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Foreword

This is the latest issue of “Science and Technology Trends — Quarterly Review”.

National Institute of Science and Technology Policy (NISTEP) established Science and Technology Foresight Center (STFC) in January 2001 to deepen analysis with inputting state-of-the-art science and technology trends. The mission of the center is to support national science and technology policy by providing policy makers with timely and comprehensive knowledge of important science and technology in Japan and in the world.

STFC has conducted regular surveys with support of around 3000 experts in the industrial, academic and public sectors who provide us with their information and opinions through STFC’s expert network system. STFC has been publishing “Science and Technology Trends” (Japanese version) every month since April 2001. The first part of this monthly report introduces the latest topics in life science, ICT, environment, nanotechnology, materials science etc. that are collected through the expert network. The second part carries insight analysis by STFC researchers, which covers not only technological trends in specific areas but also other issues including government R&D budget and foreign countries’ S&T policy. STFC also conducts foresight surveys periodically.

This quarterly review is the English version of insight analysis derived from recent three issues of “Science and Technology Trends” written in Japanese, and will be published every three month in principle. You can also see them on the NISTEP website.

We hope this could be useful to you and appreciate your comments and advices.

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Executive Summary

Life Sciences

1 Status and Direction of Infectious Disease Research

— Understanding the Molecular Mechanism of Infection and Development—

p.13

Due to the emergence of severe acute respiratory syndrome (SARS) and avian influenza, infectious disease measures are now an urgent issue. The emergence of unknown infectious diseases, the re-emergence of infectious diseases that were considered conquered, the increased risk of importing pathogens along with the increased circulation of supplies and people, the emergence of drug-resistant bacteria resulting from antibiotic overuse and bioterrorism are particularly important issues concerning infectious diseases. It is unlikely that the factors underlying these issues will be eliminated, so continuous effort must be made for infectious disease measures.

The process of pathogen infection to disease development depends on the interaction between the pathogen and the host. To establish new prevention or treatment methods other than existing vaccine-mediated prevention and symptomatic treatment, it is important to understand the molecular mechanisms of host-pathogen interaction and utilize the results to develop new prevention and treatment methods. Unfortunately, little has been achieved so far from molecular mechanism studies, and further research must be promoted.

The following are two strategies for promoting infectious disease research.

Newly emerging pathogens are likely to be members of known taxonomic groups in pathogen classification. Therefore, basic knowledge about major known pathogens and experimental techniques developed for them should prove useful in taking effective measures against novel pathogens. In this respect, it is essential to foster and secure human resources and research funds in this area. Moreover, considering their significant influence on public health and the unpredictable nature of their epidemics, infectious diseases are issues that need to be continuously studied.

Currently, there is no operative facility satisfying Biosafety Level 4 (BSL4) requirements in Japan, but since pathogens potentially causing imported infectious diseases include those that can only be handled in BSL4 laboratories, establishing such facilities is also an important task for Japan.

(Original Japanese version: published in April 2004)

2 Production and Use of Cloned Human Embryos

— Status of Therapeutic Cloning —

p.21

Cloned human embryos are cells (embryos) produced by implanting human somatic nuclei into enucleated eggs. By purpose of use, human cloning can be classified into “reproductive cloning,” which intends to produce cloned human individuals, and “therapeutic cloning,” which uses cloned embryos for medical treatment. While international opinion is against the production of cloned human individuals (reproductive cloning), research on therapeutic cloning has been approved in some countries. Including the report on the successful establishment of ES cells from cloned human embryos, some research has contributed to realizing regenerative medicine, while other research has implicated the limited potential of current technologies. Under these circumstances, Japan has been discussing whether or not to pave the way to therapeutic cloning. This report overviews the status of cloned human embryos, both from a biological and a social point of view.

In addition to the various abnormalities found at the level of the individual, animals derived from cloned embryos differ from normal at the tissue and cellular levels. Whether this could generate risk in regenerative medicine, which is the ultimate goal of therapeutic cloning, has been discussed. A non-genetic, epigenetic modification of genomic gene functions called “reprogramming” seems to be deeply involved in these abnormalities, but its mechanism is not yet fully understood. Meanwhile, the practical potential of therapeutic cloning has been demonstrated by an experiment in which mouse ES cells differentiated from cloned embryos were used in gene therapy through genetic recombination. Ethical issues concerning the procurement of eggs may be solved by a new alternative means, such as the use of materials removed in surgical operations, or eggs (or egg-like cells) produced from ES cells as tools for reprogramming. In Japan, clinical studies on regenerative medicine using somatic stem cells have already been conducted, and medicine that uses cells derived from ES cells may also develop rapidly within a few years.

The pros and cons of therapeutic cloning have been socially discussed. As long as society demands and expects regenerative medicine and research in this area, protocols and systems for implementation that gain the acceptance and confidence of both sides must be established, based on social debate. An appropriate system will comprehensively involve the participation of citizens and society, conduct risk management as well as the qualitative control of medical treatment and research, and will protect subjects’ rights, through a structure in which a specialized intermediary agency is the core. An intermediary agency is an organization that plays an intermediary role between scientific technology and society. Japan must consider the application of a governance system that can secure confidence through the participation of citizens.

(Original Japanese version: published in May 2004)

3 Trends in Gene-silencing Research

p.32

Research areas concerning the mechanisms for gene expression and suppression are showing remarkable growth. Such areas include “gene-silencing research,” which involves study of the mechanism of gene suppression without genetic change (mutation) in the genomic DNA itself.

The area of gene suppression research has become active, because it is expected that the development of techniques for controlling gene expression will lead to the development of new drugs for preventing or treating various diseases.

Gene silencing was first reported in 1990 in plants. Since 1998, the phenomenon has been extensively researched in nematodes, and its fundamental mechanism was elucidated by 2001.

In 2002, the phase of gene-silencing research shifted to applied research toward medical application using animal models for human diseases. The area will shift into the clinical research phase in the near future.

Analysis of research papers demonstrates that the area of gene-silencing research has expanded through the fusion of several research areas. The drastic increase of research papers reflects the rapid growth of this research area. In addition, comparison of the total numbers of citations between countries shows that the U.S leads the area. However, the number of citations of papers by Japanese authors is increasing, which implies the rapid growth of this area in Japan.

Although gene-silencing research is shifting from basic research to clinical research, various research issues for basic or applied research remain unresolved.

In order to advance gene-silencing research toward medical application, these research issues must be resolved. This requires not only applied or clinical research but also basic research, especially basic research involving problem-identification and problem-solving approach. Since gene silencing is the basis underlying various phenomena commonly found in all organisms, its principles must be understood through basic research to resolve research issues.

Since breakthroughs in this area were derived from the adoption of research from other areas, it is important to establish an environment promoting information exchange between researchers from various areas.

(Original Japanese version: published in June 2004)

Information and Communication Technologies

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Research Trends in Computer Science and Challenges for Japan

— Findings from the International Science Awards —

p.44

The Turing Award is one of the international science awards in the field of computer science. Since its establishment in 1966, the Turing Award has been reviewing and recognizing outstanding research achievements. Recent laureates include the inventors of RSA cryptography, a public key encryption method. There are other awards and prizes for contributions to computer science, such as the Gödel Prize, for basic theory, and the Japan Prize and the Kyoto Prize, which are both granted by Japanese organizations.

The selection criteria of these awards and prizes can be categorized in two types: the first type assesses research papers on a relatively short-term basis of a few years, and the second type recognizes achievements whose significance has been widely accepted in the academic or industrial community. In the case of the Turing Award, whose selection criteria fall into the second type, it took 25 years for public key cryptography to be awarded since the publication of the first paper on the subject. An overview of Turing Award recipients helps identify key research achievements in the field of computer science.

One recent trend is that essential research accomplishments tend to in innovative and extensive new applications of computers. Typical examples include cryptographic methods, program design concepts, and the web. Computer science is expected to have, in addition to the ripple effect on industry, a considerable influence on other science and technology fields in terms of application.

For this reason, the level of basic research in the area of computer science continues to be critical issue in science and technology policy. To promote such research activities, Japanese governmnet should establish goals from a wide perspective on application fields and a long-term view of the direction of technological evolution.

(Original Japanese version: published in April 2004)

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Recent Trends in Semiconductor Microfabrication Equipment Technology

— Proposals for Industry-Academy Collaboration on Research and Development in Japan —

p.52

From the beginning of this year, driven by hot sales of mobile devices and digital consumer products, electronic companies in Japan are seriously intending to invest capital in microfabrication equipment. As this equipment controls the key features of leading-edge semiconductor devices, they are strategically very important for Japan in securing a leading position in certain areas of semiconductor technology and its industry. Technologies supporting these products have been developed through industry-industry collaboration between optical makers and electronic makers, especially in Japan, by applying the essence of high technology, by repeated refinement of optical technology, and by pursuing the limits of precise mechanical control technology. Japanese companies have also secured the top share in business worldwide. However, as our position has recently been threatened and a breakthrough technology called "liquid immersion" has been triggered by MIT in U.S, we cannot be optimistic.

This report reviews the strategies to be pursued to maintain our international competitiveness in developing microfabrication equipment, an area in which Japan has excelled, and to secure the top position in the international market. This will be conducted considering industry-academy collaboration between corporations and university application research groups. We make two proposals.

The first is how to proceed with research and development to produce innovative technologies. We should be aware that the development field in corporations is a crossroads of the needs of the market and the seeds of scientific knowledge, and that emerging technical issues provide us with opportunities for invention and discovery. Thus, university researchers involved in application research in Japan should be more deeply engaged than ever in sharing technical issues with corporate engineers. In addition, the management and protection of IP (Intellectual Property) should always be assured. In this regard, TLOs (Technology Licensing Organizations), which are already established in universities and governmental institutions, need to legally build an equal partnership considering the protection of the rights of the corporations as well as the rights of the university. Moreover, corporations should disclose technical issues in the front-line of development to universities under the joint supervision of the IP department of the corporation and the TLO of the university. In return, excellent research staff of the university can be used by the corporation.

The second point is that we need to consider patent strategy to improve efficiency in obtaining patent rights for inventions that TLO already has. University researchers involved in industry-academy collaboration should only aim for fundamental patents that bring huge returns but have the lowest potential for success, but should steadily and exhaustively apply for patents for existing technologies with corporate engineers, so that there is extensive patent coverage. Furthermore, as the cost of patent maintenance is high, the cooperation with the corporate IP department should impose a strict screening process for patents that have already been applied for.

Under the "give and take" rule between corporations and universities based on a legally equal contractual relationship that includes patented technologies, a project team will be organized by researchers or engineers with experience in developing leading-edge technologies and products. The team should aggressively pursue development to attain the goal of productization. This will result in world-class industry-university collaboration in research and development.

(Original Japanese version: published in May 2004)

6

Research Trends toward Intelligent Computing

— Promotion of Multidisciplinary Research in Cognitive Science and Artificial Intelligence —

p.64

In Japan, the ubiquitous society is approaching now that the nation's population of broadband subscribers has reached 15 million. Even now, however, computers are still difficult for many people to use, and intelligent processing capability of software is not sufficient. An environment in which people can use computers effortlessly and where computers are user-friendly is now required. If these elements become a reality, smooth teamwork between human beings and computers will be facilitated, resulting in improved intellectual productivity.

Studies to implement "intelligent computing," the concept of creating systems that support human beings in their intellectual activities and naturally interface with them, have been conducted as part of research in artificial intelligence. Artificial intelligence studies, aiming to develop machine intelligence on the computer, began shortly after the invention of the computer and have continued. Since the intellectual capacity of artificial intelligence systems has been slow to increase, there has been criticism over research activities in this field. As the computer's processing speed increases, however, greater performance on intelligent processing is now available, allowing the commercial use of artificial intelligence. Today, the results of artificial intelligence research have been embedded in a number of information systems in fragments, although they are not easily recognizable as artificial intelligence technologies. In the artificial intelligence research fields, data mining using machine learning algorithms has recently been attracting attention, and studies in this area have greatly contributed to advances in security technology.

One emerging challenge is that mathematical and mechanical approaches solely dependent on computer processing capability are not sufficient for developing highly sophisticated intelligent systems. It is expected that a human mechanism-oriented approach will help overcome such limitations. The development of noninvasive brain observation technologies since the 1990s has resulted in major advances in research into the mapping between cognitive function and brain activation, partially revealing correlations between the visual/auditory senses and action. While many central cognitive mechanisms, which are related to reasoning and thinking, have yet to be explained, the results of research in behavioral cognitive properties obtained mainly through cognitive psychology experiments have been incorporated into the design of user interfaces for certain information devices.

Traditionally, researchers in cognitive science have emphasized achievements within the framework of basic research and have not attempted practical application. Engineers in the information and communications sector have simply used findings in cognitive science with little interaction with scientists. The boundary between the two areas must be eliminated because new developments can be derived from such activities as addressing the existing challenges in the field of information and communications in the new light of cognitive science.

The U.S. has recently been implementing projects to encourage multidisciplinary research in the areas of cognitive science and artificial intelligence. While promoting application-oriented basic research as well as the subsequent applied research, the U.S. is planning to build a center for integrating these activities to secure its position as the world leader in this field. Since research in the information and communications sector is rapidly proceeding, its application is developed very quickly from basic research results.

Japan has not been successful in embodying or applying excellent new concepts found through basic research. Another discouraging element of Japanese research initiatives is that multidisciplinary research teams usually dissolve once the project ends, reducing the opportunity for the results to be further studied and developed. Japan should consider a program of constructing a research center dedicated to cognitive science and artificial intelligence, while seeking more flexible operation of research organizations at universities by, for example, adopting a 'scrap-and-build' approach. Yet another weakness of Japan is its lack of effort in linking basic research with applied research. Possible solutions by the government are to increase incentives to promote interchange ideas between basic and application initiatives to encourage application-oriented basic research activities. In the meantime, the business sector should also make proactive approaches to universities, such as proposing joint research projects, to facilitate the commercialization of potentially fruitful findings.

(Original Japanese version: published in May 2004)

7 Trends and Issues in Computing Curriculums

p.76

Most activities, whether industrial, public, academic research or everyday life, rely on the technical advances of software. In Japan, software production totals approximately 20 trillion yen, producing extensive ripple effects in various industries. There is a growing awareness of the importance of software production capabilities, as that signifies national competitiveness. Presently, more than 10,000 university students receive computing-related professional training every year. This paper examines the content of such professional training.

In the United State, which is ahead of others in this area, the Association for Computing Machinery (ACM), the world's biggest organization of its kind, developed a model curriculum called CC2001 three years ago. This curriculum differs significantly from previous ones, because it includes enhanced "software engineering" programs, which lead directly to software production. Behind the development of CC2001 is the fact that information technology has penetrated various business areas, and that there has been rapid progress in software design and production technology.

In Japan, the conventional educational curriculum has little focus on software engineering. In order to develop human resources to meet the needs of the industrial world, it is necessary to strengthen the education content in this area further. Curriculums for professional education may improve, if accreditation (third-party evaluation) that meets criteria developed by JABEE or others is promoted. However, it is difficult to apply such evaluation systems in Japan, because they were attributed to the development in the US.

Considering the present situation, this paper recommends measures to implement education that satisfies the needs of the industrial world in the field of software engineering, without incurring large-scale organizational change. First, more flexibility in personnel rating, introduction of a training system for enhancing the content of education, and provision of educational assistance from business people are considered effective in motivating instructors. Second, strengthening the relationship between the existing qualification systems such as the one designed for technicians and curriculum. Also, the introduction of an internship program that directly leads to employment opportunities, and positive evaluation of skills that leads to wage increase are considered effective in supporting students.

(Original Japanese version: published in June 2004)

Environmental Sciences

8

Trends in Japanese Zero Emission Systems that Lead the World

— Creation of Recycling Systems Centering on Materials Industries —

p.85

A number of recycling systems have been developed in Japan, based on the concept of "zero emission." The systems that center on materials industries (e.g., the steel, cement and non-ferrous metal smelting industries) are worth noting. An initiative similar to "zero emission" is also underway in some cities in the U.S, such as the "Eco Industrial Park (EIP). Kalundborg, Denmark, is noted for creating recycling chains (linkages) between different industries. Successful cases, however, are rare. Japanese recycling systems that center on materials industries are unique in their scale of operation and contribution to waste disposal, etc.

Three major factors are behind the creation of such recycling systems. First, they have an overwhelming advantage over other alternatives; they do not require initial investment as they capitalize on existing processes. Not only manufacturers but also some waste disposal businesses take part in recycling efforts. (The latter are entitled to charge waste disposal fees by obtaining a "waste disposal business" license in accordance with the Waste Management Law.) The government subsidizes the construction of recycling facilities in line with initiatives such as the "Eco-Town Area." Second, a compulsory system for recycling materials has been in place, with the Packaging Recycling Law and the Home Appliance Recycling Law enforced in compliance with Extended Producer Responsibility (EPR), through which manufacturers and waste producers shoulder the cost of recycling. Third, these recycling systems involve high-temperature thermal processes that can dispose of hazardous substances, and have the potential of treating a massive amount of waste.

Qualitative conversion processes that are linked to the processes of materials industries should be researched and developed to further improve Japan's recycling systems, e.g., a system that feeds molten fly ash (containing high-quality copper, zinc and lead generated by the waste melting process) back into the non-ferrous metal smelting process, and a system that decomposes and gasifies packaging plastics by heat, which are then converted to hydrogen for use in the production of ammonia and other chemicals. Qualitative conversion processes, which here refer to pyrolysis/gasification/melting processes, are key technologies essential to these two systems.

Innovative recycling systems that link complex, mixed waste with materials industries, through these new qualitative conversion processes and the abovementioned socioeconomic conditions that support the systems, could be models of Japanese industrial systems. It is thus recommended that the government support the research and development of new qualitative conversion systems and their transfer to other countries, focusing on the global market.

(Original Japanese version: published in June 2004)

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Structure Maintenance Technology and Risk Based Maintenance (RBM)

p.96

Confidence in the safety of Japan's industrial facilities has been shaken recently by events such as the occurrence of major industrial accidents. As a mature society, Japan possesses a vast amount of social and industrial infrastructure assets in the form of structures. The time has come for such structures to be maintained and utilized with care.

The deterioration of structures, declining numbers of maintenance-related engineers, inadequate transmission of techniques to new generations, and outdated regulations have been pointed out as problems leading to those recent accidents. At the same time, increasingly harsh international competition necessitates cost cutting in all manufacturing industries. Furthermore, it is necessary that aging structures in the social infrastructure be maintained at low cost without compromising safety. The importance of rational maintenance to keep structures in the social as well as the industrial infrastructure must be recognized.

With steel's long history as a major component material in industrial infrastructure, its failure mechanisms leading to accidents are well understood, and research into life prediction technology has also been carried out. It is necessary that those research results be transformed into means that are broadly and easily accessible, yet in recent years R&D in maintenance-related fields has been in decline and the shortage of personnel is remarkable. In the case of concrete, most of the failure mechanisms are understood, but life prediction technology has only recently become a research subject.

Based on the above circumstances, examination of S&T policy including technical development related to steel and concrete, personnel development, and standardization is an urgent task. This article proposes the following policies.

(1) Among maintenance technologies, life prediction methods, risk assessment methods (software), and maintenance related (failure case studies, materials characteristics, etc.) databases should be highly accessible, and assessment standards must be based on broad consensus. Furthermore, the responsibility of maintaining the majority of social infrastructure should belong to the national government. At present, using national government funds to drive research in RBM, which is drawing the joint attention of industry, government, and academia, would be effective.

(2) Maitenance-related engineering fields are mature, and their attraction as research fields is weak and student interest is also low. Nevertheless, they are vital engineering fields if structures are to be maintained safely.

Taking them from the new perspective of safety, those engineering fields can be seen as a new R&D/academic discipline including social science fields. In Europe and the United States as well, maintenance is not systematized. It should be organized into an academic discipline, with graduate school majors in maintenance science and maintenance technology research centers that draw a broad range of personnel from Japan and abroad and promote education in the field.

(3) Government and the private sector should work together to prepare maintenance-related standards and to implement the setting and revising of standards in accordance with technical progress.

(4) With the number of maintenance engineers decreasing, the quality of those few engineers must be ensured. National government should actively encourages maintenance-related academic associations to set qualification standards for maintenance engineers

(Original Japanese version: published in June 2004)

Science and Technology Policy

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Science and Technology Policy Trends in the United States

— Report on the AAAS Annual Forum on Science and Technology Policy —

p.106

On April 22 and 23, 2004, the American Association for the Advancement of Science (AAAS) Annual Forum on Science and Technology Policy was held in Washington D. C. This year over 500 people attended and took part in vigorous discussions, including government officials such as John H. Marburger, III, Director of the Office of Science and Technology Policy; members of Congress such as Senator Tom Daschle (D); heads of university research departments; analysts from relevant think tanks; lobbyists from scientific associations; and foreign experts on science and technology policy.

