingly today, experts are pointing to our lack of knowledge in this area as a key problem and calling for scientists to accumulate a new kind of basic knowledge to answer questions that cannot be answered by applying our existing store of scientific knowledge.

Thus we can see why one often finds, when attempting to develop technology that will be of use to industry, that the basic knowledge on which the desired technology must be built does not exist. And the more the desired technology differs qualitatively from the technology of the past, the greater the probability that this phenomenon will occur. There is no doubt that if the technology we are attempting to develop at AIST is to assist the transition to sustainable industry, it should be qualitatively different from the technology of the past. The need for a highly accurate theory to predict the shifting of matter within the geologic strata in order to develop a technology for underground disposal of radioactive waste is only one example among many. A great deal of new basic knowledge will be needed to realize the technologies required for sustainable industry.

As the foregoing makes clear, AIST researchers are called upon to conduct basic research in new areas with the understanding that a lack of basic knowledge has hindered research into industrial technology. Here we see a new image of the researcher that was never envisioned in traditional science and engineering. The topic of such a researcher’s project may shift midway from engineering to science. In some cases the same researcher may continue with the changed topic, while in other cases the original researcher may hand off the new topic to another. In either case, the fact remains that any researcher involved in these areas must have a deep understanding of science as well as engineering, and this can raise difficulties. However, at AIST our researchers overcome such difficulties, motivated by the shared overarching goal. This is the first characteristic of AIST.

The second characteristic is that the institute provides an environment conducive to research carried out with the overarching goal of creating sustainable technology. On the basis of the foregoing discussion we know that such an environment is, above all, one that supports the process of creating ad hoc disciplines of study and moving back and forth between science and engineering — that is to say, an environment that supports the process of switching between different modes of thinking. This process is not something that was traditionally required of researchers, and for that reason it is fair to say that the structure for supporting it did not exist previously in any public research facility. At universities, for example, science and engineering have always been clearly separated from one another; even if the two were linked in name, they were never fused in deed. The different fields of study that must be merged to create an ad hoc discipline have always been treated as discrete disciplines and have carried out both research and education separately. Under these circumstances there was never even an awareness of the possibility of such a process. Thus, if there is one unique thing that AIST offers the people who work here in relation to professional growth, it is an environment that supports this process. This environment is what we call Full Research.
We at AIST regard the concept of Full Research as the foundation on which the Institute’s mission is carried out. Full Research was conceived as a mechanism for fostering the development of knowledge born from basic research into practical technology that can contribute to advances in industry. Thus it can be regarded as one approach to research management. However, as the preceding discussion makes clear, it also provides a setting conducive to growth for a certain type of researcher. Following this line of thought, we can say that it is setting that nurtures researchers accomplished in two types of thinking, the analytical thinking characteristic of science and the synthetic thinking characteristic of engineering, and further, who can understand the position of their own academic discipline relative to other disciplines. In such a setting researchers use both analysis and synthesis as appropriate to a given phase of research; they respect and accept other disciplines when mapping out a course of research; and they willingly learn and cooperate. This is one ideal image of the type of researcher that the research community needs today. It is diametrically opposed to the traditional image of the researcher as one who works independently, shut off from the outside world, totally absorbed in one field of study and dedicated exclusively to expanding the frontiers specific to that field. Both types of researcher are necessary to scholarly research, that is, to the solution of the myriad issues facing humankind, and neither is more important than the other. The important thing is that any given research facility be deliberately and clearly designed to foster one type of researcher or another.

AIST has been designed with an awareness that an organization is, by nature, something formed by people. Our organization is designed not to restrict or constrain people, but to provide settings that offer new possibilities. It is up to each individual researcher to take advantage of these possibilities. AIST offers the possibility for people to learn on their own and develop as members of a new breed of researcher while working toward the shared research goal of developing sustainable technology. In this sense, AIST is not only a research facility but also an educational institution in the broadest sense of the word — a learning institution. Here both researchers and research managers grow as they acquire the unique abilities needed to support their particular type of research.

Another principle on which AIST operates is that an organization can best perform its mission when the abilities of each of its members are utilized to the fullest. It is our hope that this principle will come to be applied throughout Japan. In our own case — applying it to people conducting basic research oriented to industrial technology — we would like to be a place where universities, research institutes, and corporations network with one another, providing a setting for varied yet systematic learning. Recently there has been considerable emphasis on the need to nurture human resources in the area of science and technology. Needless to say such activity cannot be focused solely in the creation of new organizations. All existing facilities need to think about partnering to create new learning environments. I would like 2006 to be the year such a partnership takes shape, with AIST leading the effort.
Everyone hopes to remain healthy

Everyone hopes to remain healthy, and upon experiencing illness, to return to good health rapidly. The maintenance of good health allows one to fully address one’s work and hobbies, and to enjoy everyday life. Some individuals lead a very cheerful life in spite of disease. In particular, perfect health is generally very rare for senior citizens. However, such individuals also hope to live a happy life without serious diseases, such as cancers, cardiac diseases, cerebrovascular disorders, and diabetes.

If the population requiring hospitalization expands, the social vitality will decline and the national finance will become tighter, due to the swelling cost of medical insurance. It is therefore necessary to minimize the health risks present in the social environment, to maintain and enhance the health of individual residents, and to establish systems for medical examination and treatment in order to discover and cure diseases before they become serious.