This year's Annual Forum was held a year after the war in Iraq, and it provided a glimpse of the large shadow cast over US science by security issues since the terrorism of 2001. That shadow takes forms such as difficulty in securing budgets for non-defense research and development (R&D), visa issues, and issues concerning oversight of life sciences research laboratories. In particular, the US scientific community feels a strong sense of crisis because non-defense R&D budget decreases in the next five years due to financial issues and the tendency to put priority on anti-terrorism policy.

China was the focus of much attention and awareness as a powerful economic rival of the United States. Although the US and Japan maintain their leads in areas such as overall R&D funding and papers published, China's presence is rapidly increasing. Japan's presence is in relative decline.

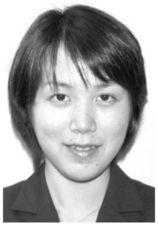
In addition, “research on the mind” or “cognitive science” continued to come to the fore as the next major topic of research and development. Currently there are no national-level projects on cognitive science in the United States, but it is possible that a national project on the subject will be carried out in conjunction with fields such as nanotechnology, information technology, and biotechnology. It is necessary to watch for future developments.

(Original Japanese version: published in May 2004)

1

Status and Direction of Infectious Disease Research

— Understanding the Molecular Mechanism of Infection and Development —



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1 Introduction

Due to the worldwide epidemic of severe acute respiratory syndrome (SARS) from 2002 to the winter of 2003 and the emergence of avian influenza in 2004 in and around Asia, infectious disease measures are now an urgent issue. "Policy for the allocation of budget and human resources to science and technology for 2004 (Council for Science and Technology Policy, June 19, 2003)" states that "measures against emerging infectious diseases and bioterrorism are new and important considerations that must be researched." "Infectious disease research" and "biodefense research" are both recognized as important issues in the United States. The budget message for fiscal 2005 announced on February 2, 2004 designated infectious diseases as priority areas to be dealt with in National Institutes of Health (NIH)[1,2].

By the 1970s, advances in diagnostic, prophylactic and therapeutic agents encouraged people to believe that infectious diseases are conquerable threats. However, the emergence of unknown infectious diseases and the re-emergence of infectious diseases that were considered conquered, as well as the need for anti-bioterrorism measures, have heightened the urgency of infectious disease research.

This report provides general information on infectious diseases and discusses the importance of basic research on infection and disease development mechanisms that will serve as the basis for developing prevention and treatment methods.

2 Infectious diseases

Infectious diseases are result from infection by pathogens. Symptoms develop due to interaction between the pathogen and the infected host. Pathogens can be parasites, fungi, viruses, bacteria or prions, which are all parasitic agents that are further classified by size, the presence or absence of genomes, and self-propagation ability (Table 1). Organisms with nuclei such as parasites and fungi are called eukaryotes, while those without nuclei such as bacteria are called prokaryotes.

Table 1 : Classification of pathogens

Microorganisms	Size	Propagation as parasites	Genome	Self-propagation
Prion	—	Capable	Absent	Incapable
Virus	0.02 ~ 0.3μm	Capable	Present	Incapable
Bacteria	0.1 ~ 5μm	Capable	Present	Capable
Fungi	~ 50μm	Capable	Present	Capable
Parasite	—	Capable	Present	Capable

Source: Prepared by Professor Akio Nomoto of the Graduate School of Medicine, the University of Tokyo.

2-1 Parasitic infections

Parasites are medically defined as parasitic eukaryotes other than fungi and can be further classified into unicellular protozoans, such as malaria and trypanosoma, and multicellular helminth represented by filaria. Diseases caused by parasites are called parasitic infections.

The Special Programme for Research and Training in Tropical Diseases (TDR) of the World Health Organization (WHO) have designated malaria, trypanosomiasis, leishmaniasis, filariasis, schistosomiasis and leprosy as the six hard-to-conquer diseases, all of which are parasitic infections except leprosy.

In Japan, the number of intestinal parasites has decreased with improved water and sewerage systems, but the Japanese habit of eating raw fish is still causing a high anisakiasis infection rate. Moreover, cryptosporidiosis caused by contaminated tap water broke out in 1994 and 1996 in Kanagawa and Saitama Prefectures, respectively[3].

2-2 Bacterial infections

Bacteria are prokaryotes that can make copies of themselves through self-replication wherever nutrients are available. Based on their activities and their influence on human beings, bacteria are classified into three groups, i.e., harmless, harmful, and effective bacteria, which co-exist in the human intestine. Effective bacteria produce lactic acid by breaking down proteins, while harmful bacteria produce ammonia, amines or indoles through putrefaction. In bacterial infection, the toxins produced by the bacteria trigger disease development[4].

Typical examples of bacterial infections are enterohemorrhagic E. coli (strain O157) infections, pertussis and dysentery. Antibiotics are effective against bacterial infections, but their overuse has resulted in the emergence of drug-resistant bacteria such as drug-resistant tuberculosis, methicillin-resistant staphylococcus aureus (MRSA) and vancomycin-resistant enterococcus (VRE). VRE is an especially difficult disease because most antibiotics currently used for treatment of infection prove ineffective in most cases.

2-3 Viral infections

Viruses have a simple structure consisting of a genome for replicating itself and proteins and lipids for protecting the genome. It cannot replicate by itself due to the absence of functions such as nutrient consumption, energy production and protein synthesis, and must therefore live on other cells to utilize their functions and replicate.

The first step in viral infection is the infection and propagation of the virus at the site of damage to a mucous membrane or the skin. Whether it infects the respiratory mucosa or the digestive mucosa depends on the kind of virus. Some viruses replicate and symptoms develop in the first target cell, while others enter the capillaries to travel through the body in the bloodstream to reach the final target tissue where they replicate and the disease develops[5,6].

Vaccines utilizing the immune function of the host have been used for preventing viral infections. As a result, worldwide eradication of smallpox was achieved in 1979. Eradication of poliomyelitis is also in progress under the leadership of WHO.

Among the considerable number of viral infections known today, SARS caused by coronavirus infection and influenza caused by influenza virus infection are perhaps attracting most public attention. In addition, koi herpesvirus infection found in carp cultured in Kasumigaura has become a serious problem because of its economic consequences, while avian influenza has become a great concern due to both its economic influence and the possibility that it will infect humans.

2-4 Prion diseases

Prion diseases such as sheep scrapie were considered to be special forms of viral diseases with a long incubation period following viral infection. However, in the 1980s, it was proposed that these diseases are caused by abnormal prion proteins, and this has been confirmed through an experiment demonstrating that abnormal prion proteins are capable of inducing neuronal disease. Prion disease is a general term for diseases thought to be caused by abnormal prion proteins. To date, little is known about the infection mechanism or the action of prion proteins[7].

Examples of prion diseases are sheep scrapie, bovine spongiform encephalopathy (BSE) and human Creutzfeldt-Jakob disease (CJD).

3 Major problems concerning infectious diseases

Infectious diseases, the most common cause of human fatalities, have always been and will remain a problem that must be overcome. Awareness of infectious diseases is growing. The following are some major issues concerning infectious diseases.

3-1 Emerging and re-emerging infectious diseases

WHO defines emerging infectious diseases as "those due to newly identified and previously unknown infections that cause public health problems either locally or internationally," and re-emerging infectious diseases as "those due to reappearance and increase of infections that are known, but had formerly fallen to levels so low that they were no longer considered a public health problem"[6,8]. Examples of emerging and re-emerging infectious diseases are listed in Table 2.

It is unlikely that emerging infectious diseases are caused by completely new viruses; rather, they are considered to be caused by zoonotic viruses (those infecting humans as well as other animals). Such viruses remained undiscovered, coexisting with their natural hosts away from human beings, but once they encounter human communities, they start emerging as 'new' diseases.

3-2 Imported infectious diseases

Aircraft and other transportation means have increased the circulation of supplies as well as people. This has also increased the risk of importing infectious diseases from other areas.

In 1967, an infection with a fatality rate of 23% attacked workers in Behring Laboratory in Marburg. This disease, named Marburg disease, was caused by a virus carried by an African green monkey shipped from Uganda. Ugandan monkeys were also exported to Japan around the same time, although they were uninfected by the virus.

In 1976, an American woman returning from Sierra Leone was found to be infected by the Lassa virus, and 552 people who had potentially had contact with her were placed under surveillance for 3 weeks. Fortunately, no secondary infection was observed in this case.

In 1987, a Japanese technician also returning from Sierra Leone was diagnosed as having Lassa fever after receiving medical treatment at the Research Hospital of the Institute of Medical Science, The University of Tokyo.

Table 2 : Examples of emerging and re-emerging infectious diseases

	Emerging infectious diseases	Re-emerging infectious diseases
Parasitic infections	Cryptosporidiosis	Malaria Leishmaniasis Echinococcosis
Bacterial infections	Enterohemorrhagic E. coli (strain O157) infections Novel strain of cholera (Bengal cholera) Legionellosis	Fulminant type-A streptococcus infections Plague Diphtheria Tuberculosis Pertussis Salmonellosis Cholera
Viral infections	Ebola hemorrhagic fever Hantavirus pulmonary syndrome HIV (AIDS) Adult T-cell leukemia Nipah virus encephalitis SARS	Rabies Dengue/ dengue hemorrhagic fever Yellow fever

Source: Prepared by the author based on the Reference [3].

3-3 Drug-resistant bacteria

Since the discovery of penicillin and its first clinical application in 1941, many kinds of antibiotic have been put into practical use. Antibiotics are effective against infectious diseases, especially against bacterial infections, and have contributed to the dramatic reduction in many acute infections, at least in developed countries. Antibiotics have also been effective against certain chronic infections, such as tuberculosis, which has drastically reduced the number of tuberculosis patients. However, while exerting such dramatic effect against bacterial infections, antibiotics have generated the new problem of the emergence of drug-resistant bacteria.

3-4 Bioterrorism

Japan's Aum Shinrikyo's dispersal of anthrax and botulinum as well as sarin in a sarin gas attack and U.S. anthrax mail threats in 2001[7] have impressed the reality of bioterrorism on the international community.

This has raised the demand for anti-bioterrorism measures, especially in the United States, where the budget for anti-bioterrorism measures has been increased[2] over the past few years.

4 Importance of understanding the molecular mechanisms of infection and development

Various factors are involved in the emergence of drug-resistant bacteria and emerging or re-emerging infectious diseases. For example, delay in public health improvement due to poverty or jungle exploitation that accompanies rapid population expansion has increased the risk of encountering unknown pathogens, and abnormal weather patterns consistent with global warming have increased or altered the distribution of the natural hosts of pathogens. Furthermore, inadequate or excessive use of antibiotics and the aging of society have lead to the emergence of symptoms that cannot be controlled by the immune system. These problems cannot be easily solved, yet they are likely to grow into even more serious problems. Therefore, we must work harder to strengthen measures against infectious diseases.

To establish new prevention and treatment methods other than existing vaccine-mediated prevention and symptomatic treatment, it is important to understand the molecular mechanisms of infection and disease development and to utilize the results to develop new prevention and treatment methods.

4-1 Importance of understanding the molecular mechanisms of infection and development

Developing new prevention and treatment methods requires elucidation of the molecular mechanisms of the infection process and the disease development process.

For example, focusing on the fact that viruses cannot propagate without using the molecules or systems of their hosts, research projects are in progress to identify the host-derived molecules determining the species-, tissue- or cell-specificity of viruses to reveal the biological processes by which viruses adhere to or invade cells, replication of the viral genome, virus particle formation and cell death. Unfortunately, the molecular mechanisms of infection and disease development have only been partially elucidated, even for substantially eradicated viruses such as poliovirus.

Research on bacterial infections has been promoted to understand the molecular mechanisms underlying the processes of bacterial fixation and invasion into tissues or cells at infection sites, and inflammation resulting from bacterial phagocytosis due to the release of macrophages and cytokines. However, these mechanisms are not yet fully understood.

4-2 Process of virus infection research

The following example of virus infection research illustrates the process for elucidating infection and disease development mechanisms.

The first step of invasion into a host organism is the propagation of the virus at the first target cell. The disease then develops at this site, or travels through the host to other tissues where they propagate and where the disease develops. However, if the host lacks the receptor that binds to the virus, infection does not occur.

Pathogenicity studies of viruses aim to elucidate “the mechanism of species or tissue-specificity determination,” “in vivo transmission mechanism” and “the capacity to damage the final target cell.” Viral propagation depends on the compatibility of molecules between the virus and the host. The mechanism and route of the in vivo transmission of viruses to the final target cell are the important steps in disease development.

For example, poliovirus shows species-specificity that limits its infection to primates and tissue-specificity that limits its site of propagation to the central nervous system and the intestines. After in vivo transmission, polioviruses release their toxins in the final target, the nerve cells. They use a cell-surface receptor molecule (poliovirus receptor) for infection that has been cloned and that is suggested to be the determinant for species-specificity. In addition, the application of genetic transformation technology has revealed the genomic sequence of viruses with tissue-specificity (central nervous system-specificity). The mechanism of the in vivo transmission of the virus is being currently studied using an infection model established with mice[5].

The elucidation of the molecular mechanism of viral infection and disease development is very important, as it serves as a basis for developing infectious disease measures such as prevention and treatment methods. Findings on the process of viral invasion into the host can be applied to developing measures to be taken at the initial stages of infection, while findings on in vivo transmission and viral replication in target cells can be used to suppress disease development (Figure 1).

5 Suggestions

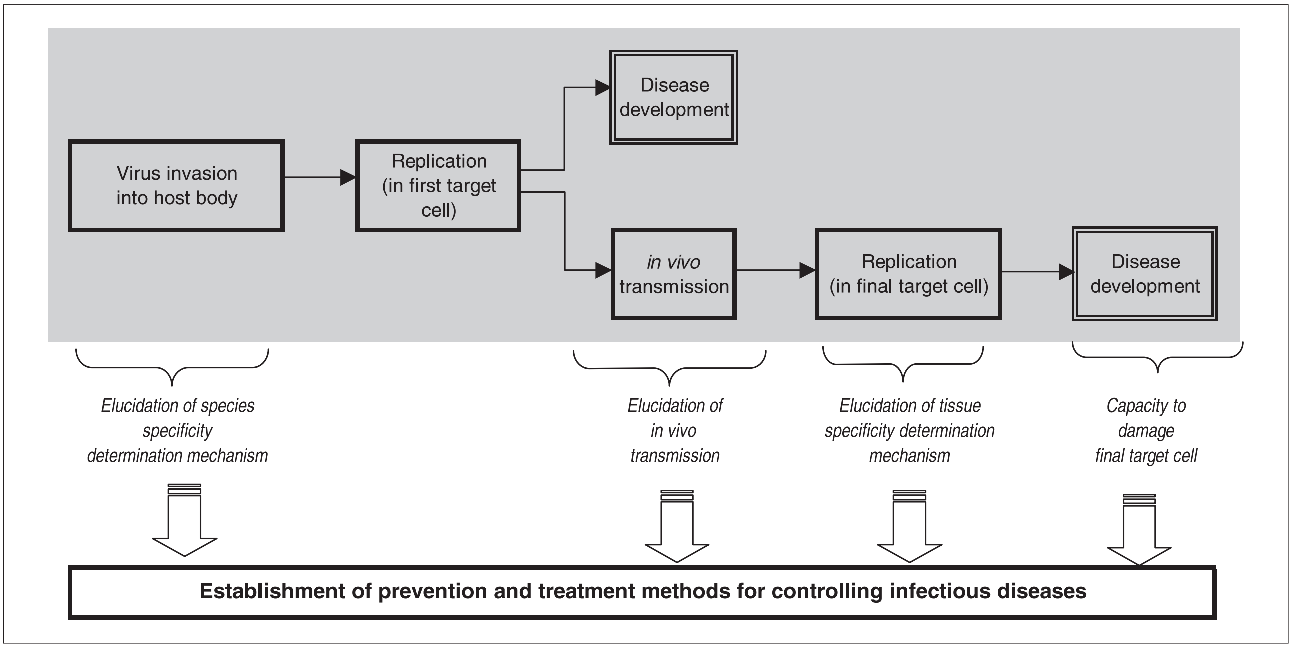
— Infectious disease research for public safety and peace of mind —

As mentioned in Section 3, there are many problems concerning infectious diseases, and it is essential to promote infectious disease research to establish a safe society with peace of mind in Japan. Here are some suggestions for strategies to be taken.

5-1 Fostering and securing human resources and research funds

Emerging infectious diseases are likely to be caused by pathogens belonging to known taxonomic groups in the pathogen classification. Therefore, basic knowledge of major known pathogens should prove useful in taking effective measures against novel pathogens. For example,

Figure 1 : Process for elucidating viral infection and disease development mechanisms



measures against SARS caused by a newly discovered coronavirus were developed based on knowledge and techniques already established for other coronaviruses.

Therefore, it is important to establish a system for supporting basic research on major pathogens. While further research should be conducted for pathogens that have already been researched, research on non-researched pathogens must also be enhanced to encourage this entire area of research. Such projects must be promoted to prepare for the future emergence of emerging and re-emerging infectious diseases.

To promote research on molecular mechanisms, the routine gathering of fundamental knowledge and establishing of experimental methods and techniques, it is essential to foster and secure human resources and research funds in this area. However, compared to the United States, Japan has allocated an extremely small amount of human resources and research funds to the infectious disease research area (Table 3).

Considering the significant influence on public health and the unpredictable nature of their epidemics, infectious diseases are an issue that must be continuously tackled. Fundamental knowledge on molecular mechanisms and experimental methods cannot be established without accumulating research results, and specialists handling peculiar pathogens cannot be raised in a short time. Reduced emphasis on infectious disease research may result in reduced research support and ultimately in the outflow of researchers to other research areas. This must not happen.

5-2 Enhancement of Biosafety Level 4 facilities considering linkage with other countries

Experiments using infectious disease pathogens require special research facilities (hardware) and appropriate action (software) by workers to prevent infection and environmental contamination.

Standards for handling pathogenic microorganisms have been established by WHO and set out in the Laboratory Biosafety Manual. In the United States, standards have been jointly established by NIH, the largest domestic institution in U.S. responsible for biomedical research, and Centers for Disease Control and Prevention (CDC), an international organization playing a central role in infectious disease measures. In Japan, the National Institute of Infectious Diseases has established safety management principles, while the Bioscience Sector in the Subdivision on the Focused Promotion of Basic and Fundamental Research and Development, Council for Science and Technology, has established “Manual for the Safe Management of Research Microorganisms in University Laboratories, etc.” in January 1998. Various academic societies have also established their own guidelines (Table 4).

“Biohazard,” the abbreviated term for “biological hazard,” refers to a hazard caused

Table 3 : An example of allocation of human resources and funds to infectious disease research

Human resources	U.S	Centers for Disease Control and Prevention (CDC)	About 3,400 people*
	Japan	National Institute of Infectious Diseases	About 400 people

* The value was predicted based on the assumption that the proportion of personnel engaged in infectious disease research, which was assumed to have been about 40% in 1997 based on reference material in 1997, has not changed since then.

R&D expenditures	U.S	Centers for Disease Control and Prevention (CDC)	About 57 billion yen**
	Japan	National Institute of Infectious Diseases	About 3.3 billion yen***

** This also includes the expenditures for chronic diseases, etc., other than infectious diseases

*** The value obtained as the sum of the 2002 annual research budget allocated for the institute (about 1.8 billion yen) and competitive funds such as research grants from the Ministry of Health, Labor and Welfare (about 1.5 billion yen)

Source: Prepared by the author based on the reference material distributed in the 34th Council for Science and Technology Policy.

Table 4 : Criteria for biosafety levels and example microorganisms

Level	Criteria	Examples (virus only)
1	Agents not that cause serious disease in humans or animals	Live-vaccine viruses (other than vaccinia and rinderpest vaccine)
2	Agents that cause disease in humans or animals but has low risks of causing severe hazards among laboratory personnel or domestic animals	Dengue virus, Herpes simplex virus (1and 2), Influenza virus, Japanese encephalitis virus, Measles virus, Adult T-cell leukemia virus, Hepatitis virus (A, B, C, D and E)
3	Agents that cause serious disease in humans but are rarely transmitted from a diseased person to other individuals	Hantavirus, HIV (1 and 2), Rabies virus (street strain)
4	Agents that pose high risk of life-threatening disease and are easily transmitted either directly or indirectly from a diseased person to other individuals, or agents without any effective prevention or treatment method.	Ebola virus, Lassa virus, Marburg virus, Smallpox virus, Yellow fever virus

Source: "Manual for Safe Management of Research Microorganisms in University Laboratories, etc. (January 1998)."

by organisms (microorganisms) harmful to humans or the environment. The fundamental rule in biohazard measures is the containment of pathogens, and action taken for this purpose consists of two steps, i.e., primary isolation and secondary isolation. The former is to protect workers from exposure to pathogens, while the latter is to isolate the laboratory from the outside environment. These actions are assigned Biosafety Levels (BSL) 1-4[9] according to the degree of hazard.

In Japan, the National Institute of Infectious Diseases and the Institute of Physical and Chemical Research (RIKEN) each has a laboratory that satisfies the conditions required for BSL4 facilities. In both laboratories, maintenance such as the replacement of filters and other equipment as well as occasional inspections are conducted, but to date, neither is planned to be used as a BSL4 laboratory.

Pathogens potentially causing imported infectious diseases include those that can only be handled in BSL4 laboratories, such as the Ebola virus and Marburg virus. Furthermore, BSL4 laboratories may be needed for handling unidentified pathogens. The lack of operational BSL4 laboratories is retarding progress in domestic research on highly hazardous pathogens.

To promote such research projects, it is important to establish operational BSL4 laboratories where high safety levels are ensured. Linkage with overseas facilities should also be considered to create a research environment equipped with available BSL4 laboratories.

Table 5 : Major Biosafety Level 4 facilities in the world

Asia	Japan	2
North America	U.S.	6
	Canada	1
EU	Sweden	1
	Germany	2
	France	1
	U.K.	4
	Spain	1

Source: Prepared by the author based on the reference material distributed in the 34th Council for Science and Technology Policy.

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2

Production and Use of Cloned Human Embryos
— Status of Therapeutic Cloning —

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1 Introduction

Cloned human embryos are cells (embryos) produced by implanting the nuclei of human somatic cells into enucleated eggs. By purpose of use, human cloning can be classified into "reproductive cloning," which uses cloned embryos for producing cloned human individuals, and "therapeutic cloning," in which cloned embryos are used for medical treatment and research purposes.

International opinion is against the production of cloned human individuals (reproductive cloning), represented by an international treaty banning human cloning discussed in the United Nations. Over this issue, the United Nations has split into (1) those appealing for a complete ban on human cloning and (2) those accepting therapeutic cloning, claiming that banning should be limited to the production of cloned human individuals and that regulating production and using cloned human embryos should be the decision of individual governments. The discussion started in 2001, but no agreement has been reached, and it will continue until this December (2004).

In October 2003, the Inter Academy Panel (IAP), an international science academy forum with membership of over 80 academies from around the world including the Science Council of Japan and the U.S. National Academy of Sciences has issued a statement on human cloning regulation. In this statement, IAP urges the United Nations to ban cloned human individual production (reproductive cloning) but also claim that "therapeutic cloning" intended to establish ES cells for research and therapeutic use should not be banned, considering its potential contribution to medical and scientific progress.

While the application of cloning technology to human beings has become a controversial issue in many areas, in March 2004, Korean and U.S. researchers successfully established ES cells from cloned human embryos and published the results of their research in the American journal, Science[1]. ES cells derived from cloned embryos had already been established in experimental animals, but the report demonstrates that they can also be established in humans. At the same time, the low success rate of the reported method, i.e., merely a single ES cell line could be obtained from 242 eggs, suggests that, in addition to ethical issues, there are a number of scientific and technical barriers to overcome before applying similar methods in practice.

In Japan, the Bioethics Committee of the Council for Science and Technology Policy has been discussing whether or not to pave the way to the production and use of cloned human embryos (therapeutic cloning). This report overviews the status of cloned human embryos, both from a biological and a social point of view.

2 Laws and regulations concerning cloned human embryos

In Japan, any research concerning cloned human embryos must be conducted in compliance with the laws and regulations. Currently, governmental guidelines with de facto legal force prohibit research on the production and use of cloned human embryos. From an international standpoint, some countries have laws concerning human cloning, while others do not, and some laws prohibit any human cloning at all, while others prohibit only reproductive cloning. In December 2000, Japan enacted the “Law concerning Regulation relating to Human Cloning Techniques and other Similar Techniques” (2000 law no. 146, hereafter referred to as the “Law concerning human cloning”), which legally prohibits the implantation of cloned human embryos into a uterus (prohibition of the creation of cloned human individuals) and imposes criminal charges (imprisonment of up to 10 years or a fine of up to 10 million yen) for any violation. Based on this law, the Minister of Education, Culture, Sports, Science and Technology has established “Guidelines on handling specified embryos” (hereafter referred to as the “Guidelines for specified embryos”) that instruct users to follow the guidelines when handling specified embryos such as cloned human embryos and chimeric or hybrid embryos (mixtures or hybrids between human and other animals) and impose substantial criminal charges for any violation. In other words, anyone whose research has been judged to violate the guidelines by the Minister and who does not follow the Minister’s improvement or suspension orders, etc., will face imprisonment of up to 1 year or a fine of up to 1 million yen.

Table 1 : Classification of specified embryos employed in laws and guidelines in Japan

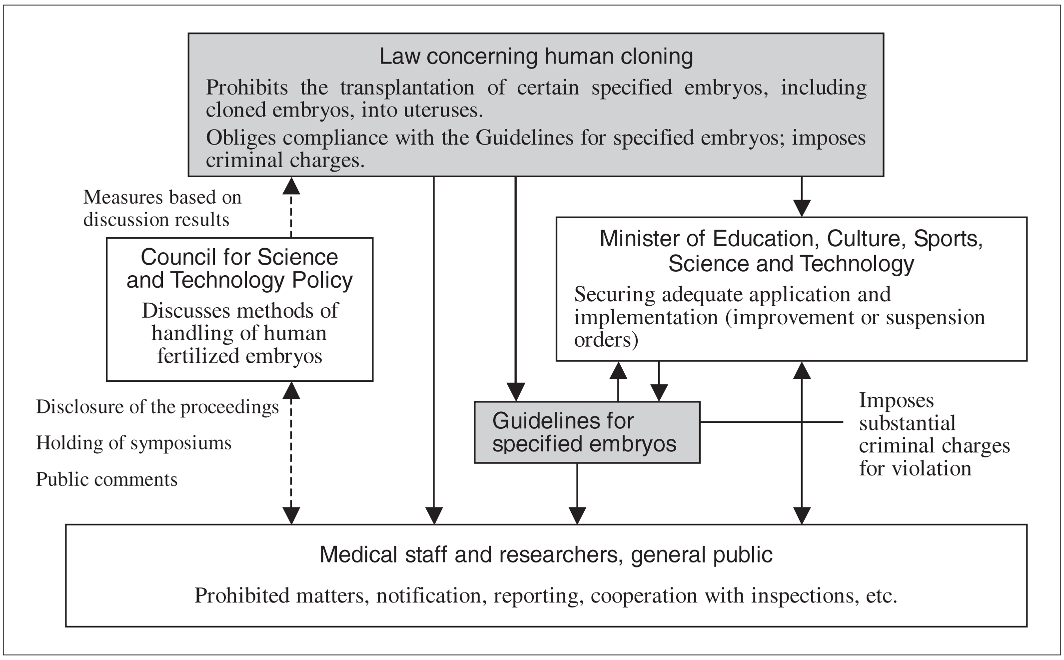
Specified embryos (simplified forms of the definitions given in the Law concerning human cloning):

(1) Human somatic clone embryo : human enucleated unfertilized egg + human somatic nucleus
(2) Human-animal chimeric embryo : human embryo + animal embryo
(3) Human-animal amphimictic embryo : human gamete fertilized with an animal gamete (or a clone obtained using its nucleus)
(4) Human-animal hybrid embryo : animal enucleated unfertilized egg + human cell nucleus (including the embryo)
(5) Human split embryo : embryo produced by splitting the human early embryo (the developing embryo)
(6) Human-human chimeric embryo : human embryo + human cell (including the embryo)
(7) Human embryonic clone embryo : human enucleated unfertilized egg + human early embryo nucleus
(8) Animal-human hybrid embryo : human enucleated unfertilized egg + animal cell nucleus
(9) Animal-human chimeric embryo : animal embryo + human cell

Definitions of the terms used

Human : contains a human nucleus
Animal : contains an animal nucleus
Chimeric embryo : an embryo produced by mixing no fewer than two embryos. Chimaera embroyo
Amphimictic embryo : a hybrid embryo produced through the fertilization of gametes, and a cloned embryo obtained using its nucleus
Hybrid embryo : an embryo produced by transplanting a nucleus into an enucleated egg or a fertilized egg

Figure 1 : Structure of regulations concerning human cloned embryos



The Guidelines for specified embryos prohibit any production or use of specified embryos given in the list, except for the production of animal-human chimeric embryos. In other words, not only the implantation of cloned human embryos into uteruses but also their production is prohibited by the guidelines.

3 Significance of therapeutic cloning

The greatest value of therapeutic cloning is its potential to produce patients' own cell transplants, thus avoiding the immunological rejection that occurs in regenerative medicine. This section summarizes the situation surrounding this aspect of therapeutic cloning.

Regenerative medicine refers to technologies to regenerate functionally disturbed or incompetent tissues or organs through the active use of cells. Using various techniques, cells, tissues, etc., are artificially adapted to perform their intended functions and then implanted into dysfunctional organs or tissues so that their lost functions and health are restored.

In organ/tissue transplantation, immunological rejection occurs in individuals (recipients) whose cells, tissues, etc., have received implants. For successful results in regenerative medicine, this rejection must be adequately suppressed. Immunosuppressants are usually used, and the improvement in immunosuppressants (emergence of cyclosporin) has largely contributed to the establishment of the medical transplantation techniques used today for the heart, lungs, liver, kidneys and other organs.

The immunosuppressants used to prevent and suppress immunological rejection are accompanied by certain adverse effects listed in Table 2 (listing only drugs generally used in renal transplantation. Other immunosuppressants such as antilymphocyte antibodies and anti-IL2 receptor antibodies are not shown). After transplantation, patients usually receive two or more kinds of immunosuppressant in combination and must continue taking them for rest of their lives (as long as they have the implants within them).

The results of an investigation conducted in 1983 show that one-year graft survival rates after cadaveric transplantation were 72% and 52% when dosing with cyclosporin alone (117 cases) and dosing with other agents (steroids/azathioprine, 115 cases), respectively[5]. The graft survival rate after cadaveric transplantation has increased to 88.7% through combination therapy (calculated from 268 cases examined since 1983[6]).

As can be seen, eliminating immunological rejection is essential in medical transplantation as well as in the cell transplantation employed in regeneration medicine. Since rejection is due to variation in immune-related genes (differences in tissue antigens) observed among individuals, rejection is in theory suppressed by establishing ES cells derived from embryos (with the genomic genes of the patients) cloned from the patients themselves and by implanting cells appropriately differentiated from such ES cells.

In mice, the use of ES cells derived from cloned embryos has actually proved effective in avoiding rejection in regenerative medicine[7].

Table 2 : Immunosuppressants

Immunosuppressants	Adverse effects
common to all agents	reduced resistance to infectious diseases
cyclosporin	nephropathy, hepatopathy, encephalopathy symptoms, neuro-Behcet-like symptoms, acute pancreatitis, thrombotic microangiopathy, hemolytic anemia, rhabdomyolysis, lymphoma, lymphoproliferative tumor, malignant tumor, hirsutism, trembling of hands, etc.
tacrolimus	nephropathy, diabetes, trembling of hands, cardiopathy, etc.
steroids	peptic ulcer, diabetes, hypertension, glaucoma, cataract, obesity, moon face, etc.
mycophenolate mofetil	leukopenia, anemia, diarrhea, inappetence, etc.
azathioprine	leukopenia, inappetence, nausea, liver dysfunction, etc.
mizoribine	leukopenia, liver dysfunction, inappetence, nausea, stomatitis, pancreatitis, etc.

4 Status of cloning technology

This section overviews the technical aspects of the process of establishing ES cells from cloned embryos, from the perspective of applying cloned human embryos to regenerative medicine.

Cloned human embryo production involves techniques that take the nucleus of a somatic cell (containing genomic genes principally identical to the donor of the somatic cell) out of the target individual to be cloned, transfer it into an egg, and treat the egg appropriately to promote embryo development without the involvement of gametes (sperm and eggs) or fertilization. From the resulting early embryo (at the blastocyst stage), a specific group of cells (inner cell mass) is removed and used to establish ES cells. This is how ES cells are established from cloned human embryos. Achievements in bioresearch in this process are discussed in the following paragraphs.

To date, cloned individuals have been obtained in sheep, mice, cattle, goats, pigs, rabbits, cats, mules, horses and rats using cloning technology. Success in the production of cloned individuals depends on the type of abnormality observed, etc., and these are different among the above species. Mice in particular, which are generally used in animal experiments, have great physiological differences from other mammals.

Phenotypic abnormalities are believed to be caused by (1) technical factors such as artificial handling that may damage the eggs, (2) genetic factors, such as abnormalities in the genomes of the somatic cells used for nuclear transplantation, or the genetic variation observed in the differentiation or the aging process or (3) non-genetic factors (epigenetic factors are explained later) concerning reprogramming (to obtain a condition suitable for development) or egg activation.

4-1 Abnormalities observed in cloned individuals

The scientific and technical aspects of cloning technology have been developed by analyzing results obtained from experiments on the production of cloned individuals from cloned embryos using domestic or experimental animals. The findings from these cloned animal production experiments should help us understand the nature of cloned human embryos used for therapeutic cloning.

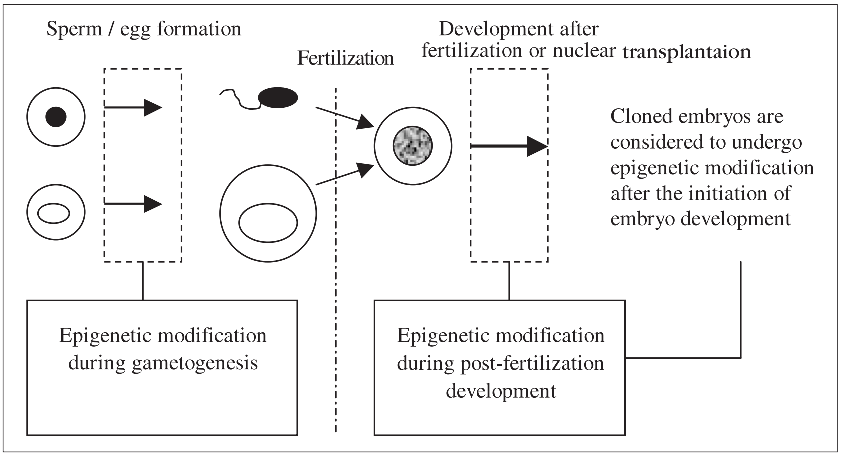
(1) In animal experiments, when embryos produced through cloning are implanted into the uterus, most early mouse embryos die immediately after their implantation, i.e., at the stage of placenta formation, while cattle and sheep embryos stop developing in late pregnancy, resulting in a high percentage of stillborn and abnormal babies. Moreover, the size of the newborn babies and their placentas is unusually large, and this commonly observed independent of species. After birth, a wide range of abnormalities is observed in respiratory function, kidneys, liver, heart, brain, etc., and obesity, oncogenesis and short life are observed after growth.

(2) The risk of inducing abnormal traits partially depends on the type of donor cell (fibroblasts, ES cells, etc.) used for nuclear transplantation. With ES cell nuclei, cloned embryo production is 10-20 times more efficient than production using other somatic cells.

(3) Abnormalities observed in cloned individuals are considered to be induced by abnormal reprogramming or egg inactivation, the use of abnormal donor cells or in vitro culture. For example, the efficiency of microfertilization can deteriorate due to technical factors, even in the absence of non-genetic abnormalities. However, in biological terms, epigenetic factors[*1] such as genome imprinting, rather than technical damage or genetic factors, seem to be the main cause of abnormal cloned individuals.

(4) Reprogramming is an epigenetic process required to achieve a state suitable for initiating embryo development. The process appears to have two stages, i.e., during the formation of the gametes (sperms or eggs) in the reproductive organs, and after the fertilized eggs and embryos have started

Figure 2 : Process involving epigenetic modification



developing. Since the nuclei of cloned embryos skip the process of gametogenesis, they cannot achieve a completely reprogrammed state (Figure 2).

Even in embryos derived through usual sexual intercourse, the absence of normal epigenetic reprogramming after fertilization results in abnormal development. For example, parthenogenesis of an egg results in the formation of teratoma, while an embryo with only a sperm-derived nucleus results in developing vesicular mole.

Furthermore, the epigenetic factors involved in gametogenesis include a mode of gene modification called imprinting (mechanism for regulating gene expression which leads to differential expression between paternal and maternal genes) and the modification of non-imprinted genes, and the factors involved after the initiation of development include X-inactivation and telomere length regulation. Cloned embryos undergo normal epigenetic processes after the initiation of development, i.e., X-inactivation and telomere length regulation.

(5) Cells consisting of various organs in cloned individuals differ greatly from those found in individuals produced through ordinary reproduction in terms of the kinds of gene expressed, DNA methylation patterns, expression levels of various substances, etc.

4-2 Procurement of eggs

The biological significance of using eggs to prepare cloned embryos is their capability of reprogramming the transplanted nuclei. Reprogramming is required to modify the cells, which have once experienced differentiation and are functioning as somatic cells, so that they can form early embryos again (initiate development).

(1) Eggs can be provided (i) by female volunteers or (ii) from eggs obtained for fertility treatment or through other medical procedures.

From the viewpoint of human rights and gender issues, there is a great fear that females may be treated as a means of supplying egg materials for human cloning. In the United Nations, African countries have expressed their concerns about “poor women in African countries becoming exploited as egg factories.” Moreover, egg retrieval imposes physical risks such as the use of ovulation-inducing agents, anesthesia and surgical operation. For instance, ovulation-inducing agents may induce severe symptoms such as ovarian hyperstimulation syndrome.

Meanwhile, eggs may be obtained through medical procedures other than fertility treatment, such as from ovaries removed in surgery.

(2) There is no established method for the cryopreservation of eggs. However, the use of frozen eggs has resulted in successful in vitro fertilization in a number of cases. Advances in cryopreservation technologies should enable the preservation of individual

eggs or of eggs as a part of the ovary tissues.

(3) Alternatives to using eggs collected or provided from living bodies to reprogram the somatic nuclei of donors are currently being developed, such as the use of eggs differentiated from human ES cells or eggs derived from other species. In 2003, Hübner, et al. reported that egg cells could be differentiated from mouse ES cells[9]. This report suggests that, although less efficiently than egg cells derived from living bodies, a large number of egg cell-like cells can easily be obtained (from ES cells through only in vitro treatment) as a tool for reprogramming somatic nuclei and initiating the development of cloned embryos. This report implicates that cells required for medical cell transplantation can be supplied on an industrial basis.

(4) In the future, the development of new techniques for the reprogramming process, such as the direct reprogramming of somatic cells, may eliminate the necessity of eggs derived from living bodies to obtain rejection-free cells that inherit the immunological characteristics of the patients themselves. Unfortunately, much of the biological mechanism underlying the reprogramming process remains unexplained, even at the level of animal experiments.

4-3 Low success rate

With sufficient technical skill, ES cells can generally be established from blastocysts derived from fertilized embryos with a 100% success rate. In comparison, establishing ES cells from cloned human embryos has a low success rate. Hwang et al. collected 242 eggs from 16 females and used them for nuclear transplantation to achieve 30 blastocysts (12%). However, only one ES cell strain could be obtained, resulting in an extremely low success rate compared to the rate using fertilized embryos. The ultimate success rate was 0.4%, which is impractical considering the use of eggs derived from living bodies.

Nevertheless, their report is significant in that it demonstrates the possibility of establishing ES cells from cloned human embryos, and technical issues should be solved by future research and development. As discussed in the section on abnormalities observed in cloned individuals, cloned embryos skip the process of nuclear reprogramming in the gametogenesis process, and developing an alternative means to this natural process requires basic research using experimental animals. Currently, there is no clear vision concerning the development or the results of such basic research, and scientific and technical breakthroughs are awaited. Nevertheless, including the use of ES cell-derived eggs (or cells similar to these) in research, we must establish a system under which research involving cloned human embryo production can be conducted within an appropriate framework.

5 Status of regeneration medicine research using ES cells

To date, transplantation experiments with animals using cells differentiated from ES cells have been reported on hematopoietic cells, dopamine-producing nerve cells, motor cells and insulin-producing cells, which are applicable to hematopoietic diseases, Parkinson's disease, spinal cord injury and diabetes, respectively. Among these reports, an experiment using immunosuppressed mice simultaneously succeeded in differentiating ES cells derived from cloned embryos and using them in gene therapy through genetic recombination. The success of this experiment is based on the potential of cloned embryos in regenerative medicine and the technical advantage of using ES cells in genetic recombination.