Challenges in health engineering

In order to facilitate the early identification of disease symptoms, methods must be developed for precise physiological testing, to check for organ disorders. More precision is also required in existing tests (e.g., a check of blood protein changes, measuring cellular activity in organs, and visual tests with contrast media). Furthermore, additional improvements are required in the treatment of symptoms associated with serious diseases identified via the above tests. On the other hand, an improvement in lifestyle is also necessary, to reduce the incidence of lifestyle-related diseases. The guidelines for necessary lifestyle improvements should be established based on scientific studies.

Beyond physical health, simultaneous efforts must also be made to pursue appropriate methods for maintaining a balanced state of mind, which fosters a mentally and physically healthy life. Numerous factors in the living environment pose threats to the public health. It is also important to develop technologies to measure and remove these factors.

Strategic targets in life science at AIST

To meet the aforementioned requirements, AIST established the following five strategic targets in life science in April of 2005, when AIST initiated its second stage:

- Promoting preventive medicine through
Engineering at AIST for Better Human Health

Hisao Ichijo
Director, AIST Shikoku

Health engineering is a developing field for which a comprehensive system of engineering has not yet been established. Also, its relevant concepts and technological subjects have not yet been defined. However, it is expected to emerge as a new field of industrial technology, to be promoted by AIST towards the establishment of a safe, secure, and sustainable society based on technologies to maintain and enhance health, rather than simply dealing with diseases and patients.

In the Shikoku region, where the decline and aging of the population continue, there are great expectations for the health-related industry. This sector therefore forms an important part of the plans of Shikoku’s industrial cluster. Many leading companies in the Shikoku region are engaged in the development of welfare and nursing equipment, health and functional foods, diagnostic and testing devices, and medical apparatuses.

At AIST Shikoku, departments in charge of collaboration between industry, academia, and the administration will cooperate with the Health Technology Research Center, which was opened in April of 2005, to promote activities as a center for research and partnership in the development of the health industry in Shikoku. In addition, the Next-generation Bio-nano Industrial Technology Workshop was established in 2004, and has initiated examinations to make project proposals linking the nano- and bio-technological fields, in cooperation with industrial, academic, and administrative representatives.

We at AIST Shikoku plan to establish a forum for the participation of researchers from businesses/corporations, universities, and public institutions who have been engaged in research and development in close collaboration with us, via joint research projects and technical consultations. Also planned are activities to further the formation of health industry mini-clusters, with the Health Technology Research Center as their hub.

Health engineering at AIST and the Health Technology Research Center

AIST research fields extend to nano-technological materials and information science, to conduct health-related studies in diverse areas. Research subjects cover, for instance: anthropometry, drug delivery systems, new diagnostic technologies, artificial organs, and risk reduction in human environments. The strong points of AIST lie in its capability to challenge new tasks linking the life sciences to other areas.

We have 14 research units in the life science area, which respectively address different projects concerning the predictive diagnosis and prevention of diseases. In addition to genomic studies, we also conduct, for example, physiological research on the influence of physical exercise on circulatory organs at the Institute for Human Science and Biomedical Engineering.

The Health Technology Research Center was recently opened at AIST Shikoku, and is expected to serve in the integration of health engineering-related studies at AIST. We hope that applicable studies underway at many AIST research units will be linked to each other, and generate excellent achievements in collaboration with external businesses and institutions, thereby furthering their contributions to the development of the health industry.

the development of technologies for early diagnosis, and realizing tailor-made medicine based on genomic information;

• Realizing safe and effective medicine with detailed diagnosis and regenerative medicine;

• Extending the healthy lifespan by evaluating and rejuvenating human functions;

• Producing bio-products with an efficient production process, using biological functions; and,

• Establishing an infrastructure to promote the development and application of medical equipment and to support a more competitive bio-industry.

We thus place an emphasis on health engineering, featuring diagnostic and other related technologies.
Promoting Health through Technological Approaches

Tomokuni Kokubu
Director, Health Technology Research Center

Health maintenance as a social task

In the 21st century, Japan is experiencing a typical sociological aging. The percentage of senior citizens in the total population continues to rise, with the country’s population expected to take a downward turn in 2007, due to the declining birth rate.

This will lead to serious social phenomena, including a diminishing labor force and a swelling in national medical expenses. The latter is expected to grow to ¥41 trillion in 2010, from ¥30 trillion in 2001 (estimation by the Ministry of Health, Labour and Welfare).

To help to provide a sustainable, secure, and fulfilling life for national citizens under these circumstances, the Japanese government is examining policies to deregulate working age restrictions for older people, and to reduce medical expenses via disease prevention and health maintenance/enhancement.

The social importance of health maintenance and enhancement is drawing increasing attention in the U.S. and Europe, as well.

Technological approaches to health

The Health Technology Research Center was established in the Shikoku region in April of 2005 for solving the above-mentioned social problems, and it has 22 regular members. This center is designed to contribute to society, and promote health-related industries, through engineering studies on the analysis of physical health as physiological phenomena, thereby maintaining and enhancing the healthy state.

Humans receive diverse stimuli from both inside and outside of the body, via signs from perception and movement. Human health is maintained by the homeostatic mechanism that arranges the central nervous, immune, endocrine, and other internal systems, in response to such stimuli (Figure 1).

Therefore, a very wide range of research fields must be covered in health studies, including the interaction between humans and the natural or living environment, the retention of physiological homeostasis, the physiological and psychological impacts of various stresses in social life, and the recovery from physical or physiological dysfunctions.

Based on such studies, we must ultimately determine methods to maintain and enhance the healthy state of human individuals, both mentally and physically. Therefore, the major goals of health engineering lie in: (i) identifying the physiological state of individuals by integrating information from genetic, cellular, individual, and other perspectives; (ii) establishing technologies to treat problems identified in (i); (iii) discovering, analyzing, and evaluating risk factors (existing or unknown) that threaten health; and (iv) establishing technologies to effectively protect individuals from the risks identified in (iii).

Health engineering thus has many problems to solve in its pursuit of health maintenance and enhancement, which was initiated only recently. In practical research activities, we must accumulate knowledge from diverse related areas including biotechnology, human engineering, environmental engineering, information technology, materials engineering, and social engineering, and integrate these technologies with new technologies specifically developed in the pursuit of health engineering.

AIST Shikoku has been engaged in advanced research at the global level, on such subjects as the technologies and devices for predictive diagnosis, based on the performance analysis of biological materials involved in cancers and lifestyle-related diseases. We have also developed technologies to remove and detoxify trace toxic substances, in order to ensure potable water and medical solutions in living areas.

The Health Technology Research Center
is designed for the further promotion of these studies, and also aims to establish advanced diagnostic technologies capable of identifying the physiological status of humans in the pre-clinical (“mibyo”) stage, thus assisting disease prevention. For this purpose, the center plans to incorporate a research team for the analysis and assessment of functional materials in the human body, such as saccharides and glycolipids possessing many unknown properties in vivo. The center also seeks to promote the development of technologies to eliminate diverse risk factors present in the living environment, and to feed back these achievements to society to provide individuals with a safer life (Figure 2).

**As a center of health engineering research**

As described above, health-related studies require the assistance of a very wide range of scientific fields. We at the Health Technology Research Center therefore plan to promote its studies effectively, through close collaboration with AIST research units in charge of health engineering-related studies, the Ministry of Health, Labour and Welfare, and related businesses and universities. The center is thus expected to promote health-related industries, as well. Shikoku is a typical region in Japan, which is characterized by a declining birth rate and an aging population. The Shikoku regional governments expect lifestyle-related and other diseases to expand rapidly. We hope to contribute to the society of Shikoku and other parts of Japan, through research and development at the Health Technology Research Center, as a hub of promotion for health-related industries (Figure 3).

Health-related research will continue to expand throughout the world. We believe that this center will contribute to the development of health engineering as a young scientific sector, and to the promotion of health-related industries, through the development of technologies for predictive diagnosis, and for the reduction of risk factors threatening the public health.
Presence of various health risks

The increasing sophistication and globalization of industries will provide great convenience and possibilities for our society. Concomitantly, the potential for health risk caused by a wide variety of chemical substances or previously unknown pathogenic bacteria and viruses are expected to increase in the surrounding environment (i.e., the living environment). Arrival of various substances may enhance the risk of health damage, because such substances can be hazardous even in trace amounts, or accumulate without notice due to a long latency period. In addition, recent worldwide viral infections suggest that the globalization of our society may produce harmful health effects on people all over the world. In order to sustain social development, the maintenance of human health by reducing these risks is therefore critical. Health risk factors (Figure 1) interact with the human body and result in symptoms, particularly when entering into the body. Technological inventions for preventing risk factor invasion via removal or external detoxification are important challenges required for health risk reduction.

Basic technologies to resolve health-related issues

First of all, materials that recognize and capture objects harmful to health (e.g., ions, molecules, and microorganisms) in a highly selective manner are essential to the development of technologies to deal with health hazards. For health risk reduction in a variety of surroundings, it is very important to specifically recognize the minimal concentration of noxious objects, even when embedded in a multi-component system.

We have studied the recovery of uranium and lithium from seawater, and have created original technologies to design materials that are capable of recognizing and isolating specific target ions in a multi-component system, such as seawater. We have proposed an ion-templating technique for designing cation exchangers. Ion exchangers with sieving effects on target cations are produced by mixing target cations (template ions) with inorganic oxides to form composite-oxide precursors under specific conditions. The precursors are then treated with acids to elute only the template ions, without altering the crystal structures of the matrices. Using this technology, we have succeeded in developing the first practical lithium-ion exchanger to selectively adsorb lithium ions from seawater. To date, ion exchangers specific for sodium or potassium ions have been developed. We have successfully conducted joint research with industry on the production of ultra-high purity potassium chloride and sodium chloride, by utilizing the respective exchangers.

We have challenged to extend the concept of ion sieving to the separation of anions, and recently have demonstrated that inorganic layered compounds specifically adsorb oxo-anions, when interlayer distances are appropriately adjusted. Our final goal is to develop materials that can selectively recognize different substances in the size range from < 1 nm to 100 nm, including organic compounds and viruses (Figure 2). To achieve this goal, we design appropriate capturing sites based on the chemical properties and sizes of the target compounds.

Figure 1 : Multiple risk factors in the living environment
substances. These systematic approaches are expected to be a significant methodology to reduce health risks.