In Japan, the Institute for Frontier Medical Science of Kyoto University has established the 3 human ES cell lines (KhES-1, 2 and 3) shown in Table 3 and has already begun distributing some of them (human ES cell project information disclosure website). Their nature as ES cells is currently being confirmed, such as whether they are capable of stable self-replication (the forms of cells and colonies), their pluripotency, normal chromosomes (karyotype) and the expression of markers for undifferentiation (ALP, SSEA-4, TRA-1-60/81, Oct-3/4, Rex-1, etc.). The nature of ES cells is not fully understood, and therefore requires further research, e.g., to elucidate the molecular mechanism of self-replication.

In addition to the various abnormalities found at the level of the individual, animals derived from cloned embryos differ from normal at tissue level. This generates risks in the application of cloned embryos to regenerative medicine, i.e., the use of artificially generated (naturally non-existing) cloned embryos as cell transplants. These abnormalities are believed to depend on reprogramming, but as mentioned earlier, their mechanisms are not fully understood, even in experimental animals. Meanwhile, the difference between cloned embryos and normal cells may be significant in the process of ontogenesis, but as long as they retain the functions required for cell transplants to treat adults, their safety and benefits may not be considered as practical problems. Furthermore, ethical issues concerning the procurement of eggs may be solved by a new alternative means, such as the use of materials removed in surgical operations or eggs (or egg-like cells) prepared from ES cells as tools for reprogramming.

Based on these points, various patterns of ES cell establishment are shown in Figure 3. A number of attempts have been made to establish ES cells applicable to regenerative medicine, not only ES cells derived from fertilized or cloned embryos but also egg-like cells derived from ES cells or the application of cell fusion techniques. Moreover, the British scientific journal, Nature, has recently published a report[10] by Japanese and Korean researchers who generated eggs with a mutation in a gene (H19) potentially involved in epigenetic genome imprinting in mice, and who successfully initiated development without fertilization in individual reproductive mice. This study clearly demonstrates the involvement of epigenetic phenomena in reprogramming, and other studies are also being conducted to elucidate the reprogramming mechanism.

6 Somatic stem cells and ES cells

In contrast with ES cells, which are derived from cloned human embryos, somatic stem cells are obtained from the tissues of adult individuals. Although their biological properties differ from those of ES cells, somatic stem cells are also useful in regenerative medicine. Unlike human embryos or cloned human embryos, the use of somatic stem cells is free from ethical issues. Here are some important points concerning somatic stem cells compared with cells derived from

Table 3 : Examples of human ES cell strains established in various countries

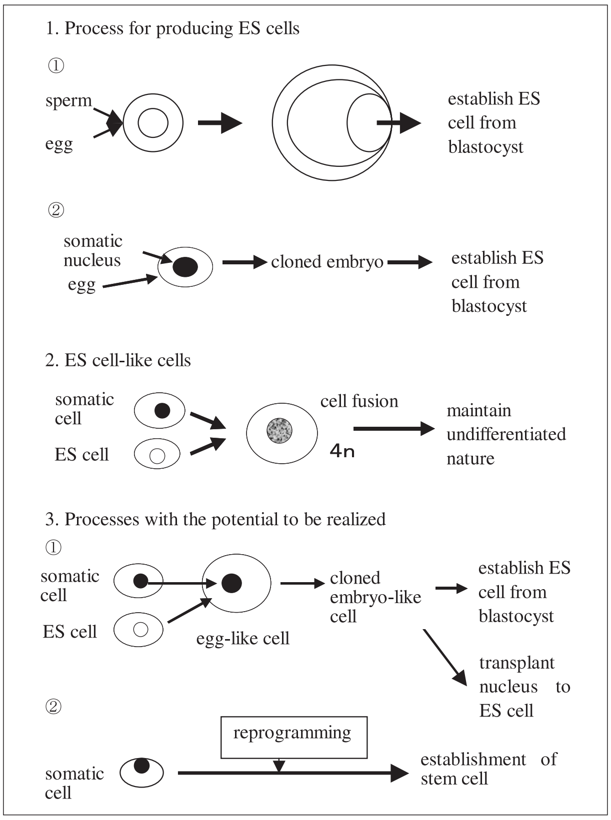
U.S.	27
Sweden	25
India	10
South Korea	6
Australia	6
Israel	4
Total	78

Source: Prepared by the author based on the NIH Stem Cell Registry that presents the number of human ES cell lines approved by U.S. NIH by August 2001

Japan	3

ES cell lines established in May and October 2003 by the Institute for Frontier Medical Sciences of Kyoto University

Figure 3 : Process for producing ES cells, etc.



cloned embryos or ES cells.

(1) Unlike cells artificially derived from cloned embryos, immature ES cells or cells derived from such cells, somatic stem cells are originally part of the body and can therefore be assumed to be safer when returned to the same body in medical transplantation.

(2) Somatic stem cells potentially have various differentiation potencies and practical uses, as demonstrated in an attempt to differentiate mouse bone-marrow cells into myocardial cells. Transplantation therapy against leukemia, etc., using cord blood cells is already equivalent to bone marrow transplantation in terms of the number of patients receiving this therapy (cord blood cell transplantation requires a long recovery period and has a high risk of bleeding and infection in adult recipients, but strategies to overcome these disadvantages, such as alleviating preoperative myelosuppression and using in vitro culture, have been discussed).

Stem cells have limited differentiation potency, but as an exception to this, Jiang et al. (2002) have reported the isolation of pluripotent somatic stem cells[11]. These stem cells have been isolated in mice, rats and humans, but their application has not yet been researched. Some reports doubt the pluripotency of somatic stem cells, and their potential for future application is unclear.

(3) Compared to ES cells, somatic stem cells are difficult to collect and propagate (ES cells can be propagated and maintained without limit over a long period of time).

(4) Some of the advantages of ES cells are that their genes can be modified, they can be supplied in large amounts with consistent quality, their sublines can be established, and their supply can be stabilized and standardized. On the other hand, such advantages are unknown or are hardly observed in somatic stem cells.

Mamoru Ito et al., Central Institute for Experimental Animals, have developed immunosuppressed mice (NOG mice: NOD/SCID/γ (gamma) C^{null}) intended for studying the clinical application of somatic stem cells and ES cells. They are expected to serve as a means of examining in vivo regeneration, and the differentiation and the safety of cell transplants.

As mentioned above, somatic stem cells and ES cells each have different advantages and disadvantages. If collected from the individual to be treated, somatic stem cells require neither the use of fertilized embryos nor the preparation of cloned embryos. However, they seem to have limited capacity for differentiation, propagation and retrieval from living bodies. Therefore, research must be promoted for both cell types.

According to the "Surveys on the clinical application of somatic stem cells in Japan" conducted by the Health Sciences Council in 2002, 90, 3 and 16 facilities were at the stages of research, pre-clinical research and clinical study, respectively (based on data from the references[3]). At least in these facilities, transplantation of the epidermis or bone, or transplantation therapy for vascular occlusion diseases, has already been performed on actual patients in clinical trials. Furthermore, a Japanese patient with a spinal cord injury has received spinal cord regenerative medicine using olfactory ensheathing cells in China. Establishing regulations and guidelines for regenerative medicine has become an urgent social issue for Japan.

7 Debates on therapeutic cloning

7-1 Debates in Japan

Article 2 in the Supplementary Provisions of the "Law concerning Regulation relating to Human Cloning Techniques and other Similar Techniques" (2000) states that "the Government shall, within three years of enforcement of this Law, take necessary measures in accordance with the results of its study and examination of the provisions under this law, based on the results of the examination by the Council for Science and Technology Policy concerning the method of handling of human fertilized embryos as the beginning of human life." The deadline is June 2004, and the Expert Panel on Bioethics of the Council for Science and Technology has announced an interim report, "On basic concepts concerning the handling of human embryos." In response to comments by the public on the report, the committee is continuing discussion to reach a public decision on whether to permit therapeutic cloning and whether to pave the way to regenerative medicine research.

There are various arguments concerning therapeutic cloning. From the ethical viewpoint, arguments in favor of therapeutic cloning are based on medical, scientific and humane reasons. Meanwhile, those against therapeutic cloning are mostly based on religious and personal ethical convictions, or fear of scientific uncertainty, and some even claim that regenerative medicine itself is unnecessary or that the potential to increase exploitation of the human body is not acceptable. Complete agreement has not yet been reached through these arguments, and neither is it expected in the future. Therefore, we should return to the original purpose of achieving both respect of individual rights and public benefit. In other words, the government must establish a social system that approves the independence of individuals with various ethical values and that ensures social safety and peace of mind.

7-2 Trends in therapeutic cloning in the United Nations and other countries

As mentioned earlier, the United Nations has not reached an agreement between those in favor of and those against therapeutic cloning. Complete prohibition of human cloning, suggested by Costa Rica, is supported by more than 50 countries including the United States, African countries, the Vatican, Spain and Italy, while prohibition of only reproductive cloning is supported by more than 20 countries including Belgium, Germany, France and Japan. The United States, which supports complete prohibition, imposes regulations on NIH concerning the use of funds, but does not have any federal law that directly regulates the handling of human embryos including human clones. In other words, the country has no federal regulation on privately funded human embryo research, so human embryo technology has been developed in the private sector. The President's advisory council announced "Human Cloning and Human Dignity" concerning cloning, "Monitoring Stem Cell Research" concerning stem cell research and "Reproduction and Responsibility" concerning assisted reproduction technologies in July 2002, January 2004 and March 2004, respectively. In these reports, the Council only mentions the necessity of social debate, the fact that the Council has been divided over this issue, and that the bill prohibiting both reproductive and therapeutic cloning of human has passed the House but has not been approved in the Senate. Meanwhile, ES cell research has been supervised by NIH (encouraging studies using existing ES cells that have been registered) based on a presidential statement in 2001. At the individual state level, state laws concerning cloning vary greatly, but the law in California approves therapeutic cloning (production of cloned human embryos).

In "The Ethical Implications of Research Involving Human Embryos" and the "Commission Staff Working Paper: Report on Human Embryonic Stem Cell Research" in 2000 and 2003, respectively, the EU suggests establishing strict conditions on the production of human fertilized embryos for research purposes. However, the organization principally respects decisions made by individual governments concerning the production of human embryos for research purposes or therapeutic cloning. In 2001, the European Parliament rejected a bill prohibiting the contribution of public funds to human embryo research (CNN).

To the author's knowledge, countries prohibiting the establishment of ES cells from human embryos are Norway, Austria (imported ES cells are under discussion), Germany (imported ES cells are approved), France (under review), Spain (under review) and Ireland. Switzerland approves the establishment of ES cells but explicitly prohibits both reproductive and therapeutic cloning by law. On the other hand, in countries such as U.K., Belgium, South Korea, China, Israel, Luxembourg, Italy (under discussion) and Taiwan, therapeutic cloning is permitted either explicitly by law or substantially through freedom from legal restrictions. In

France, a revision of the Bioethics bill is currently under discussion in Parliament, and while moving toward an acceptance of research using human embryos for limited purposes, the Parliament is divided over therapeutic cloning. A public poll conducted in France revealed that 65% of people distinguish between reproductive and therapeutic cloning, while 31% make no distinction. The results also indicate that 45% are in favor of therapeutic cloning, while 20-30% are against it (the Science Generation Initiative). In Singapore, a bill that allows therapeutic cloning is currently under discussion and should be approved in the near future (ABC Online).

As in Japan, methods of handling of human embryos are controversial in many developed countries. Discussion concerning the acceptance of ES cells seems to be entering a new stage, while therapeutic cloning has already been socially accepted and researched in some countries.

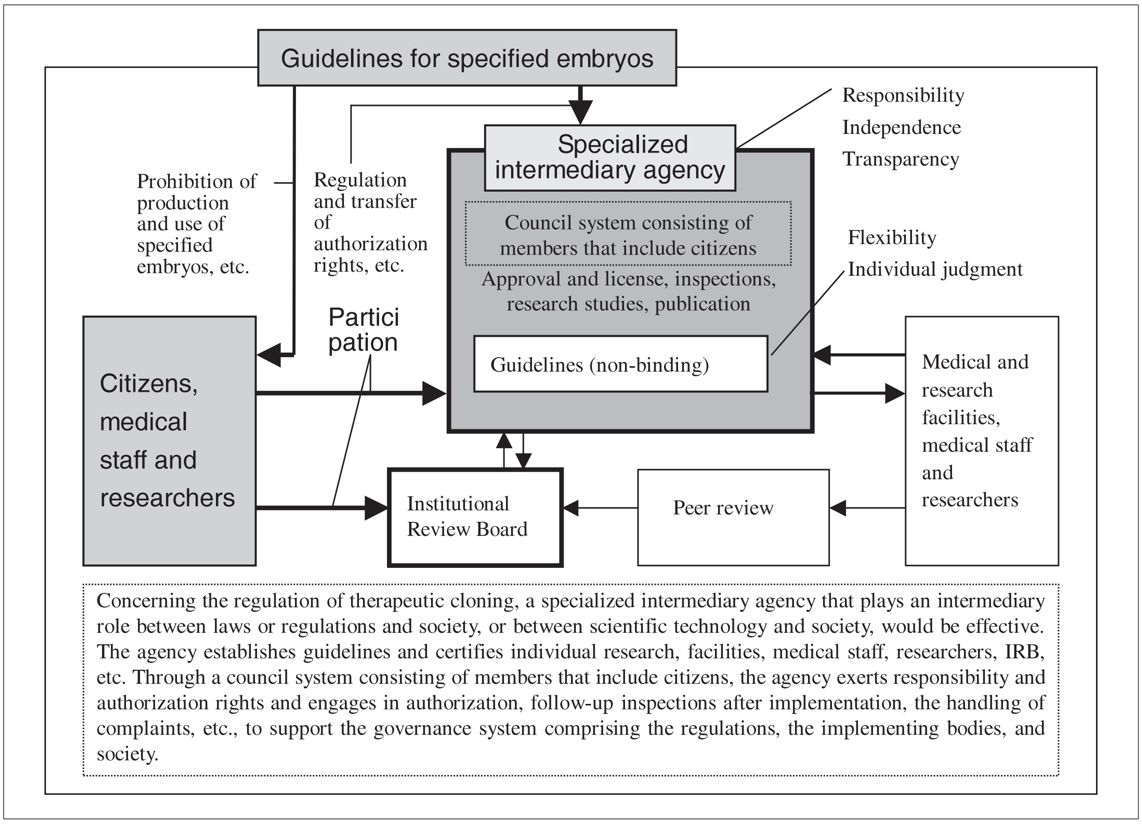
8 Conclusion

The pros and cons of therapeutic cloning have been socially discussed. As long as society demands and expects regenerative medicine and research in this area, protocols and systems for implementation that gain the acceptance and confidence of both sides must be established, based on social debate. As a candidate for such a system, the 2nd Policy-Oriented Research Group of the National Institute of Science and Technology Policy suggests a “social governance system of life science technology”[15], which comprehensively involves the participation of citizens and society, conducts risk management as well as the qualitative control of medical treatment and research, and protects subjects’ rights, through a structure in which a specialized intermediary agency is the core. An intermediary agency is an organization that plays an intermediary role between scientific technology and society. As an example, the structure of a system for therapeutic cloning is depicted in Figure 4. Japan must consider the application of a governance system that secures confidence through the participation of citizens.

Acknowledgements

The author thanks Dr. Terutaka Kuwahara, Director of the Science and Technology Foresight

Figure 4 : Example of social governance system concerning the handling of therapeutic cloning



Concerning the regulation of therapeutic cloning, a specialized intermediary agency that plays an intermediary role between laws or regulations and society, or between scientific technology and society, would be effective. The agency establishes guidelines and certifies individual research, facilities, medical staff, researchers, IRB, etc. Through a council system consisting of members that include citizens, the agency exerts responsibility and authorization rights and engages in authorization, follow-up inspections after implementation, the handling of complaints, etc., to support the governance system comprising the regulations, the implementing bodies, and society.

Center, for providing this opportunity to write this report. The author also thanks those who kindly advised me, especially Dr. Teruhiko Wakayama (RIKEN), Dr. Shinichi Nishikawa (RIKEN) and Dr. Satoshi Teraoka (Tokyo Women's Medical University).

Notes

*1 epigenetic: a mode of non-heritable modification involved in the regulation of gene expression, etc., without changing the gene. The modification involves DNA methylation, histone protein modification, the higher-order structure of chromosomes, etc[8].

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3

Trends in Gene - silencing Research

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1 Introduction

Advance in genome research has provided tools such as DNA microarrays that can be used to analyze the expression and suppression stage in several genes at once. This revealed the fact that not all cells *in vivo* are expressing the same genes in the same manner, but that each cell shows a specific pattern of gene expression. For example, a skin cell and a liver cell each express different genes. This implies the presence of *in vivo* mechanisms for controlling gene expression.

In cancer cells found in cancer-developing tissues or organs, genes that are suppressed in normal cells are expressed while those expressed in normal cells are suppressed, implying the involvement of abnormal gene expression in cancer development. In addition to cancer, abnormal expression or suppression of genes is involved in many lifestyle-related diseases such as diabetes.

Research on mechanisms of gene expression and suppression are showing remarkable growth. Such areas include “gene-silencing research,” which involves study of the mechanism of gene suppression without genetic change (mutation) in the genomic DNA itself.

As shown in Table 1, various subjects are studied in gene-silencing research, such as DNA methylation, chromatin modification, structural change in chromosomes and RNA-mediated suppression of gene expression (RNA interference)[1].

Gene suppression mechanism research is active, because the development of techniques for controlling gene expression will lead to the development of new drugs for treating various diseases.

Nucleic acid compounds are chemically synthesized and introduced into cells to suppress gene expression through stoichiometric inhibition of gene transcription or translation. Typical examples of such nucleic acids are single-stranded synthetic DNAs or RNAs and RNA enzymes (ribozymes). Small double-stranded RNAs are attracting attention for their stability and high efficacy in gene suppression.

Unlike conventional synthesized nucleic acid compounds, small double-stranded RNAs suppress gene expression employing a biological mechanism which all organisms retain. This report triggered the advance in gene suppression mechanism research and facilitated the expansion of gene-silencing research.

This report describes the trends in gene-silencing research with the focus being on research on the small double-stranded RNA mechanism, and further discusses the potential of gene-silencing research for drug development. In addition, this paper describes various strategies for further development in this area.

Table1 : Subjects studied in gene silencing research area

Research target	Research subjects
Mechanism of gene suppression without genetic change in the genomic DNA itself	DNA methylation, chromatin modification, structural change in chromosomes, RNA interference (RNAi), siRNA, suppression of gene expression mediated by synthetic nucleic acid compounds

2 The history of gene-silencing research (years 1990-2001)

The present section covers the gene-silencing research (basic research) conducted since the phenomenon was first reported in 1990 until 2001 and introduces breakthrough studies in this area.

2-1 Gene-silencing research originated from studies of plants

The suppression of gene expression called “gene silencing” was first reported in 1990 in studies of plants[2,3].

The phenomenon was discovered almost by coincidence, when the transformation of petunias with transgenes involved in purple pigmentation for artificially producing dark-colored flowers unexpectedly resulted in white flowers. It was considered that the overexpression of transgenes had suppressed the expression of the endogenous pigment genes.

Subsequent research on the mechanism of gene silencing suggests that the phenomenon were not induced by DNA suppression but rather by RNA suppression.

2-2 Gene-silencing research concerning double-stranded RNA started in nematodes

The suppression of gene expression by the introduction of exogenous single-stranded RNAs into cells was first reported in 1985[4], but it was not until 1988 that double-stranded RNAs were found to be directly involved in gene suppression.

The introduction of large (300kbp or larger) double-stranded RNAs into the cells of nematodes suppressed gene expression more selectively and efficiently than in the case of single-stranded RNAs[5,6].

The suppression of gene expression by double-stranded RNAs was named “RNAi (RNA interference)” and has been reported in invertebrates such as hydra, drosophila and plants.

Single-stranded RNAs suppress gene expression by binding to target mRNAs and mechanically inhibiting their translation into proteins. Double-stranded RNAs suppress gene expression using a gene-silencing mechanism that originally existed in vivo but has recently been discover. The mechanism is explained in Section 2-5.

2-3 Discovery of small RNAs as performers of gene silencing

Large double-stranded RNAs introduced into plant or nematode cells are broken down into small double-stranded RNAs of about 22bp within cells. These small double-stranded RNAs induce gene silencing, which was demonstrated in a series of reports published in 1999-2000.