**Technologies to reduce health risks**

I would like to introduce several unique approaches relating to health risk reduction (Figure 3). Nitrate ions (NO$_3^-$) are known to cause developmental disorders in infants (methemoglobinemia) and to have carcinogenic potential. Water quality standards for drinking water provide that the concentration of NO$_3^-$ should be 10 ppm or lower. We have recently developed an inorganic layered compound that sieves out NO$_3^-$ ions. Adjustment of interlayer distances by controlling the types and composition of constituent metal ions generates the sieving effects. This ion exchanger has been demonstrated to adsorb trace quantities of NO$_3^-$ in seawater. Owing to its very high specificity, the NO$_3^-$ ion exchanger can selectively adsorb NO$_3^-$ ions and effectively remove them in an aqueous system containing anions other than NO$_3^-$. According to data obtained from the measurement of groundwater quality in 2003, approximately 7% of the groundwater in Japan exhibits NO$_3^-$ levels exceeding that defined by the water quality standards. The NO$_3^-$ ion exchanger can provide safe water, for example, in emergency situations caused by disasters, in which utilization of groundwater may become necessary.

A similar idea has been adopted for continuous antibacterial activity in aqueous systems, which is a completely different attempt. Silver-based antibacterial agents are safe and well-known, but function poorly in systems containing chloride ions. We have inserted silver ions or silver complex ions between layers of inorganic layered compounds to ensure sustained ionic release, and thus continuous antibacterial effects regardless of the presence or absence of chloride ions. Antibacterial effects in seawater have already been observed with some complex ions. The development of methods for maintaining these effects will be an important issue hereafter.

Unlike materials previously used for resource collection, recognition materials for health risk reduction must be composed of safe substances. To maximize effects, nano-sized recognition materials need to be dispersed and embedded in porous polymer matrices, prior to being shaped. Therefore, the development of a nano-particle fixation method is also required as a basic technology to overcome nano-risks. We hope to realize health risk reduction in the living environment, through the development and integration of these advanced technologies.
Fusion of Biotechnology and Nanotechnology: What It Brings

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Professor, Graduate School of Engineering, Nagoya University

Nanotechnology breaking fresh ground in medicine

To advance the creation of new technologies through a combination of nanotechnology and biotechnology, we have undertaken research on the basic technologies shown in Figure 1 (single-molecule DNA analysis, diagnostic nano-bio devices, and single-cell diagnosis), and the combination of them. This research provides a foundation for the practical application of new systems that enable us to comprehend physical conditions, and diagnose diseases based on individual genetic information. Mobile or wearable devices for evaluating an individual’s condition at home are the fruition of these research efforts. In addition, our recent invention to fuse semiconductor nanoparticles and biomolecules has attracted attention. This innovation has produced encouraging results and provided a new perspective on nanotechnology. It may lead to “super” early diagnosis, as well as new cancer treatments. In the future, these research efforts will contribute to the development of the predictive diagnostic technology, facilitate the transformation of treatment-oriented health care into a prevention-oriented one, and realize an active aging society.

Development of a genetic diagnostic device requiring only a fraction of the blood

Using our semiconductor technology, and in collaboration with Kyoto University and Starlite Co. Ltd., we have developed a technology for producing plastic chips for genetic diagnosis at a lower cost. An electromicrograph of the chip is shown in Figure 2. This extremely small chip possesses 10 microchannels, with a width and depth of 50 µm, which allows the simultaneous analyses of blood samples from 10 individuals. We have succeeded in placing 10 channels within a 1-mm width. By expanding this technology, one chip with a size of several centimeters will be sufficient to analyze the genes of more than 1,000 individuals. Moreover, a highly sensitive device that can rapidly analyze genetic information on chips and make diagnosis has been contrived.

Figure 2 illustrates the genetic diagnosis of lung cancer. Conventional genetic tests require 1-2 days to obtain the results. Our device has successfully shortened the diagnostic time, requiring approximately 10-20 minutes. In addition, the amount of blood necessary for testing has been reduced to 1/100 or less. Our technologies will also lower the cost of genetic testing to 1/10-1/100 or less, relative to previous tools. These improvements are believed to reduce the burden on patients. The system is roughly the size of a desktop computer at present, but will be downsized to the size of a laptop computer,
we have developed a new technology to fuse quantum dots with proteins. Using this technology, quantum dots can be fused to lectin molecules that specifically recognize cancer cells, or to antibodies that recognize specific proteins. These fusion quantum dots, together with single-cell diagnostic chips, are employed in the cytopathological diagnosis of cancer. As shown in Figure 3, the addition of quantum dots to cancer cells followed by irradiation with ultraviolet rays produces a bright green fluorescence resulting from the binding of quantum dots to the surface of cancer cells. In contrast, no fluorescence was observed in normal cells, due to the absence of an interaction between the quantum dots and normal cells. The presence of disease is revealed using this technology, which may detect cell populations as small as a few to several dozens of cancer cells. Cutting-edge diagnostic imaging systems, including magnetic resonance imaging and positron emission tomography are costly and do not detect cancer tissues smaller than 1 millimeter in size. Considering the above, the improvement of the sensitivity and accuracy of quantum-dot technology will lead to “super” early diagnosis and more effective cancer treatment.

Novel applications of nanotechnology to medicine

The devices and quantum dots mentioned above, as well as other technologies utilizing nanostructures can introduce new physical phenomena into the field of biotechnology, and allow us to invent unimaginable revolutionary technologies. For example, very small amounts of disease-related proteins present in cells will be detected using different types of quantum dots. Though fluorescence diminishes when conventional fluorescent reagents are used in combination, such an effect is not observed in quantum dots, which facilitate the highly sensitive detection of target proteins.

Furthermore, it has been elucidated that approximately 60 minutes of ultraviolet irradiation induces apoptosis in cancer cells, but not in normal cells, following the diagnostic test described above. Quantum dots absorb ultraviolet energy, a portion of which reacts with oxygen to generate noxious oxygen species, including the radical oxygen that causes apoptosis in cancer cells. Such an event may occur only when nanomaterials are used. Combining these technologies with an endoscopic approach, not only “super” early diagnosis, but also the treatment of detected cancer cells by inducing apoptosis will become practical. The development of technologies that integrate diagnosis with treatment is not fantasy (Figure 4).

Future perspectives

The application of nanodevices and quantum dots to the biomedical field has just begun. Further research will lead to the development of technologies that make the early diagnosis of diverse diseases possible. The fusion of nanotechnology and biotechnology will realize health care that has been considered impossible with conventional diagnostic tools and treatment measures.
A New Scheme of Adaptively Trainable Motion Image Recognition
Achieved World’s Best Performance for Human and Motion Recognition

A new scheme has been developed for automatic recognition of persons and movements out of a monitored video image, a key step of automatic video-surveillance such as an anti-crime camera. The method is an extension of adaptive learning recognition scheme based on the Higher-order Local Auto-Correlation (HLAC) feature extraction developed for two-dimensional static images. To cover the feature extraction of "target's movements" in motion images, HLAC was extended to Cubic HLAC (CHLAC). The technology is characterized by enhanced versatility, high speed and high accuracy.


Figure: Examples of human abnormal movement detection (Normal: walking through, Abnormal: tumbling over).
Doppler-free spectroscopy using continuous-wave optical frequency synthesizer

A continuous-wave optical frequency synthesizer was developed using a monolithic type continuous-wave optical parametric oscillator (cw-OPO) and an optical frequency comb. The cw-OPO was phase-locked to an optical frequency comb that was phase-locked to an atomic clock. The output frequency of the cw-OPO was frequency-shifted with an electro-optic modulator (EOM), which made it possible to tune the frequency continuously over 10 GHz. Furthermore, Doppler-free spectroscopy was performed using the optical frequency synthesizer for a cesium D1 line at 895 nm.

On-demand cell manipulation based on photo-induced cell capturing

A new photo-responsive cell culture substrate has been developed. The substrate was based on photo-responsive polymer, and cell adhesion to the substrate can be modulated by irradiation of lights with specific wavelengths without affecting cell viability. This substrate enables us to control the adhesion (capturing or removing) of individual adherent cells on our demand by irradiating spot light under a microscope, and is expected to provide an innovative technique to manipulate living and adherent cells.
Multi Cell Sorter on a Chip

We have developed a new method of particle retrieve for a chip-based multi-cell sorter. Optical gradient force can change direction of target dielectric particles, such as cells, and retrieve particles against hydorodynamic force by irradiation of a laser in a microfluidics device. We are putting the developed method to practical use of a multi-cell sorter in a chip for applications of life science and medical technology.

Development of a high strength Fe–Cr alloy without a brittle sigma phase using a novel powder method

Fe-48at%Cr alloy has been synthesized using mechanical alloying (MA) of Fe and Cr powder and consolidated using pulsed current sintering  (PCS). The obtained Fe-48at%Cr alloy has consisted of fine grains without a brittle sigma phase, which precipitated inevitably in Fe-48at%Cr cast alloy. Fe-48at%Cr alloy fabricated by the newly proposed process (MA-PCS) has showed a high strength of over 1GPa and a high elongation more 10% at room temperature.

Figure: Effect of milling time on mechanical properties of Fe-48at%Cr compacts.
An accurate method for quantum chemical computations of biomolecules

The fragment molecular orbital method (FMO) delivers the accuracy and generality of \textit{ab initio} quantum chemistry. It can be applied to chemical reactions, excited states and other complicated problems. Using the method on the AIST Super Cluster, we have been able to perform the world record all electron calculation of a system containing more than 20,000 atoms. To facilitate its application in the field of bioscience, it was implemented in a general quantum chemistry program GAMESS and is being distributed free of charge. The intra- and intermolecular interaction analysis is a promising tool for drug design and other applications.

![Interaction energy diagram](image)

\textbf{Figure 1: Interaction between thymidine Phosphorylase and its ligand (PDB:1uou).} Attractive (residues 77,79,152,167,171) and repulsive (residue 159) interaction between protein and its ligand constitutes useful information for drug design.

![Protein polarization](image)

\textbf{Figure 2: Protein polarisation by the ligand.} The difference in the electron density of the protein in vacuum and in the complex with the ligand is plotted. Areas where the density increased are shown as blue and the decreased areas are white. Due to the interaction with the ligand, polarisation is especially large in the area (indicated by the red frame) around the two oxygen atoms (red). Protein atoms are not shown.

New "Geological Maps of Volcanoes" were Published

New “Geological Maps of Volcanoes”, Miyake Jima Volcano and Iwate Volcano, were published. The series of “Geological Maps of Volcanoes” shows geological maps and eruption history of active volcanoes in Japan. These new maps discribe new distributions of volcanic ejecta, craters and the development history of the Miyake Jima (Miyake-Jima) and Iwate volcanoes. We hope these maps will help those who are interested in volcanoes, and will be useful to reduce damage from volcanic disaster.