In 2001, an enzyme decomposing the double-stranded RNAs was discovered from drosophila and was named “Dicer”[7], which was also later discovered in mammalian cells[8].

The discovery of this enzyme suggests that gene suppression by double-stranded RNAs is a common phenomenon found in all organisms. The next step was to search for the small double-stranded RNAs that actually function in cells.

2-4 Introduction of double-stranded RNAs also induced gene silencing in mammals

Because the mammalian mechanism for gene silencing is different from those in plants or invertebrates such as nematodes, it is considered that gene suppression mediated by double-stranded RNA is not applicable to mammalian cells. When long double-stranded RNAs of 30 bp or larger are introduced into mammalian cells, the cells mistake it for virus invasion and release interferon, ultimately inducing cell death instead of gene suppression.

Based on the results of gene-silencing studies conducted in nematodes and plants, small double-stranded RNAs of the same size (21 bp) as those decomposed by Dicer, were introduced into mammalian cells instead of the large double-stranded RNAs. This attempt succeeded in inducing gene silencing in various cultured mammalian cells, including human cells, without causing cell death[9].

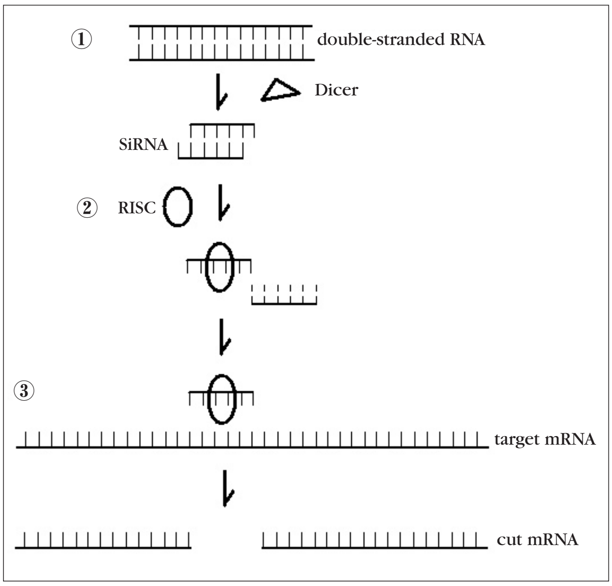
This discovery was a breakthrough in the use of double-stranded RNA in mammals. Small double-stranded RNAs (small interference RNA, siRNA) has rapidly drawn attention as a universal tool for suppressing gene expression.

2-5 Mechanism of gene silencing mediated by double-stranded RNAs

Figure 1 illustrates the mechanism of gene silencing mediated by double-stranded RNAs. This is considered a universal mechanism commonly found among all organisms including mammals.

(1) Dicer cuts double-stranded RNA that enter cells into small fragments of about 22 bp to form small interference RNAs (siRNAs).
(2) One of the two strands of the siRNA binds to a RISC (RNA-induced silencing) complex, while the other is decomposed.
(3) The RNA-bound RISC complex binds to a messenger RNA having a sequence complementary to the RNA strand and decomposes the complementary region, resulting in the inhibition of protein synthesis.

Figure 1 : Mechanism of gene silencing mediated by double-stranded RNAs



2-6 Small RNAs involved in the regulation of in vivo gene expression

Several small RNAs are present within the cells and are involved in the regulation of gene expression.

These short double-stranded RNAs of 18-25 bp, called miRNAs (micro RNAs), were first reported in 2001[10]. RNAs (pseudodouble-stranded RNA) having hairpin secondary structures are cut by Dicer to form miRNAs. miRNAs consist of mRNA portions corresponding to non-translated regions.

The miRNA suppresses gene expression through a mechanism similar to that of siRNA, but unlike siRNA, which completely binds to the target mRNA sequence, miRNA only partially binds to the target mRNA, resulting in no decomposition of mRNA. Therefore, miRNA is considered to inhibit protein synthesis stoichiometrically. Moreover, since miRNA binds to the non-translated region within the mRNA sequence, it is believed that miRNA acts by binding to a region involved in the control of gene expression.

Hundreds of miRNAs can be found within a nematode or plant cell and are reported to be controlling the timing of development or regulation of stem cells. It is assumed that 200-250 miRNAs are present within human cells[11], and their functions have been actively researched.

Table 2 chronologically lists breakthrough studies in gene-silencing research. As can be seen,

Table 2 : Breakthrough studies in the area of gene silencing research (basic research)

Year	Content	Research target	Highlights
1990	Suppression of flower color gene through gene transfer	Plant	Discovery of modification in phenotypic traits through gene transfer
1998	Gene suppression mediated by double-stranded RNAs (siRNAs)	Nematode	Discovery of a novel gene suppression technique
2001	Discovery of an enzyme (Dicer) decomposing double-stranded RNAs (siRNAs) in vivo	Drosophila	Elucidation of gene suppression mechanism
2001	Gene suppression in mammalian cells by small double-stranded RNAs	Mammal	Discovery of a gene suppression technique for mammalian cells
2001	Discovery of small double-stranded RNAs (miRNAs) considered to be involved in the regulation of gene expression	Mammal	Discovery of a molecule essential to in vivo regulation of gene expression

much of the research was performed in 2001.

3 Overview gene silencing

Based on its own database of research papers called Essential Science Indicators, Thomson Scientific analyzes research papers concerning particular research areas. In December 2003, the company reported the results obtained from their analysis of gene silencing[12].

The present section provides an overview of gene silencing based on the report by Thomson Scientific as well as the results obtained from our own research using the ESI database.

3-1 International comparison of gene-silencing research

Thomson Scientific performed a search on papers published during 1993-2003 using "gene silencing" as the keyword and extracted 1,505 papers written by 4,540 authors representing 898 research institutes from 48 nations and published in 365 academic journals[12] (the papers were searched by keywords by abstracts and authors).

- **The United States is leading the gene-silencing research**

According to Thomson Scientific, the United States was ranked the highest (17,073 citations from 697 papers) for the total number of citations of gene-silencing related papers on a country basis, followed by the United Kingdom (6,374 citations from 168 papers), Germany (3,166 citations from 128 papers), France (2,460 citations from 117 papers) and Scotland (1,716 citations from 47 papers). Japan was ranked 12th, with 649 citations from 111 papers[12].

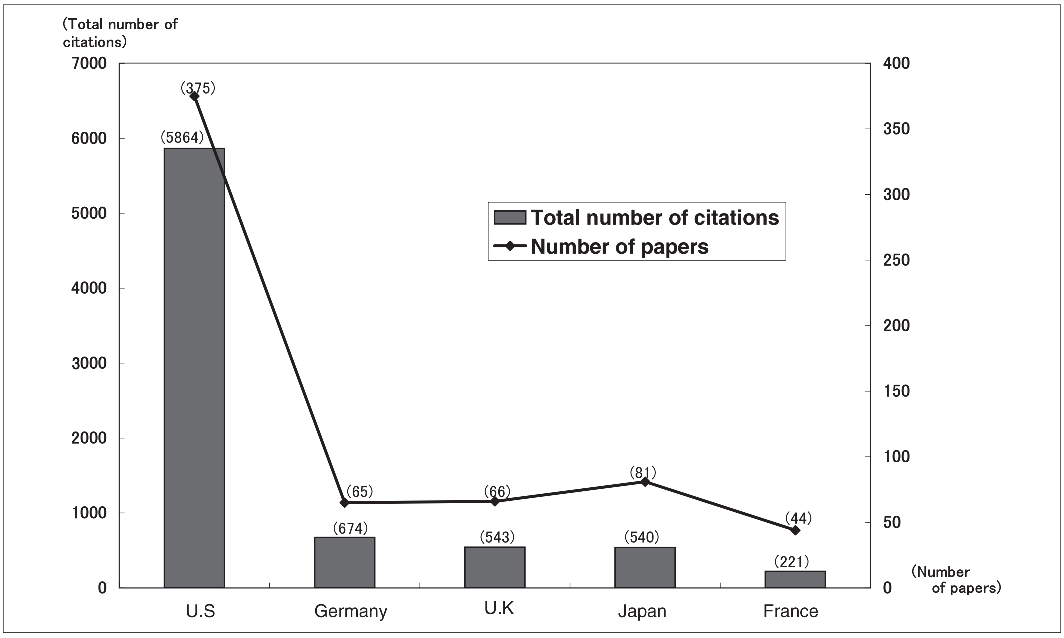
- **The number of citations for Japanese papers are increasing**

In order to compare the numbers of citations on a country basis for the last two years, a similar search was performed using the ESI database.

Figure 2 shows the number of citations of papers published during the last two years (2002-2003) for various countries. As in the analysis performed on years 1993-2003, the U.S. had the largest total number of citations for the last two years.

The total number of citations for Japanese papers increased to a level substantially equivalent to that of Germany or the U.K. Furthermore, about 70% of the papers published during 1993-2003 were published within these two years. This indicates that it has not been long since the research area has become active in Japan.

Figure 2 : Comparison of total numbers of citations of papers in gene silencing research area between countries (2002-2003)



3-2 Characteristics of gene-silencing research

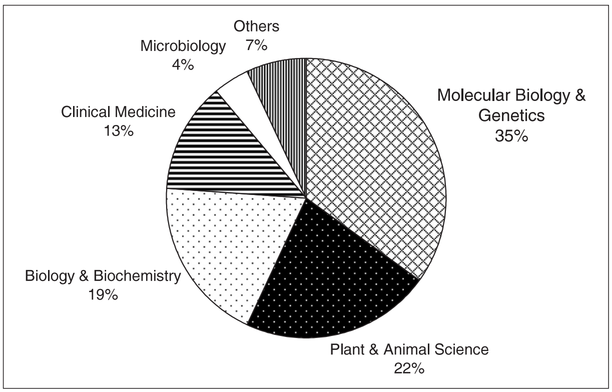
The characteristics of gene silencing were analyzed based on the ESI database.

- **Gene-silencing research is a multidiscipline area**

The papers concerning gene-silencing research are classified by the academic area of the journals in which they are published. As a result, 35% of the papers fall under Molecular Biology & Genetics, while 21%, 19% and 13% fell under Plant & Animal Science, Biology & Biochemistry and Clinical Medicine, respectively[12] (Figure 3).

The analysis indicates that many academic areas are involved in the gene silencing.

Figure 3 : Classification of papers in gene silencing research by academic area



- **The two major subjects dealt with in the ten most-cited papers were DNA methylation and RNAi**

Table 3 lists the ten most-cited papers in gene silencing. The classification of these papers by their research subjects reveals the presence of two major subjects.

One is the mechanism of RNA-mediated gene silencing and the other is the mechanism of gene silencing mediated by DNA or histone methylation found in mammalian cells.

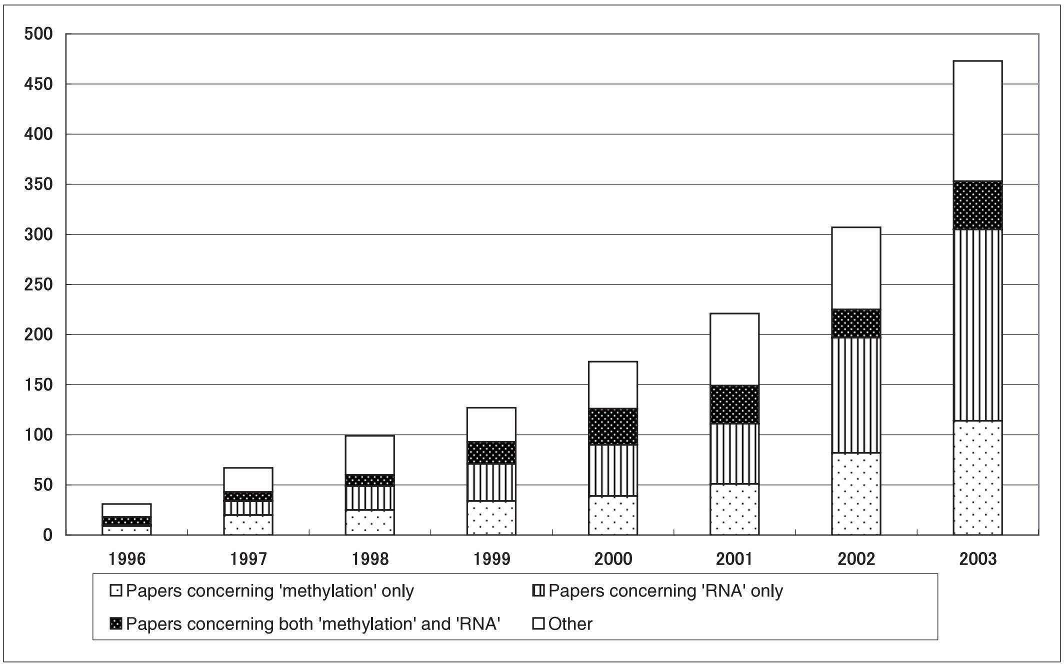
3-3 Shift in gene silencing research

Temporal changes in gene silencing were revealed by analyzing the number of papers using

Table 3 : Ten most-cited papers

	Number of citation	Titles	Subjects	Authors (Nationalities)	Journals (Years of publication)
1	913	Methylation-specific PCR: A novel PCR assay for methylation status of CpG islands STATUS OF CPG.	Methylation	Herma, JG et al. (U.S.)	PNANS (1996)
2	627	Duplexes of 21-nucleotide RNAs mediate RNA interference in cultured mammalian cells.	RNAi	Elbashir, SM (Germany)	NATURE (2001)
3	584	Methylated DNA and MECP2 recruit histone deacetylase to repress transcription.	Methylation	Jones, PL (U.S, Belgium, Italy)	NATURE GENETICS (1998)
4	522	Cancer epigenetics comes of age	Epigenetic	Jones, PA (U.S.)	NATURE GENETICS (1999)
5	411	Methylation of the 5'-CpG island of the P16/CDKN2 tumor-suppressor gene in normal and transformed human tissues correlates with gene silencing.	Methylation	Gonzalezzulueta, M (U.S.)	CANCER RESEARCH (1995)
6	345	A species of small antisense RNA in posttranscriptional gene silencing in plants.	Antisense RNA	Hamilton, AJ (U.K.)	SCIENCE (1999)
7	339	Selective recognition of methylated lysine 9 on histone H3 by the HP1 chromo domain.	Methylation	Bannister, AJ (U.K., Scotland)	NATURE (2001)
8	308	Methylation of histone H3 lysine 9 creates a binding site for HP1 proteins.	Methylation	Lachner, M (Austria)	NATURE (2001)
9	293	An RNA-directed nuclease mediates post-transcriptional gene silencing in Drosophila cells.	RNAi	Hammond, SM (U.S., U.K.)	NATURE (2000)
10	264	RNA interference is mediated by 21-and 22-nucleotide RNAs.	RNAi	Elbashir, SM (Germany)	GENES & DEVELOPMENT (2001)

Figure 4 : Shift in the number of papers and research subjects in the gene silencing research area (1996-2003)



the ESI database.

The number of papers published in each year was investigated using "gene silencing" as the search keyword. Only 31 papers were published in 1996, but the number of papers has continuously increased since then and drastically increased since 2001 (Figure 4).

In addition, as mentioned in Section 3-2, since "RNA" and "methylation" were the major subjects researched in the most-cited papers in the gene-silencing research, these keywords were each combined with "gene silencing" to examine the temporal shift in research subjects within the area (Figure 4).

The result demonstrates that the mainstream has shifted from methylation to RNA research; the former was dominant until 1997 while the latter became dominant after 2002. This reflects the shift of researchers' interest into small double-stranded RNAs after the mechanism for RNA-mediated gene silencing was fundamentally understood by 2001.

Furthermore, many reports suggesting the mutual involvement of "RNA" and "methylation" in the gene-silencing mechanism were successively published in 2004[13-15]. Therefore, the two subjects that were dealt with separately are likely to be integrated into a single research area.

4 Development of applied research on gene silencing toward disease therapy (2002-2004)

Experiments using mammalian cells or mice have been conducted in expectation of the development of new drugs and therapeutic or prevention methods using the small interference RNAs (siRNAs)[16]. The target candidates are diseases that are potentially cured by suppressing gene expression, such as virus diseases (e.g. HIV/AIDS, influenza, SARS, virus hepatitis), neurologic diseases (e.g. Parkinson's disease, Alzheimer disease), cancer and autoimmune diseases (e.g. rheumatism).

Table 4 lists the breakthrough studies that contributed to the development of such applied studies.

4-1 Research on disease therapy by gene silencing

The following cases are examples of applied research on gene silencing performed using animal models for human diseases.

- **Inhibition of HIV virus infection**

In rapidly dividing cells, the absolute number

Table 4 : Breakthrough studies in the area of gene silencing research (applied research)

Year	Content	Research target	Highlights
2002	Gene suppression by injection of small double-stranded RNAs into mice through tail vein [17]	Mice	Successful in vivo delivery through an ordinary means
2003	Prevention of hepatitis using small double-stranded RNAs in hepatitis model mice [18]	Mice	Establishment of the principle for therapies mediated by small double-stranded RNAs
2004	Discovery of a novel molecule from a known signaling pathway through an RNAi-based screening system [19]	Human	Establishment of a large-scale screening system enabling search for novel targets for drug

of siRNAs per cell decreases as the cells divide and propagate, so the effect of siRNA-mediated gene silencing only lasts for about 5 days. This was considered a drawback of siRNAs when using them as drugs, but research conducted in 2003 provides a solution to this[20].

HIV viruses invade the macrophages by binding to CCR5 receptors present at the macrophage surface, so the inhibition of their binding to the receptors should prevent their infection. Moreover, macrophages do not undergo cell division, so siRNA-mediated gene suppression was expected to last over the long term.

siRNAs that suppress the expression of the macrophage CCR5 receptor genes and siRNAs that suppress the expression of HIV virus genes were produced and used in combination to test their effectiveness in preventing HIV virus infection.

The preliminary introduction of the siRNAs suppressing the CCR5 receptor gene expression into macrophages successfully prevented HIV-infection of the macrophages. Moreover, siRNAs suppressing the expression of HIV virus genes proved effective for preventing the replication of viruses that have already infected the macrophages. These results demonstrate the potential of siRNAs, not only as preventive drugs but also as therapeutic drugs.

- **Prevention of aggravation in liver diseases**

Many liver diseases are accompanied by apoptosis (cell death) in liver cells mediated by Fas protein. The death of liver cells deteriorates liver function, resulting in symptoms such as liver cirrhosis. Therefore, the prevention of cell death in liver cells by suppressing the expression of Fas protein should prevent the progression to severe status such as liver cirrhosis.

In 2003, siRNA-mediated gene silencing was reported in autoimmune hepatitis model mice. Development of hepatitis in the hepatitis model mice was successfully prevented by injecting siRNAs that contain sequences corresponding to the Fas gene via their tail veins[18].

4-2 Drug development research by gene silencing

Instead of being used as drugs, the small interference RNAs are used as tools for searching in vivo targets (proteins) for developing new drugs.

- **Research on cancer drug development**

In 2003, de-ubiquitinating enzymes in cancer-related pathways were identified using RNAi. The result demonstrates that the inhibition of familial cylindromatosis tumor suppressor gene (CYLD), having no known function, enhances the activation of the transcription factor NF-κB and imparts resistance to apoptosis (cell death)[21].

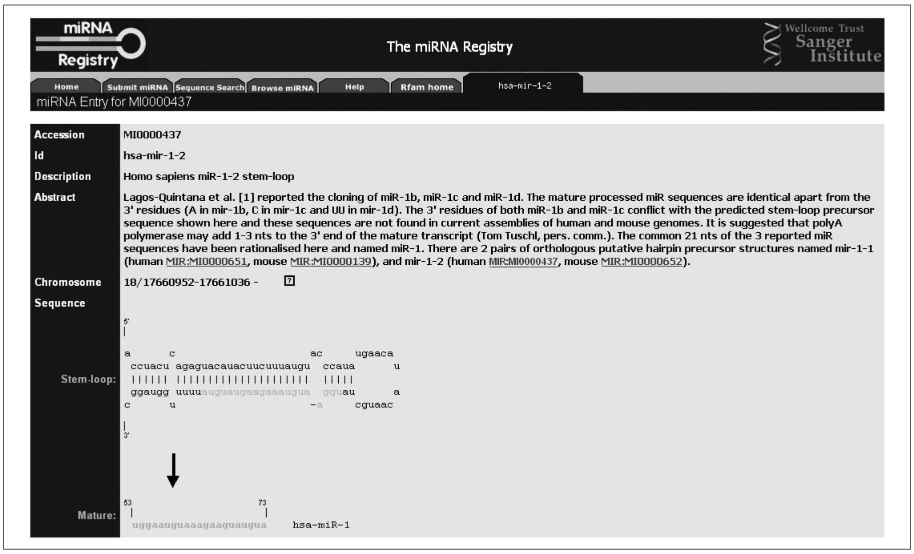
This implies that the loss of CYLD inhibits cell death and therefore inhibits the removal of abnormal cells, which leads to the accumulation of genetic mutations and develops cancer. Although the relationship between the loss of CYLD and oncogenesis has been recognized, the mechanism of CYLD-mediated oncogenesis is not understood.

Based on this research result, NF- κB inhibitors are researched as potential drugs for treating familial cylindromatosis.

4-3 Infrastructure development for promoting gene-silencing research

Databases concerning the small interference RNAs are established mainly in the U.S. and European countries to provide information such as RNAi sequence data.

Figure 5 : miRNA database



miRNA Entry for MI0000437

Accession MI0000437

Id hsa-mir-1-2

Description Homo sapiens miR-1-2 stem-loop

Abstract Lagos-Quintana et al. [1] reported the cloning of miR-1b, miR-1c and miR-1d. The mature processed miR sequences are identical apart from the 3' residues (A in mir-1b, C in mir-1c and UU in mir-1d). The 3' residues of both miR-1b and miR-1c conflict with the predicted stem-loop precursor sequence shown here and these sequences are not found in current assemblies of human and mouse genomes. It is suggested that polyA polymerase may add 1-3 nts to the 3' end of the mature transcript (Tom Tuschl, pers. comm.). The common 21 nts of the 3 reported miR sequences have been rationalised here and named miR-1. There are 2 pairs of orthologous putative hairpin precursor structures named mir-1-1 (human MIR:MI0000651, mouse MIR:MI0000139), and mir-1-2 (human MIR:MI0000437, mouse MIR:MI0000652).

Chromosome 18/17660952-17661036 -

Sequence

Stem-loop:

```
5'
|

a      c                     ac     ugaaca
 ccuacu agaguacauacuucuuuaugu  ccaua      u
 |||||| |||||||||||||||||||||  |||||
 ggaugg uuuuauguaugaagaaaugua  gguau      a
c      u                     -a     cguaac

|
3'
```

Mature:

```
53                   73
 |                   |
 uggaauguaaagaaguaugua    hsa-miR-1
```

Source: The miRNA Registry website

- **Databases of small interference RNAs (miRNA)**

The British Sanger Institute (funded by Wellcome Trust) has established a database of small interference RNAs[22,23]. To date, 899 miRNAs have been registered, and data including 78 drosophila, 166 nematode (two species) and 191 human miRNAs can be freely accessed (Figure 5).

4-4 Trends concerning drug development

Gene-silencing research has passed the applied research phase and now entered the phase of clinical studies and drug development.

- **Corporate-driven technical cooperation has been established for drug development**

Many universities and companies forged technical partnership around 2003. Examples of such partnership are presented in the following section.

A U.S. company Sirna Therapeutics, Inc. entered into a license agreement with the University of Massachusetts Medical School concerning small interference RNA (siRNA) technology.

Merck & Co. Inc. and Alnylam Holding Co. collaborated to develop RNA-based technology and therapeutics. Alnylam Holding Co. is a merged company of Alnylam Pharmaceuticals Inc. and a German company Ribopharma AG. Ribopharma AG, who already had many European patents concerning RNAi, aimed at acquiring RNAi-related U.S. patents by merging with Alnylam Pharmaceuticals Inc.

Furthermore, Alnylam Pharmaceuticals Inc., the pharmaceutical division of the Alnylam Holding Co., formed a research collaboration with Mayo Clinic, the leading comprehensive medical institute in the U.S. functioning both as a general hospital and as a research and education institution, to develop therapeutic drugs for Parkinson's disease using RNAi-based technology.

To date, no clinical study (clinical trial) such as human administration of siRNA drugs has been reported, but it is expected to begin in the near future (by the end of 2004 or 2005).

5 Unresolved research issues concerning gene-silencing research

The present section discusses the unresolved research issues for the medical application of gene silencing and suggests research required for their resolution.

5-1 Unresolved research issues in basic research

In gene-silencing research, many breakthrough studies at the basic research level were reported within a short period. This gives the impression that sufficient basic research has already been accomplished, but there are many aspects that are not fully understood.

- **Elucidation of RNA interference (RNAi) mechanism**

Some parts of "the mechanism of gene silencing mediated by double-stranded RNAs" described in Figure 1, such as the detailed structure of the RISC complex or its function, remain unclear. Further research is required to elucidate the details of the mechanism.

- **The roles of small interference RNAs (miRNAs) in vivo**

Recent studies reveal that a mammalian cell contains about 250 miRNAs, which are assumed to be controlling the expression of various genes in vivo.

These small interference RNAs (miRNAs) are assumed to be controlling the expression of genes in various steps of development and differentiation or in various organs.

Some miRNAs act as switches for turning on and off gene expression. While, some proteins have functions of "suppressing" other proteins *in vivo*. When the expression of genes for such proteins is suppressed by the miRNAs, the other proteins are freed from the "suppression" and regain their "expression."

The elucidation of the functions of all 250 miRNAs in a mammalian cell should lead to the elucidation of the *in vivo* mechanism of gene regulation and the network among genes. However, most miRNAs have not been functionally identified.

- **Relationship between suppression of gene expression and RNAi in chromosomes**

A normal chromosome has regions where the expression of particular genes is suppressed by methylation. An unstable gene suppression status prevents normal development or differentiation or induces diseases such as cancer or congenital abnormality. Recent reports suggest that such chromosomal gene suppression involves an RNAi-mediated mechanism, but the actual mechanism is unknown.

The control of gene suppression status in chromosomes should provide novel findings in development and differentiation studies and ultimately bring a breakthrough in the development of new drugs for treating diseases. It is therefore important to elucidate this mechanism.

5-2 Unresolved research issues concerning the applied research toward medical application

Since RNAi drugs have not been developed, it is difficult to estimate the size of the market concerning drug development using RNAi. RNAi is currently applied mainly to experimental techniques or reagents for research, and its market size is estimated to be $300 million. Such techniques should be involved in the development of therapeutic drugs or techniques, so the current value of the drug development market using RNAi is estimated to be $500 million. By 2010, the market is expected to increase to $1 billion[24].

Meanwhile, many research issues must be resolved before the practical application of RNAi to drugs.

- **The issue of in vivo drug delivery system (DDS)**

The drug delivery system (DDS) is an important issue for using siRNA as drugs. The siRNAs administered through ordinary means must be securely delivered to the target organs, stably exist *in vivo* until therapeutic effects are achieved and exert the effects in a sustained manner.

Some of the possible means for delivering the siRNAs in vivo are (1) the use of synthetic polymers such as liposomes as carriers or (2) the use of safe virus vectors as carriers. Such means have been discussed in gene therapy research, but sufficiently safe and efficient techniques have not been achieved.

Nanotechnology-based techniques such as the use of nanoparticles as carriers are promising DDS techniques that may be developed in the future.

- **The issue of side effects**

Highly selective drugs are thought to posses few side effects. However, even among the drugs recently developed as molecular-targeting drugs with few side effects, some drugs have been reported to exert severe effects in certain patients. In the case of gene-targeted drugs, certain combinations of the drug and the genetic status of the patients may produce unexpected side effects.

Moreover, even though the human genome has been decoded, the overall network among genes and their functions in vivo is fully understood. This means that there is a risk that the suppression of a certain gene may induce unexpected suppression or expression of other genes.

In addition to mRNAs, cells contain small RNAs present within the nuclei involved in the biosynthesis of ribosomal RNAs. The RNAi drugs introduced into the cells may be transferred into the nuclei and bind to these small nuclear RNAs[25].

5-3 Research promoting medical application of gene silencing

Drugs based on gene silencing directly or indirectly acts against the genes. Therefore, their safe, effective use requires sufficient understanding of in vivo functions of the major genes, the regulatory mechanism of their expression and the network among genes.

The following research is suggested for understanding such subjects.

(1) Basic research using model organisms

The function of vital genes are common among all living organisms, so detailed studies using model organisms should provide results applicable to humans.

Extensive research has been conducted on experimental organisms such as nematodes and drosophila, but even in such organisms, little is understood regarding the vital functions responsible for life itself, including the genes.

(2) Basic research applying problem-solving approaches

In order to promote the medical application of gene-silencing research, it is important to solve research problems that are created in applied or clinical studies. For this purpose, it is effective to conduct basic research taking problem identification and problem-solving approach.

(3) Applied and clinical studies according to needs

The medical application of gene silencing requires information of the patient types, their needs and the suitability of the gene silencing-based treatment for individual cases.

Applied and clinical studies must reflect the needs from the actual clinical environment, which requires the establishment of a system for efficiently providing the researchers with medical information.

6 Conclusions

Finally, this section characterizes the gene silencing and suggests measures to be taken for further promotion of the area.

6-1 Characteristics of this area

The following three points characterize the research area.

- **The fusion of several research areas has promoted gene-silencing research**

Gene silencing has grown rapidly over the past 4-5 years. The area has expanded through the fusion of several basic research areas such as DNA methylation and RNA-mediated gene suppression. The research targets were first limited to plants but were soon expanded to yeast and nematodes. Now the research subjects have shifted from mice and other mammals to human disease therapy.

- **Transition of the research phase is quick**

In most cases of biomedical research, the research phase has shifted from basic research to applied research and ultimately to clinical research. This shift of the research phase has been very rapid in gene silencing (Table 5).

- **The U.S. leads the area, but the number of citations of papers by Japanese authors is increasing**

Analysis of research papers concludes that the U.S. plays a leading role in this research area. However, the number of citations of papers by Japanese authors is increasing, which implies the expansion of scale of domestic gene-silencing research.

Table 5 : Research phases in gene silencing research

Research phase	Year	Period	Research subject
The first report	1990	(8 years)	The first report on gene silencing
Basic research	1998 – 2001	4 years	Elucidation of in vivo mechanism of gene silencing
Applied research	2002 – 2004	3 years	Research using animal disease models toward medical application
Clinical research	2005 – ?	?	Research concerning clinical trials performed on patients

Among the papers published in the top journals having impact factors of 10 or higher in 2002-2003, papers involving Japanese researchers as principal investigators were mostly supported by relatively large, project-type research support systems such as “21st century COE (Ministry of Education, Culture, Sports, Science and Technology),” “Grant-in-Aid for Scientific Research on the Priority Area (Ministry of Education, Culture, Sports, Science and Technology),” “Grant-in-Aid for Scientific Research (S) (Ministry of Education, Culture, Sports, Science and Technology),” “Research for the Future Program (JSPS),” “Exploratory Research for Advanced Technology Program (JST)” and “Rice Genome Research Program (Ministry of Agriculture, Forestry and Fisheries).”

6-2 Measures for further promoting the gene silencing

Measures for further promoting the gene silencing are discussed based on the characteristics of the area.

(1) Importance of basic research taking a problem-solving approach in a spiral-type research area

In gene-silencing research, breakthroughs that were derived from basic research have established the direction of the applied research toward medical application. To date, the advance in gene-silencing research has greatly contributed to the elucidation of life, but many functions and mechanisms remain unknown, especially the common mechanisms shared by all organisms. These include the regulation of gene expression in the development and differentiation processes.

Furthermore, the medical application of this technology requires the resolution of several research problems, which involves not only applied or clinical studies but also basic studies including the elucidation of gene networks.

The area of gene-silencing research does not fit a linear advance model of “basic research → applied research → clinical research” but fits a spiral advance model of “basic research → applied research → clinical research → basic research → applied research → clinical research → ” or a braid-type model in which the area is advanced through intertwining of “basic research”, “applied research” and “clinical research”.

The area is currently approaching the end of the first spiral. It is essential to start basic research taking the problem identification and problem-solving approach forward to the second spiral.

(2) Establishment of an environment promoting spontaneous adoption of research from other areas

As can be seen from the fact that the gene-silencing research started from the area of plant research, breakthroughs that expanded the research area were derived from the adoption of research from other areas. Therefore, it is important to establish an environment promoting information exchange between various research areas.

For example, a funding agency decides a subject for research adopting a task-solving approach and recruits about 10 research groups taking different approaches and belonging to different research areas. About twice a year, the agency hosts interim meetings where the research groups can exchange their results. The agency does not enforce joint research among the groups but only promotes information exchange.

Alternatively, it may be effective to organize a research meeting for researchers gathered from various areas. As in the Gordon Research Conference, the participants selected by the committee congregate together and thoroughly debate a particular research issue in a closed environment.

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4

Research Trends in Computer Science and Challenges for Japan
— Findings from the International Science Awards —

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1 Introduction

Securing top-quality research personnel is an essential for science and technology policy[1,2]. One possible measure for research promotion is to increase the number of winners of international awards and prizes[3-5]. This article focuses on trends in computer science research from the viewpoint of science awards in computer science, such as the Turing Award, and discusses how to facilitate academic development in this area.

Computer science emerged as an academic discipline in the mid 20th century and achieved rapid development. No matter how outstanding, commercial success has not necessarily been valued from the academic perspective. This means that it is a field in which academic structure and the boundaries between basic theory and application technology are subject to constant review.

In the field of computer science, which has undergone such a transformation, the Turing Award has been known for its consistent review and recognition of research results since 1966. To highlight certain aspects of research trends in computer science, this article traces the history of the Turing Award.

There are many other awards and prizes that honor achievement in computer science. The Gödel Prize is particularly intended for achievement in basic theory. The prize is given for outstanding papers in theoretical computer science. Since its institution in 1993, the prize has been presented to, among others, papers on the discovery of algorithms, proposals for computational models, and the elucidation of computational complexity. In Japan, too, awards have been established for computer science, such as the Japan Prize, the Kyoto Prize, and the Japan IBM Science Award.

By reviewing the history of these awards and prizes for the past ten years or so, this article discusses world-wide research trends in computer science. It also summarizes the current Japanese research environment surrounding computer science research through interviews with prominent Japanese researchers about the level of Japanese research and education as well as possible measures for promotion in the area.

2 What the awards and prizes indicate about recent computer science

2-1 The Turing Award

(1) Recent laureates and characteristics of the award

Essential research on the information was established in the mid 20th century, leading to the basic principles of the computer and communications. One of these fundamental principles is a concept known as the “Turing machine,” which was introduced by Alan M. Turing. His research results, represented in his 1937 paper “Computable Numbers,” later contributed to the birth of the computer and probably created a turning point in the entire world of science that furthered its advancement.

Alan J. Perlis, the first winner of the Turing Award, praised Turing’s achievement in his commemorative lecture as having “completely captured the imagination of one generation of researchers and demanded all their thinking power”[12].

The Turing Award was established in honor of Turing’s achievement, and has been recognizing outstanding research achievements since its first presentation in 1966. Currently, a prize of 100,000 U.S. dollars is provided by the Intel Corporation.

Table 1 shows the names of the Turing Award winners of the past 10 years, along with their achievements. Since the Turing Award honors “general technical achievement in the field of computer science,” each of the listed research achievements has made a significant contribution to the computer science and the development of information and communications technology today.

For example, as early as in the 1960s, Douglas Engelbart, the 1997 winner, was seeking innovative ideas about the functions characteristic of the current models of information terminals, including those on the precursor to the mouse that is in widespread use today and a camera-based interface for the personal computer. He and his colleagues were already envisioning the computer of the future in the 1960s, when ideas like the mouse and the laptop computer were revolutionary in the world of computer systems. His winning of the Turing Award was recognition of his long-lasting contribution to both the computer system and human beings.

In 2001, Kristen Nygaard and Ole-Johan Dahl received the award for their research into object-oriented technology. This was another research effort that had a significant impact on computer science. During the development process of a programming language named “Simula I,” they invented a scheme for building a layered control structure for computing, based on the notion called the “object.” This “object-oriented” programming paradigm has triggered a fundamental change in how programs are designed and developed. Not only has the award-winning scheme been strongly inherited in today’s programming languages, such as C++ and Java, which are widely used for system development, but it also exerts a considerable influence on software development processes and design concepts.

The 2002 recipients are Ronald L. Rivest, Adi Shamir and Leonard M. Adleman, the inventors of

Table 1 : Turing Award for the past 10 years

Year	Laureate Name	Achievement
2002	Ronald L. Rivest, Adi Shamir, Leonard M. Adleman	Contribution to the development of RSA cryptography and the subsequent advancement of cryptographic technology
2001	Kristen Nygaard, Ole-Johan Dahl	Establishment of the ideas fundamental to object-oriented programming through the design of the programming languages, including Simula I
2000	Andrew Chi-Chih Yao	Research in the theory of computation, especially computational complexity, cryptography, and communication complexity, based on the theory of pseudorandom number generation
1999	Frederick P. Brooks, Jr.	Contributions to computer architecture, operating systems, and software engineering
1998	James Gray	Contributions to database and transaction processing research and system implementation
1997	Douglas Engelbart	Presentation of a vision of the future of interactive computing between the human and the computer, and invention of key technologies to help realize this vision
1996	Amir Pnueli	Introduction of temporal logic into computing science and outstanding contributions to program and systems verification
1995	Manuel Blum	Contributions to the foundations of computational complexity theory and its application to cryptography and program checking
1994	Edward Feigenbaum Raj Reddy	Pioneering research on the design and construction of large-scale artificial intelligence systems, demonstrating the practical application of artificial intelligence technology
1993	Richard E. Stearns Juris Hartmanis	Establishment of the foundations of the field of computational complexity theory

Source: Compiled by the author based on Reference[7].

RSA public key cryptography. Their achievement, which is a technology providing basic principles for ensuring electronic information security, has had a significant impact on the computing world. As society becomes increasingly computerized, a framework for electronic security protection is expected to play an essential role in a variety of areas. Security capability for these purposes will be enabled based on public key cryptography.

An example of award-winning research achievement more inclined to basic theory is that of Andrew Chi-Chih Yao, who was honored with the Turing Award in 2000 for his contribution to quantum computing. He established a completely new computational paradigm based on the principles of quantum mechanics. He succeeded in proving the equivalence between quantum circuits in quantum mechanics and the Turing machine in computer science. This achievement indicates that algorithms used on regular computers can be realized at the quantum level. These findings have provided new possibilities for innovation such as the development of computer mechanisms based on new principles and ultra high-speed communications systems.

Award recipients in other theoretical fields include Robin Milner (1995) and Manuel Blum (1995), who have been described by a theoretical computer scientist as having "received the award they deserve."

(2) Profiles of the laureates

We investigated at what age the Turing Award laureates get the idea that was later recognized. The main source of the survey was the website on which the content of the Turing Lectures is posted; this information is presented by the recipients after award acceptance, together with their achievements[7].

This investigation reveals that many of the researchers awarded have opened a new field at a relatively early age (between the ages of 30 and 40) and have made continuous contributions to research progress in that field.

From the perspective of nationality, many of the Turing Award laureates acquired U.S. citizenship later in their lives, although their original nationalities varied widely. This indicates the typical way in which U.S. research personnel have been supplied in the area of natural science, particularly over the past half-century.

One characteristic of computer science is that there are many researchers who used to work in the area of mathematics or applied physics. This can be attributed to the short history of computer science as well as to the academic position of computer science as a discipline that lies on the boundary between existing academic disciplines such as mathematics, communication engineering and electrical engineering.

Another characteristic is that, for achievements in such fields as cryptography, database theory and software engineering, laureates not only write theoretical papers, but also concurrently develop practical systems. In fact, the essential objectives of their projects have often been the design of practical systems.

As these findings indicate, for a scientist to receive the Turing Award, his or her achievement must involve the discovery or elucidation of a fundamental principle. In addition to this, practical application of this principle must be demonstrated, or alternatively, a concept established by the researcher must be inherited and evolved by another, which is also the case with many projects that have won the award.

2-2 The Gödel Prize

The Gödel Prize is, like the Turing Award, a prestigious award that recognizes achievement particularly in the field of theoretical computer science. The prize selection is jointly conducted by the Special Interest Group on Algorithms and Computing Theory of ACM (ACM-SIGACT) and the European Association for Theoretical Computer Science (EATCS), a European scientific society[8].

The prize was inaugurated in honor of Kurt Gödel, a mathematician renowned for achievements such as proving "Gödel's Incompleteness Theorems." In recognition of contributions to pure theory in mathematical science, the prize is granted to papers published in the last few years. The prize includes an award of 5,000 U.S. dollars. Please refer to [8] for a list of laureates and their prize-winning papers.