![Miyake Jima map](image)

\textbf{Figure: A part of the geological map of Miyake jima volcano.} There are many fissure vents and pyroclastic cones on the flank of the Miyakejima volcano. Pyroclastic cones with "C" means newly recognized cones in the study of the geological map. At the summit area, the map shows the old caldera rim and the new AD2000 caldera.
Calibration of the Frequency Response of Photodetector Using Twice-modulated Light

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A system for calibrating hydrophone sensitivity by laser interferometry has been constructed at the AIST. The frequency response of the photodetector (PD) in the system is one of important factors in determination of total measurement uncertainty of the calibration. So a novel calibration technique using twice-modulated light was proposed. This technique can determine the frequency response of the PD with small uncertainty without using a standard PD or a standard modulator.

Figure 1: Photograph of the system for calibrating the frequency response of photodetector.

Figure 2: An example of the measured frequency response with reference to 1.5 kHz of a photodetector. The error bars show the uncertainty for each measurement.

Photochemical manipulation of structures and properties of liquid-crystal colloids

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In liquid-crystal colloids where colloidal spheres are dispersed in liquid crystals, we investigated photochemical manipulation of colloidal structures and optical properties. By modulating surface properties of colloidal spheres on the basis of photoisomerization of photochromic compounds, we achieved a control of aggregation and dispersion of the spheres. A variety of colloidal superstructures could be fabricated by illumination of appropriate patterned light onto the liquid-crystal colloids. In addition, we could manipulate light-scattering properties of the liquid-crystal colloids by photochemical modulation of phase structures of liquid crystals. It is strongly expected that the liquid-crystal colloids will be applied to practical devices in various industrial fields.

Figure: Light-induced aggregation and dispersion of micro-droplets in liquid-crystal colloids.
**Development of Hybrid Fast Neutron Spectrometer**

We developed a hybrid fast neutron spectrometer composed of three position-sensitive proportional counters and two surface barrier silicon semiconductor detectors. The hybrid spectrometer can measure energy and recoil angle of a recoil proton simultaneously. The spectrometer successfully gave a neutron spectrum with 1.7% energy resolution for a monoenergetic neutron (5.0MeV) beam.

![Diagram of the hybrid fast neutron spectrometer](image)

**Figure:** schematic drawing and photograph of the present spectrometer.

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**Fully Automated Two Dimensional Electrophoresis System**

Proteomic Device Team, Research Center of Advanced Bionics, AIST, has developed an innovative full-automatic 2D electrophoresis system in collaboration with Tokyo University of Technology, Sharp Corp., Toppan Printing Co. Ltd. and Astellas Pharma, Inc. This research has enabled us to reduce 2D electrophoresis time for longer than a day to around 1 hour. In the newly developed system, all the operations, such as injection of biological samples, isoelectric focusing, staining of proteins, rinsing, polyacrylamide gel electrophoresis and detection, are fully automated. This system has also realized highly reproducible 2D electrophoresis.

![Image of electrophoresis system](image)

**Figure:** Fully Automated Two Dimensional Electrophoresis System.
Collaboration Support by Ubiquitous Intelligence and Web Intelligence

We have been developing a collaboration support system targeting on event spaces since 2002 because event spaces have rich contents and interactions among certain interest groups and myriad sub-communities. We have been developing the integrated system by elaborately fusing web support systems based on cyber world interaction and onsite support systems based on real-world interaction. Users can easily and peacefully interact with both the support systems seamlessly causing collaboration among users more active. This is because the system is designed not to rob personal information secretly but to return greater benefit to the user as he/she wants.

Geological evidence of repeated giant Chile earthquake

Although the time since the preceding earthquake spanned 123 years, the estimated slip in 1960 Chile earthquake, which occurred on a fault between the Nazca and South American tectonic plates, equalled 250-350 years a worth of the plate motion. Geological record shows that the penultimate event occurred during 1575, and the average interval between giant earthquakes on this fault spanned 300 years. Two later earthquakes, in 1737 and 1837, produced little, if any, subsidence or tsunami at the estuary and they therefore probably left the fault partly loaded with accumulated plate motion that the 1960 earthquake then expended.
**A novel fabrication for surface microstructures on silica glass**

Two types of new apparatuses for surface micro-fabrication of UV transparent materials, based on AIST-original LIBWE (laser-induced backside wet etching) method, have been developed. One is an excimer laser mask projection system, and another is a diode-pump solid state laser beam scanning system. Both systems can micro-fabricate a silica glass surface of large area rapidly, and high aspect ratio of 60 was attained in a deep trench fabrication. Unlike conventional lithography methods, these apparatuses need no photo-resist, and can be operated under atmospheric pressure. The projection system attained 0.75 µm resolution and the beam scanning system can fabricate prototypes rapidly.

![Line patterned grating fabricated by laser beam scanning system using galvano mirrors.](image1)

**Conduction Mechanism in Semiconductor Spintronic Device Clarified**

Novel TMR (Tunneling Magneto-Resistance) devices composed of single-crystalline semiconductors with (Ga,Mn)As for ferromagnetic electrodes and ZnSe for tunnel barrier, were developed. The spin-dependent transport properties of the TMR devices were studied in detail. It has been confirmed with the semiconductor-based TMR devices that (i) large TMR effects can be obtained just like with the metal-based TMR devices, and (ii) anisotropic TMR effects reflecting hole characteristics of semiconductors can be demonstrated in contrast to the metal-based TMR devices. The results verify holding and transfer of spin information in semiconductor spintronic devices. This research will open the way to realization of spin transistors.