In the field of theoretical computer science, "computational complexity" is one of the core research areas. An important unanswered question about computational complexity is known as the "P versus NP" problem. The complexity of problems is classified as P or NP. Class P is a set consisting of problems that are relatively easy, such as asking the path of drawing a graph using a single stroke, and are solved in polynomial time. Class NP consists of problems whose positive solutions can be verified, provided that part of the solution is given, in polynomial time, such as a Hamiltonian path problem, which asks to find a path that visits each point in a given graph. While it is clear that P is a subset of NP, it remains unsolved whether there are any problems that belong to NP but not to P. The P versus NP problem asks whether such problems exist. A prize of 1,000,000 U.S. dollars is offered from the Clay Mathematics Institute for a solution to the P versus NP problem[6]. Gödel is one of the discoverers of this question.

One of the Gödel Prize recipients is Seinosuke Toda, a Japanese researcher who won the Gödel Prize in 1998, the sixth year since the prize was instituted. His research efforts contributed to the resolution of the P versus NP problem. He introduced to the NP problem the concept of the counting problem (PP problem) and proved that studying a PP problem can provide large amounts of information about an NP problem. The theorem, known as the "Toda's polynomial equation," is considered a key achievement in theoretical computer science.

In the area of computational models, Joseph Halpern and Yoram Morses received the Gödel Prize in 1997, the fifth year, for their research on distributed computing. It was a basic theory on the coordinated operation of distributed systems and was related to the implementation of parallel computing with greater granularity. Their research results are expected to serve as a theoretical proof in designing large-scale computational software based on grid computing, a technology that is currently attracting huge attention.

2-3 The Kyoto Prize

Next, let us consider the Japanese awards for world-class research. The Kyoto Prize is awarded as part of the activities of the Inamori Foundation, which was established through the initiative and benevolence of Dr. Kazuo Inamori. [10] states, "the Kyoto Prizes are international awards to honor those who have contributed significantly to the scientific, cultural, and spiritual development of mankind. The prizes are presented annually, one in each of the following three categories: Advanced Technology, Basic Sciences, and Arts and Philosophy (Creative Arts and Moral Sciences until the 1999 Prizes)." The prize money is 50 million yen.

Table 2 lists the Kyoto Prize laureates in the field of computer science and their research themes. The laureates are selected from researchers in the computer science category

Table 2 : The Kyoto Prize

No.	Year	Laureate Name	Field	Turing Award
16th	2000	Antony Hoare (UK)	Information Science	1980
12th	1996	Donald Ervin Knuth (US)	Information Science	1974
9th	1993	Jack St.Clair Kilby (US)	Electronics	—
8th	1992	Maurice Vincent Wilkes (UK)	Information Science	1967
5th	1989	Amos Edward Joel Jr. (US)	Electronics, Telecommunications, Lasers, and Control Engineering	—
4th	1988	John McCarthy (US)	Computer Science and Engineering, Artificial Intelligence	1971
4th	1988	Avram Noam Chomsky (US)	Cognitive Science (in its wider sense)	—
1st	1985	Rudolf Emil Kalman (US)	Electronics, Telecommunications Technology, Laser Technology, Control Engineering, Computer Sciences, Information Engineering and Artificial Intelligence	—
1st	1985	Claude Elwood Shannon (US)	Mathematical Sciences (including Pure Mathematics)	—

Source: Compiled by the author based on Reference[10].

Table 3 : The Japan Prize

No.	Year	Laureate Name	Field	Recognized Achievement
19th	2003	Benoit B. Mandelbrot	Science and Technology of Complexity	Creation of universal concepts in complex systems — Chaos and Fractals
18th	2002	Timothy John Berners-Lee	Computing and Computational Science and Engineering	Advancement of civilization through the invention, implementation and deployment of the World Wide Web
15th	1999	W. Wesley Peterson	Information Technologies	Establishment of coding theory for digital communication, broadcasting and storage
12th	1996	Charles K. Kao	Information, Computer and Communication Systems	For pioneering research on wide-band, low-loss optical fiber communications
6th	1990	Marvin Minsky	Category of Technology of Integration—Design, Production and Control Technologies	Establishment of the academic field of Artificial Intelligence and a proposal of fundamental theories in this field
1st	1985	John R. Pierce	Category of Information and Communications	Outstanding achievement in the field of electronics and communications technologies

Source: Compiled by the author based on Reference [11].

almost biannually. Many of these recipients are already widely recognized for their achievements in the field before being honored. They include some Turing Award winners. The laureates of the Kyoto Prize have often been selected from researchers whose achievements have already been widely recognized in the scientific community.

2-4 The Japan Prize

Another famous science award in Japan is the Japan Prize. The Japan Prize is awarded by the Science and Technology Foundation of Japan “to people whose original and outstanding achievements in science and technology are recognized as having advanced the frontiers of knowledge and served the cause of peace and prosperity for mankind,” according to [11]. An award of 50 million yen is presented to the laureates.

Table 3 lists the Japan Prize laureates in the field of computer science and their research themes.

For instance, Tim Berners-Lee, one of the 2002 laureates, was awarded in recognition of his “invention and first-ever implementation of the World Wide Web (WWW), which is the most important element of the Internet technology in information communications networks” and also of his “significant contribution to the further development and proliferation of the WWW”[11].

Benoit Mandelbrot, awarded in 2003, is known for his discovery of the Mandelbrot set, which draws complex, beautiful figures using series of complex numbers. He was awarded for having “discovered that self-similarity is the universal property that underlies complexity, and coined the expression ‘fractal’ for this concept, and illustrated its properties.” The prize-giving body also noted “the applicability of this concept has been extended even to the arts, economics and the social sciences.”

2-5 The Japan IBM Science Award

The Japan IBM Science Award is aimed particularly at young Japanese researchers aged under 45 and who are based in Japan. The award was established in 1987 to mark the fiftieth anniversary of IBM Japan, Ltd., for “contributing to the promotion of academic research in Japan and the development of excellent talent, as part of the social action program.”

The laureates in the computer science category include Seinosuke Toda, a then-professor at Nihon University, honored in 1998. He is also a recipient of the Gödel Prize mentioned earlier. See [9] for the list of the Japan IBM Science Award laureates and their recognized achievements.

2-6 Characteristics of the evaluation criteria of each award

An overview of the past recipients of each award helps to identify elements emphasized in the selection process. In addition to the above-mentioned Turing Award and the Gödel Prize, ACM recognizes excellence through many other awards based on its Policies and Guide to Establishing an ACM Award[7]. According to this guideline, ACM awards are given in honor of (i) contributions to a discipline, (ii) service to the award's sponsor and/or to a community, and (iii) the best papers published.

In the case of the Gödel Prize, which obviously adopts the third criterion for selection, it does not take long for a researcher to be recognized after he or she makes a deserving achievement. In contrast, the selection process of the Turing Award emphasizes point (ii), which suggests that an innovative concept must wait until it is evolved in the academic or industrial community before it can be appreciated and awarded. This means there are greater delays between achievement and award winning. For example, RSA cryptography, on which a paper was published in 1977, was an accomplishment that took as long as 25 years before it was honored in 2002.

In other words, when growth in the industry or development in the academic field derives from an idea obtained through research activities, the credit usually goes to the underlying research achievement in the field.

3 Current research activities in computer science and challenges to Japan

The following sections first discuss the characteristics of computer science as an academic discipline, in reference to the profiles of the awards and prizes described above. Suggestions are then made for the future promotion of computer science, based on the opinions of researchers working in this area.

3-1 What awards and prizes indicate about computer science research

One can criticize the Turing Award for not being balanced as an international award because it acknowledges contributions to a specific scientific society. However, there is no doubt that its list of laureates is filled with great names in computer science.

In particular, recent award-winning achievements such as public key cryptography and object-oriented technology are either concepts or basic principles/methods that enable the epoch-making application of information processing capabilities. The web is another accomplishment that is as highly regarded as these technologies in international science awards.

3-2 International recognition of research results

One important step in promoting computer science is to produce excellent research results originating in Japan that are recognized by the international scientific community. The level of international recognition can be measured by, for example, the number of publications in the Journal of the ACM, the most historic and prestigious journal in the field of computer science. The journal, which marked its fiftieth anniversary in 2003, has constantly been publishing 30 to 60 significant papers on an annual basis for the past few decades. The number of articles that have appeared in the journal totals over 2,300.

Of these papers, those submitted by Japanese researchers account only for 1.1%. In the last 10 years, the figure is even smaller, about 0.8%. Discussing the number of acceptances by Journal of the ACM alone is insufficient for making an adequate judgment, but it is undeniable that Japan should make more effort to raise international recognition of its research achievements.

For example, the Japanese language input system for Japanese word processors, which has had a significant impact on non-English language input systems, deserves wider international recognition and respect than it has had. Other world-class achievements in recent years include the development of an operating system for embedded systems and the acquisition of the best results in vector computing against the benchmarks.

3-3 International exchange between research communities

Today's computer science field covers a variety of research areas. It is therefore often the case that individual researchers are unable to find a domestic scientific community in which they can discuss the specific topics in which they specialize. Some call for research fund management in a manner that allows for more frequent hosting of international conferences.

Another direction for improvement can be learned from the U.S., where there is dynamism that attracts top-quality students and researchers from other counties. Many recipients of the Turing Award have been such people. While Japan also accepts many excellent students from overseas and grants a number of doctorates to foreign researchers annually, there are certain cultural aspects that make life in Japan difficult for foreigners. It is essential that Japan give further consideration to accepting foreign students as well as be more active in hiring foreign researchers.

3-4 Significance of interdisciplinary research activities

Researchers specializing in theory sometimes mention their laboratories' need for research personnel who have completed an undergraduate mathematics course. This provides an important point of view in developing course models and curricula for science and engineering departments. There have been a number of cases where advance in information processing technology has opened completely new research possibilities, as has recently happened in the area of life science. Thus, interdisciplinary research is becoming increasingly vital.

As important as interdisciplinarity in science and technology are the boundary areas between scientific and social activities. Public key cryptography has proven truly effective because of the widespread availability of electronic information. Close and continuous cooperation between industry and academia is essential for allowing scientists to achieve outstanding results. Essential elements in realizing this include an increase in the number of research projects entrusted to universities, improved mobility of research personnel, and efficient management of research organizations.

3-5 Recognizing the scientific significance of computer science

Here is a comment by a researcher that is worthwhile considering: "Japan's research and education communities related to information processing lack the intention to capture the essence of information and recognize computer science as a field of science. Engineering did not precede the invention of the computer."

There is a traditional perception that computer science serves as the basis of information processing technology. An important additional view is that, in the future, research on information will lead to new developments in a wide range of fields of science and technology. The ripple effect of information technology in other academic disciplines largely depends on breakthroughs in information processing capability. The possibility of new developments does not lie exclusively in computer science but in broader areas where computer science is the foundation. From this point of view, implementing research projects intended to explore the frontiers of interdisciplinary fields is essential.

4 Conclusion

Research in the area of computer science continues to be important because computer science is expected to have, in addition to its ripple effect on industry, a considerable influence on other science and technology fields in terms of application.

Japan has acquired a certain level of strength in computer science research specifically in the pure theory field. Moreover, the nation is affluent in industrial infrastructure as has been proven through the development of mainframe computers and the production of personal computers. More recently, Japan's strength has been shown in world leading-edge developments such as advanced mobile phone capabilities and intelligent home appliances. The right combination of these advantages promises an outcome with international impact. To achieve this, Japan should establish goals from a wide perspective in application fields and a long-term view of the direction of technological evolution.

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5

Recent Trends in Semiconductor Microfabrication Equipment Technology

— Proposals for Industry-Academy Cooperation on Research and Development in Japan —

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1 Introduction

From the beginning of this year, electric companies in Japan have been intending to invest capital in semiconductors and liquid crystal products, mainly motivated by the hot sales of digital consumer products. Capital investment is again surging from its low point of '99 to '00 after the IT bubble burst. In fact, Renesas Technology (consolidated semiconductor company of Hitachi and Mitsubishi) attained the No. 3 position in sales, if nominally, next to Intel and Samsung. A portion of their capital investment in on microfabrication equipment that transfers LSI (large-scale integration) patterns on masks onto semiconductor wafers. This equipment controls the critical features that define the specifications of leading-edge semiconductor products and LCDs. Global competition is increasing over the share of the microfabrication equipment market. Maintaining an advantageous position both in technology and in market share is strategically important for Japan to retain world leadership in the technology industry and the semiconductor industry.

Japanese companies have dominated both in technology and in the application of product segments of optical technologies such as optical disks, optical fiber components for communication, cameras, microscopes, endoscopes and laser printers. This is especially important in semiconductor microfabrication equipment that extensively uses optical technology, and the optical exposure systems that we discuss here. Optical exposure systems require the most advanced optical technology. We should not be complacent about Japan's future position since a European maker once took the No. 1 market share[1] in the semiconductor exposure system market.

This report shows that industry-academy collaboration is an important way of retaining international competitiveness in the development of exposure systems, an area where Japanese companies have been strong in an increasingly competitive semiconductor microfabrication equipment industry. In addition, we discuss the action required to make collaboration fruitful in Japan.

2 Semiconductor device roadmap and lithography solution

2-1 *Semiconductor device roadmap*

In semiconductor LSI segments produced recently, competition in development has been kept strong for MPUs (Micro Processor Units) that are the core components of PCs, which form the basis of the information-communication equipment, DRAM (Dynamic Random Access Memory) and SoC (System on Chip) for mobile devices and digital consumer products. These semiconductor devices have evolved with further integration as a goal. For example, DRAM has untiringly pursued fine patterning technology called "half pitch," or "gate length" for MPUs.

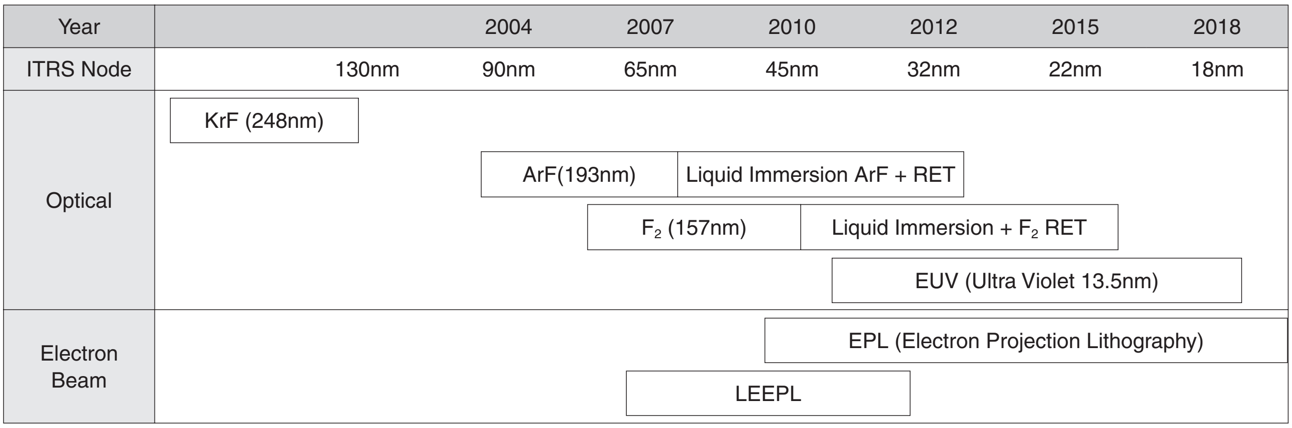
Table 1 is a roadmap indicating basic trends in integration improvement[2]. The roadmap is

Table 1 : Semiconductor Device Roadmap

Device/Year	2004	2007	2010	2012	2015	2018
DRAM	4Gb	8Gb	16Gb	32Gb	64Gb	128Gb
Half Pitch	90	65	45	32	22	18
Contact Hole	110	80	55	45	35	25
Overlay control	32	23	18	14	10	7.2
Linewidth Variation (3s)	11	8	5.5	4.3	3.1	2.2
MPU						
Half Pitch	107	76	54	42	30	21
Gate Length	53	35	25	20	15	10
Contact Hole	122	80	59	46	33	23
Linewidth Variation (3s)	3.3	2.2	1.6	1.3	0.9	0.6
SoC						
ASIC/LP gate	75	45	32	27	19	13
Contact Hole	122	80	59	46	33	23
Linewidth Variation (3s)	4.7	2.9	2	1.7	1.3	0.8

Source: Prepared by the author based on the table on the ITRS home page.

Figure 1 : Lithographic solution



called ITRS (International Technology Roadmap for Semiconductor) and is defined by major electronics companies in the world including Intel Corporation in U.S.A. At first, the minimum line width was in the order of microns, and this continuously decreased over time, and now a 90-nm node will be in production with the size of a DRAM with this line width corresponding to 4 Giga bits. The target for 15 years from now is set to an astonishing 18-nm line width for 128-Giga-bit capacity.

2-2 Lithographic solution

This micropatterning of LSI in the ITRS roadmap is created by microfabrication equipment that fully uses lithographic technologies and is called the lithographic solution at each node[3,5]. This equipment employs ultraviolet light or an electron beam as the light source, and can be classified into two categories as shown in Figure 1. We now outline these categories.

The first category is the stepper, or recently, the scanner, which employs an optical method using ArF (argon fluoride) or F_2 (fluoride gas) laser that emits ultraviolet light as the light source. This method has the advantage of optical parallel processing capability in space, as shown in Figure 2, which means all the points on the mask pattern are simultaneously transferred onto a wafer. It gives higher throughput, guarantees production and is widely used. The wavelength of the light source shortens with the generations because the line width is defined by resolution of the lens optics of the exposure system derived from the equation below, called Abbe's equation (or Rayleigh's equation).

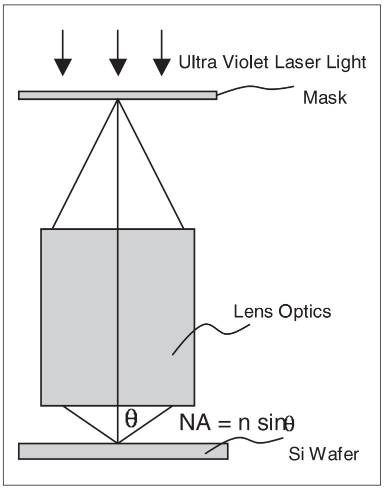
Line width: $\delta = k \bullet \lambda / NA$ ...(1)
where λ: wavelength, NA: Numerical Aperture, k: Engineering factor.
NA is given by $NA=n \bullet \sin\ \theta$ where θ is the one-half angular aperture

We now briefly discuss liquid immersion technology, which was a technical breakthrough and a strong candidate for future lithography at Microlithography2004[6] held in February 2004 in Silicon Valley (Santa Clara) in U.S.A. This technology extends the life of the ArF laser-sourced wafer exposure system. It fills the space between the projection lens and the wafer with pure water and improves effective NA because of its refractive index, 1.4. Equation (1) clearly explains the improvement in resolution. Another big advantage is the better focal depth, which reduces the need for accuracy in the mechanical position control of the system. The liquid-immersed lens has long been known for its super high-resolution microscope, but its application to the production exposure system is a historical first. Its applicability to 60nm resolution was confirmed by partial experiment and 45nm to 32nm is possible if mask pattern is simply repetitive.

The second is an exposure system with an electron beam as the source, which has a much shorter wavelength. The electron projection lithograph (EPL) is a typical piece of equipment. This technology irradiates the electron beam (with its wavelength of below 0.1 nm) to a mask pattern and projects the reduced image of the mask pattern onto a wafer. The equipment can expose only a limited area and provides less throughput than optical systems. It has never been mass-produced. However, because it gives better resolution and better focal depth than optical systems, it can be partially used for isolated pattern exposure such as contact holes. It can also be used for the microfabrication of special-purpose LSIs.

On the other hand, a new method called LEEPL (Low-energy electron-beam proximity-projection lithography) is proposed, which positions the mask and the wafer close together and projects the entire image by an electron beam. Its resolution of 65 nm has been confirmed by experiment, and development of a resolution of 45 nm is underway. The cost of the equipment is affordable and higher throughput can be achieved compared with EPL, but it still has a number of problems such as its higher mask cost because it is real-sized.

Figure 2 : Diagram of the optical exposure system



So far, we have briefly reviewed the electron beam lithography system that has been developed to replace the optical lithography system should the latter system reach its limit. However, as its productivity has not improved compared with optical systems, its major role today is for lithography research purposes and fabricating original masks for submicron lithography.

2-3 Next-next-generation EUV/F_2 lithography

As discussed so far, breakthroughs achieved through liquid immersion technology has made a 45-nm ITRS node certain, and even a 32-nm node is possible, but what about beyond these? Next-next -generation lithographic technologies, extreme ultra-violet (EUV) exposure technology and F_2 lithographic technology, are an answer to this question.