![A cross section transmission electron microscope of single-crystalline semiconductor TMR device consisting of (Ga,Mn)As and ZnSe.](image2)
Ricinus communis toxins are highly poisonous proteins once used illegally in the past. Against such bioterrorisms using toxins and pathogenic microbes in the form of the "white powders", we have to be prepared with facile detection and medical treatment methods. Recently, we developed an SPR (surface plasmon resonance) detection system applying synthetic carbohydrates as the toxin probes, which allows us a facile and highly sensitive detection within 10 min even at protein concentration of less than 1/10,000 of LD$_{50}$ value. The present analytical method may offer one of the highly effective methods against the bioterrorism.

Figure: Detection principle of our present method.
Thailand meets “Paro”: AIST participates in Thailand Science Tech 2005

At the request of the Thai government and its National Science and Technology Development Agency, AIST demonstrated its technologies at Thailand Science Tech 2005, which was held in Bangkok from August 23 to 28. Technologies exhibited included the robot seal “Paro”, photocatalysts, nanobubble water, urination sensors, root formation promoters, artificial olfaction technology, a technique for separating cells by optical means, robots (video presentation), and simulation results on the Indian Ocean tsunami resulting from the Sumatra Earthquake. The most popular of the exhibits was Paro, which instantly attracted a great deal of attention after being reported on by the local media. The news was even broadcast by NHK in Japan. During the event, AIST delegates were able to discuss joint research opportunities with NSTDA and various Thai enterprises.

Thailand Science Tech is an event held under the auspices of the Thai government with the aim of enhancing public understanding of science and technology. This year it attracted some 100,000 visitors per day with a total of about 600,000 people, including many children. The exhibit was a great success, as the picture shows.

AIST presented one Paro unit to Princess Sirindhorn and this was covered by local newspapers. The Princess visited AIST’s booth personally and asked the researchers several questions.

South African delegation led by Deputy Environmental Minister visits AIST Tsukuba to see environmental technologies

On October 12, Ms. Rejoice Mabudafhasi, South African Deputy Minister of Environmental Affairs and Tourism, visited AIST Tsukuba West, together with 21 delegates, including her ministry’s executive officials and four provincial ministers. The delegation exchanged opinions with AIST officials on environmental and 3R (reduce, reuse and recycle) technologies and toured related research labs. After welcoming remarks from AIST’s Senior Vice President Kodama and an introduction to AIST by International Affairs Department Director-General Matsuo, the Deputy Director of the Research Institute for Environmental Management Technology, Mr. Kobayashi, explained his institute’s research into 3R technology. The delegation then visited the labs involved in metal recycling research (led by Tanaka) and the development of technology for recycling waste plastic into fuel and other materials (led by Senior Research Scientist Kodera). The Deputy Minister and other delegation members said that South Africa was addressing recycling and 3R strategies seriously and that they were very interested in the advanced technologies of AIST and other Japanese organizations. They expressed their desire to strengthen ties with Japan in this area and eagerly inquired about legal systems and collaboration with industry for the promotion of 3R implementation.
Second AIST-VAST workshop and visit of VAST Director General Dang Vu Minh to AIST

The second joint workshop between AIST and the Vietnamese Academy of Science and Technology (VAST) was held on October 3 and 4 at AIST Tsukuba. This workshop was based on the memorandum of understanding (MOU) signed by the two institutes. During the workshop, participants from both parties exchanged views on the potential for joint research projects. Discussions covered a wide range of topics including environmental and energy-related technologies, such as waste water treatment, biomass, coastal environment and marine geology, and geogrid and information technologies, including multilingual open source software and grid computing. On October 6, a delegation from VAST including VAST Director General Minh and some of his deputy directors visited AIST Tsukuba. They held discussions with AIST President Yoshikawa, Senior Vice President Kodama, and related research coordinators over the future promotion of AIST-VAST joint research and agreed on an action plan. On the same day, the delegation toured the Research Center for Photovoltaics, the Grid Technology Research Center, Science Square Tsukuba, and the Geological Museum. The next day, they visited the AIST Tokyo Waterfront and Akihabara sites, where they met with Vice President Nakajima, Information Security Research Center Director Imai, and Information Technology Research Institute Director Hashida.

AIST signs cooperation agreement with ITRI Taiwan

AIST signed a cooperation agreement with the Industrial Technology Research Institute (ITRI) of Taiwan on September 26 in Hsin Chu, Taiwan. ITRI was founded in 1973 as a non-profit research organization by integrating Taiwan’s three national laboratories specializing in industrial technology. Today, the organization is recognized as a leading Taiwanese research institute in industrial technology. The research areas of ITRI are similar to those of AIST, covering a broad range of industrial technologies. There have been previous instances of research collaboration between AIST research units and ITRI laboratories, on an individual project basis. However, the newly concluded agreement officially sets the guidelines for mutual cooperation by defining the handling of intellectual property, the procedures for dispute settlement, and other details. Now that the agreement has been signed, AIST expects that its research units will be able to conduct joint research and exchange information with ITRI more easily.
Delegation from Vietnam’s National Science and Technology Policy Council visits AIST Tsukuba

A delegation from Vietnam’s Science and Technology Policy Council, led by Chairman Chu Tuan Nha, paid a courtesy visit to President Yoshikawa at AIST Tokyo Headquarters on October 25. The delegation visited AIST Tsukuba, where they heard Director Kodama’s welcoming remarks, followed by Vice President Yoshikai’s explanation of AIST’s second medium-term program. Vice President Nakajima gave a presentation on major developments and future plans concerning the research partnership with VAST (Vietnamese Academy of Science and Technology). Research Coordinators Yamabe, Ohmaki and Tsukuda described the progress of AIST-VAST research cooperation, including the discussions held and the action plan developed at the joint workshop in early October. After this meeting, the delegation toured Science Square Tsukuba, the Geological Museum, and the lab of the Energy Technology Research Institute’s Clean Power System Group at AIST Tsukuba East. Noting AIST’s emphasis on environmental research, Chairman Nha mentioned the need for Vietnam to take measures against the environmental destruction associated with industrialization.

Mongolian Deputy Minister of Education, Culture and Science visits AIST Tsukuba

Professor Sanjbegziin Tumur-Ochir, the Mongolian Deputy Minister of Education, Culture and Science, and the Minister-Counsellor of the Mongolian Embassy visited AIST Tsukuba on October 28. They met with Vice President Nakajima, who made welcoming remarks, and International Coordinator Miyazaki, who provided an overview of AIST. He also met with AIST researchers who have connections with Mongolia (Kaoru Obuchi and Hitoshi Iwahashi in life science; Mahito Watanabe, Yoshio Watanabe, Yasushi Watanabe and Sereenen Jargalan, a visiting researcher from Mongolia, in geology; Koichi Sakuta and Kenji Otani in environment and energy). The researchers presented summaries of their research. Obuchi spoke about his research on technology to inhibit the fermentation of sea buckthorn berries. (Sea buckthorn is a Mongolian plant that belongs to the Elaeagnaceae family and its berries can be used as an active ingredient in nutritional foods.) The geological researchers discussed GSI (the Geological Survey of Japan) and mineral resource development and surveying. The environment and energy researchers described their photovoltaic power generation experiments in the Gobi Desert. The delegation then visited Science Square Tsukuba and learned about AIST research activities in a wide range of areas. The deputy minister appreciated the specific description of joint research achievements with Mongolia and expressed his willingness to extend his country’s cooperative relationship with AIST beyond the three current research fields.
German-Japanese Forum on IT

The German-Japanese Forum on Information Technology is a conference that aims to deepen the two countries’ mutual understanding and promote exchange in the information technology field. It also serves to promote human resource interaction and the development of information technology through close cooperation. This year’s forum, the 15th conference, was hosted by AIST and Fraunhofer-Gesellschaft and took place at AIST Akihabara on November 1 and 2.

Experts from both countries held wide-ranging discussions on selected topics, such as grid technology and human-technology interaction, which are emerging areas of information technology. During the symposium on the first day, AIST SOA (Service Oriented Architecture), the institute’s ongoing research initiative to revolutionize industry, attracted the attention of participants as an attempt to comprehensively address both forum themes. The working sessions on the second day were dedicated to an in-depth debate on the possibilities for future research collaboration. This year’s forum was also one of the events celebrating “Germany Year in Japan 2005/2006”.

Gfarm Workshop 2005 takes place

Gfarm Workshop 2005 was held on September 9 at Akihabara Convention Hall. The event was hosted by the Grid Technology Research Center, AIST under the auspices of Grid Consortium Japan.

Gfarm is a next-generation network shared file system being developed by a group led by AIST, and has been available as open-source software since November 2003.

In the workshop, participants learned about new functions of Gfarm 1.2, whose release coincided with this event, and listened to eight presentations on Gfarm research, utilization and commercialization. The presenter of Gfarm’s latest enhancements referred to improved performance, higher fault tolerance, and accessibility from Windows PCs via Web browsers, and even demonstrated high-speed access from a Windows PC to the Gfarm file system consisting of 66 distributed PCs in Tsukuba and Otemachi.

The event attracted 74 participants from industry, academia and other sectors. At the round table conference to conclude the workshop, Gfarm developers and participants held a lively debate over the future of Gfarm. The Gfarm Workshop was broadcast live across Japan over the Internet in RealVideo format, with the support of IIJ-MC and SOUM Corporation.
A New Unit Starts on October 1st

The Biomass Technology Research Center was established with two major objectives: the production of ethanol and Ethyl Tertiary-Butyl Ether (ETBE) from woody biomass resources that have the highest capability for carbon dioxide fixation; and the production of BTL-FT diesel fuel by developing a Biomass to Liquids (BTL) total system involving gasification, hot gas cleaning, Fischer-Tropsch (FT) synthesis and hydrocracking. Also, the production processes for these biomass-derived liquid fuels are to be systematically evaluated through simulation in order to promote the substitution of biomass and other renewable energy resources for petroleum and other fossil fuel resources and to develop a practical biomass transfer process with high cost-benefit performance that can contribute to the creation of a society based on energy recycling. The major research areas include the following:

1) Development of a highly efficient ethanol production method combining constituent separation of woody biomass, hydrothermal and mechanochemical treatment and enzymatic saccharification. Incorporation of the resultant ethanol into ETBE materials.


3) Preparation of a database on the physical, chemical and biological reactions of various types of biomass. Development of systematic simulation technologies to evaluate the economic and environmental performance of the conversion processes in use.

4) Diffusion of technologies involving biomass energy use to other parts of the world in cooperation with biomass research institutions in other countries, especially in Asia, where large amounts of biomass resources are available.