EUV technology proposed by Prof. Kinoshita of University of Hyogo, ex-NTT, is an innovative idea from Japan to be proud of. This lithographic technology can use, for example, extreme ultra-violet light (wave length, 13.5 nm) emitted from high-temperature plasma gas generated by the radiation of a high-power laser light to a stream of water ejected from a nozzle in a strong vacuum. Competition among Japan, U.S. and Europe is also fierce in this area. Peculiar to EUV technology is that there is no glass that transmits EUV light. For this reason, a reflective mirror is used, and most of the continuity with the existing optical exposure system will be lost. Hence, the total development costs of the exposure system are estimated to be 43 billion Yen (ca. US $400 million) including basic, measurement, and production technologies. This exceeds the 15 billion Yen for ArF lithography and the 20 billion Yen for F_2 lithography, and this is far more than one company can afford.

Thus, EUV technology in Europe and U.S. is promoted by industry-academy-government collaboration with plenty of funding from, for example, MEDEA+[7] (Microelectronics Development for European Applications +) in Europe, EUV LLC[8] (Limited Liability Company), VNL (Virtual National Lab./Lawrence Berkeley, Lawrence Livermore, Sandia) and ISMT[9] (International SEMsATEC) all in U.S.A. With this background, EUVA[10] (Extreme Ultra Violet Lithography Association) was organized in June 2002 and March 2005 as a consortium through industry-academy-government collaboration with the support of NEDO (New Energy Development Organization) and under the initiative of the Ministry of Economy, Trade and Industry. Amidst international competition, it is developing future technologies including equipment cost reduction. With this situation, Intel announced in autumn 2003 that they would focus on EUV exposure for beyond 32 nm and would skip F_2 lithography. Still, EUV exposure has a number of problems including huge costs, a poor mirror optics record and the necessity for EUV light source development.

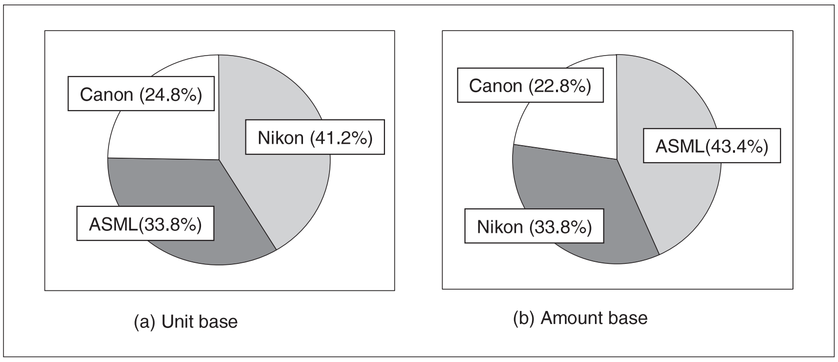
On the other hand, there are also problems with F_2 lithography, such as production technology for the large crystal growth of CaF_2 (Calcium Fluoride) for lenses. However, it may have an advantage over EUV because it is an extension of the existing optical system that has produced fruitful results as an exposure system. To reinforce this view, ASML delivered an experimental F_2 exposure system in April 2003, priced at over 12 billion Yen to InterUniversities MicroElectronic Center (IMEC[11]) in Europe for the early identification of technical hurdles in production. Zeiss in Germany, a well-established optical technology company in the world, is responsible for the ASML optical system. In Japan, F_2 lithographic technology is driven in the "Asuka Project" of Selete[12] to be completed in March 2006. Whether to pursue F_2 or EUV beyond this needs a high level of decision as it is very complicated, not only in its technology, but also in its development time and the huge amount required for investment.

3 Share of the worldwide market and the international competitiveness of Japanese companies

In worldwide market share of semiconductor products, it has been almost ten years since a Japanese company lost the No. 1 position. However, thanks to the strong digital consumer product and mobile product market, and perhaps due to corporate reorganization, Renesas Technology (consolidated semiconductor company of Hitachi and Mitsubishi) attained the No. 3 position in sales, if nominally, next to Intel and Samsung. This raised the intention of Japanese electronic companies to invest capital for semiconductor and LCD products. This is a good chance for Japanese companies to retrieve international competitiveness in semiconductor microfabrication equipment. We now consider the market share of semiconductor microfabrication equipment and the international competitiveness of Japanese companies, which is the subject of this report.

The international market share of semiconductor exposure equipment is shown in Figure 3. The market is oligopolized by three companies, Nikon and Canon, the world's preeminent optical makers in Japan, and ASML (in the Philips group in the Netherlands) carrying Zeiss optics with a long history in optical technologies. In Figure 3, (a) is the unit base and (b) is the amount base. Nikon has the best sales by unit, but ASML has the best sales by amount. So far in the semiconductor manufacturing equipment market, Japanese companies have taken a strong world both in

Figure 3 : Market Share of Optical Exposure Systems in 2003



(a) Unit base

(b) Amount base

Source: Prepared by the author based on data from Press Journal Ltd.

technology and business. Recently, however, on the business side, ASML sometimes beats Japanese companies, emphasizing customer service and supplying easy-to-use products to the market. This causes great problems for Japanese companies. Customers choose ASML products even though the price is higher. Through the process of acquiring and improving international competitiveness, Japanese companies are expected to offer better customer services that emphasize usability and maintenance.

In U.S.A, optical makers like Kodak and Perkin-Elmer did good business in optical equipment such as cameras, instruments and others in the past, but they have lost their competitive edge today. For some time, SVGL was active in optical exposure systems, but they were acquired by ASML several years ago. As seen here, the lithography system industry in U.S. is losing its energy. However, universities in U.S. are still energetically researching and developing, and are responsive to front-line technical issues, as is seen with liquid immersion breakthroughs. What made this happen?

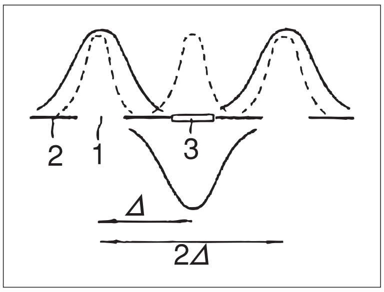
4 Technical advantage of Japanese companies and the success of universities in U.S.

So far, a roadmap of semiconductor microfabrication technologies and corresponding lithographic solutions has been explained, and semiconductor devices and the market share of microfabrication equipment has been reviewed. We will next analyze the international competitiveness of Japan in the semiconductor industry using two representative cases. The first case is an ultra resolution technology in which Japanese companies have been especially strong, from basic technology, to application through industry, to industry collaboration between optical and electronics companies. The second case is the success of U.S. universities that triggered the breakthrough in liquid immersion technology.

4-1 Industry to industry collaboration on ultra resolution technologies in Japan

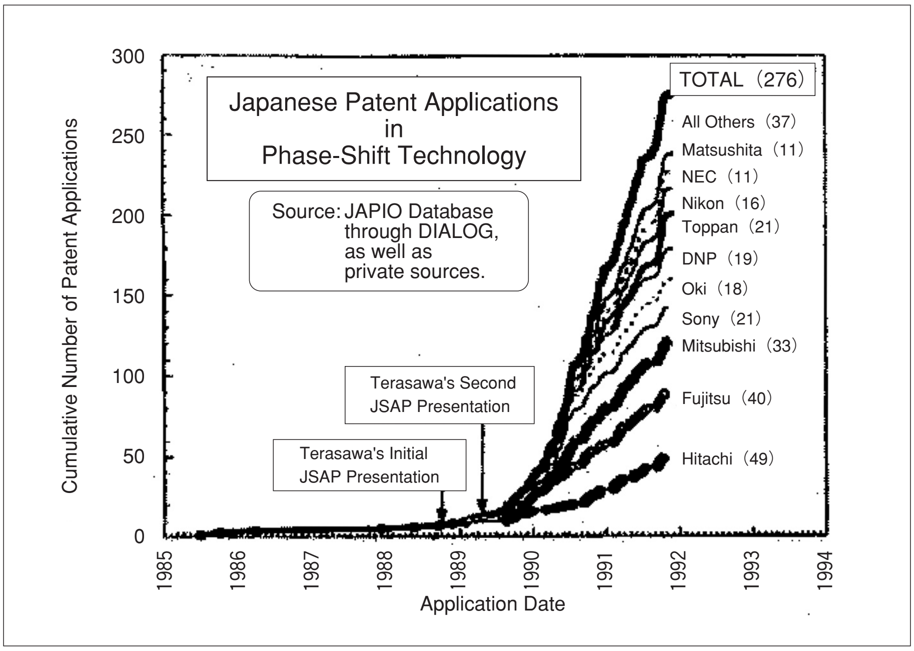
According to Equation (1) in Chapter 2, the minimum line width of semiconductor microfabrication can be made smaller by reducing the K-factor, even if the wavelength of the light source and the numerical aperture are kept the same. Resolution enhancement technology (RET) is a technology based on this idea, and the phase-shift technology shown in Figure 4 is representative of it. It shifts the phase of adjacent patterns on the mask by 180 degrees to divide electric field intensity into two. This is to improve the lithographic resolution by almost 200%. The basic idea was invented by Mr. Masato Shibuya,

Figure 4 : Principle of the phase-shift method



Shift phases of adjacent patterns on the mask by 180 degrees for a resolution improvement of about twice

Figure 5 : Trends in of number of patents related to the phase-shift mask, i.e., a champion of RET (Resolution enhancement technology)



Source: Presentation materials by F. Schellenberg at Microlithography2004

then working for Nikon, and now Prof. of Tokyo Polytechnic University, and the patent application was made by Nikon[13]. After this, Dr. M.D. Levenson at IBM independently proved its effect, and a group working under Dr. Shinji Okazaki of Hitachi opened the way to actual application.

Figure 5, with the vertical axis showing the number of patents for the phase-shift mask, shows that Japanese companies led in this area. The chart was presented by Mr. Frank Schellenberg of Mentor Graphics, an authority on lithographic technology, in his keynote speech entitled “Resolution Enhancement Technology: the Past, the Present, and Extensions”[14] at Microlithography 2004 mentioned above. Phase-shift can be applied only to repetitive patterns, and it is difficult to use for isolated patterns such as contact holes, but it is a general technology compatible with KrF, ArF and the F_2 exposure system since it does not limit the wavelength of the light source.

In summary, ultra resolution technology that was a breakthrough in optical lithography, is a good example of a technology developed by Japanese companies ahead of the rest of the world, then raised by American companies and put into practical use by the Japanese companies that predominated other countries. It should be acknowledged that technologies from Japanese companies contributed not only to production technologies and yield improvement, but also to solutions to fundamental technical issues. At Microlithography2004, a new award was established using the name of Zernike, who won the Noble prize in 1953 for his phase contrast microscope. Mr. B.J. Lin received the award this year for his driving liquid immersion technology discussed in the next section. Accomplishments in RET technology will be strong candidates for the next award.

4-2 Breakthroughs from liquid immersion and the technical sense of MIT

As reviewed, Japanese engineers have generally led the optical lithography with ultra resolution technology as a typical example. However, there are too many technical options[3,5] for next-generation lithographic solutions, as stated in Chapter 2 of this article, and it is unclear which technology should be the main solution. A concern of exposure system manufacturers both at home and abroad has been that they have been unable to narrow down the options, making development investment too large and irretrievable.

In this situation, at Microlithography2004[6] held in February this year in Silicon Valley (Santa Clara), Nikon, ASML and Canon each made separate presentations on the production usage of ArF liquid immersion technology as a breakthrough to a 65-nm node and beyond. They all confirmed this technology to be their first choice. A technology development race has already started for rollout by the end of this year or by early next year. Further competition for purchase orders from customers aiming for the top market share has also kicked off. For this, resources are being focused on and selected. That is, engineers engaged in the development of other lithographic technologies have been transferred to the development of the liquid-immersed ArF stepper.

We will now see how this noteworthy breakthrough technology attracted the limelight as a technology of choice for the next generation. As is clear from Abbe's equation (1), liquid immersion technology is so well known that it appears in school textbooks as enhancing microscope resolution. In fact, the invention of the liquid recycling lithography as announced this time can be traced back to a patent applied for early in the 1980s by Mr. Akihiro Takanashi of Hitachi[15]. At that time, however, RET technology, such as the phase-shift above, had much higher priority in development than other options for next-generation technologies. Thus, liquid immersion technology remained frozen for some time. RET itself seems to be lacking innovative ideas in technology recently.

With this background, Dr. Rothschild and others of MIT Lincoln Laboratory announced an experiment on liquid immersion lithography using F_2 lasers with a wavelength of 157 nm in 2001[16]. Mr. B. J. Lin, who moved to TSMC in Taiwan after IBM, and others then established a perspective through theoretical investigation in which a 45-nm node can be supported by liquid immersion lithography. They stressed that the technology should be promoted for production use. At Microlithography2003, Dr. Soichi Owa and others of Nikon presented an idea called "local fill," a new handling technology of liquid immersion, and showed that it can be applied to production equipment. This accelerated development works at all vendors including ASML and Canon, including simulation of liquid immersion and production experiments. All three companies are in fierce competition for productization to ship the first model by the end of this year or early next year. Considering this history, it is unclear how accurately the engineering team at MIT foresaw the future of the technology, but it is certain that they were very responsive to requirements from the frontier of optical lithography and that they triggered a breakthrough in liquid immersion technology.

5 Issues of industry-academy collaboration in Japan and how to proceed

5-1 Issues of industry-academy collaboration in Japan

The development of liquid immersion technology that became a breakthrough in lithographic solutions was triggered by Prof. Rothschild of Lincoln Laboratory, Massachusetts Institute of Technology (MIT). His laboratory received funding from DARPA (No. F19628-00-C-0002) to pursue the ultimate limits of optical lithography, and contributed to the development of leading technologies, such as exposure experiments using an F_2 (157nm) laser. In other words, they ran experiments at the same level of as the development group in the industry, and they clearly understood frontline technical issues. It is not surprising that they triggered this breakthrough. As is seen in this example, universities in U.S. are much more responsive to technical issues at the forefront of the industry than universities in Japan[17]. This enables them to make breakthroughs and to breed venture companies that are rooted in real business.

Please note that we are not discussing pure research activities such as on elementary particles, but how to proceed with application research activities, like MIT in the case above, conducted by university production technology groups. Universities in Japan usually have a lot of so-called "basic research for the future" even if it is application research in reality and has strong potential. They also tend to set their target off the mainstream, which is contrary to the aim of basic research. It would be useful to calculate the number of articles whose topics ended up only in publication rather than application. For example, at Microlithography2004[6] where mainstream technology is discussed, universities in U.S. contributed 25 articles, while there were only a few from Japanese universities. In addition, as is seen from the examples at MIT and Rochester University at Microlithography2004[6], their data collection methods and simulation results were very close to those used in the industry, which indicates the quality of their work and their contribution to mainstream technology. On the other hand, presentations by universities from Japan are, in most cases, limited to the presentation of ideas and concepts only using charts, and data is limited only to photos. At society meetings of optical disk technology in the past, the author sometimes felt irritated by certain presentations where the nature of the technology could have been presented more clearly using signal-to-noise ratios and efficiency information in addition to photographs.

What prevents Japanese universities from entering the mainstream of the technology? One reason may be that some universities do not have sufficient research equipment. To collect data like signal-to-noise ratios and efficiency data requires reasonably expensive equipment that some universities cannot afford. It is a concern that universities have not completely grasped leading-edge technical information about mainstream technology, including the design methods of state-of-the-art devices or expertise in measuring methods. As it is easiest and quickest for universities to learn these methods from the industry, it would be convenient if this information can be disclosed by the industry.

However, there is the a barrier of corporate confidentiality. Maintaining confidentiality in the industry is reasonable, but the limitations of working by oneself are now being questioned, and technology itself will be stifled if corporations focus on confidentiality and on the enclosure of technical information. To allow corporations to disclose their information to universities without anxiety, we need a system where the rights of the corporation are guaranteed even after the corporation discloses technical information to universities, and where corporations feel comfortable about information exchange with universities.

By closing a legal contract on confidentiality as equal partners (e.g., Nondisclosure Agreement (NDA) or Exclusive Agreement (EA)) between a university and a corporation, we need to change the relationship between both parties to obtain a win-win result through technology exchange. It has been pointed out that confidential information may be carried by students to other companies for whom they will work after graduation. However, this can be avoided if the NDA binds students engaged in collaborative work between universities and the industry.

The discussion so far indicates that there are at least two issues, other than funding, in investigating how university-industry collaboration should be managed in application university technology groups. One is the issue of patent filing for which the university TLO is usually responsible, and the other is how to manage research and development activities that result in inventions.

5-2 Status of TLOs of Japanese universities and ILP of MIT

Technology Licensing Organizations (TLO)[18] in universities in Japan is to manage intellectual property (IP) such as patents, related to the industry-academy collaboration above. The main mission of the TLO is to file patents for work undertaken by university researchers, to transfer technology to corporations, and to allocate funds for the next research project. In other words, the TLO is a legal entity, something like the Patent Department of universities that gathers and assesses the results of study by university researchers, register their patents and transfers the technology to corporations. The legal background of the TLO is “Law for Technology Transfer from Universities and Others” (a.k.a. the TLO law) which came into in effect in August 1988. A total of 36 TLOs have been founded and approved today in Japan.

In contrast, industry-academy collaboration in U.S. has a long history. In MIT[19], for example, an organization called ILP[20] (Industrial Liaison Program) was formed in 1948 in addition to TLOs. While the TLOs above handle intellectual property protection, the ILP handles leading-edge technical issues and constitutes a part of the Innovation Value Chain with more than 50 years of experience. The Innovation Value Chain is a chain of value created from technical innovation to investment return, or a productive chain of basic research - application research - productization - business - research investment. Last year, 645 companies invested in MIT, with 21 companies investing over $1M and 139 companies investing between $100K and $1M. MIT graduates had founded more than 4,000 companies by 1997, created 1,100 thousand jobs and achieved about 2,500 billion Yen in sales[20]. Revenue from patents in all of North America including MIT in 2002 amounted to about 145.3 billion Yen[21].

Revenue from patent licensing through TLOs in Japan is increasing, but the cumulative amount by 2003 was only 1.4 billion Yen[22]. It is necessary to take into account here that the full start of TLOs is very recent and that there are still a number of management issues regarding revenue from patents. Some people have considered obtaining patent revenue from basic research, but in reality, little basic research reaches production level. Even if the research does reach production level, it usually takes 20 to 30 years, and basic patents expire when the product is on the market.

For this reason, patent applications from universities should be made not only for basic technologies but also for application technologies during the productization stage for continuous and exhaustive coverage in related areas. This strategy would be unrealistic without collaboration with corporations that have sufficient experience and a proven record in achieving patent revenue. In addition, patent maintenance costs are fairly high, which calls for a strict screening process on whether right to patents already applied for should be retained or not. These are patent-related technical issues to improve efficiency in acquiring patent rights from invention. We now consider a much more important issue, i.e., how to manage research and development work that will produce inventions, and propose a solution considering issues in the industry-academy collaboration discussed above.

5-3 How to make industry-academy collaboration more efficient

The solution is first that researchers in the production application area in universities visit the development organizations of corporations and share frontline technical issues in development with corporate engineers. The intellectual property management and protection issues that always emerge in these cases can be handled through the TLOs established in universities and governmental research centers. The main mission of TLOs today is to protect the rights of universities; failure to do so will hinder progress.

Thus, the second solution is to redefine the mission of TLOs, which is not only to protect the profits of the university, but also to consider how to protect the profits of the corporation and to establish a legally contracted relationship as equal partners between the corporation and the university. Otherwise, corporations will not be any closer to universities than today, and no further collaboration between industry and universities will take place. The third solution is that corporations should disclose technical issues in frontline development to universities under the joint supervision of the IP department of the corporation and the TLO of the university, with the expectation that excellent research staff of the university be used.

If these three solutions are combined and promoted, both parties can engage in technology exchange with peace of mind since technology disclosure will not damage the IPs of each party. There will be deeper, more extensive discussion between the researchers and engineers of each party than at society meetings or conferences, and scientific knowledge and technologies will be stimulated more with the aim of making progress in technology.

Business potential that requires a higher level of judgment, it can be decided comprehensively at a meeting by management level people from each party. In summary, for each key target project, universities and corporations first agree on the “give and take” rule based on a legally equal contractual relationship. Then, based on this rule, a project team is organized by researchers and engineers with experience in developing leading-edge technologies and products. The team should pursue development steps to attain the goal of productization. This will produce world-class industry-academy collaboration on research and development. This type of process has already been realized in industry-industry collaboration between corporations and has achieved a number of promising results.

5-4 Participation in the international Innovation Value Chain

Finally, we will cover research that funds industry-academy collaboration in U.S. and Europe. In the area of semiconductor microfabrication, a consortium called ISMT[9] (International SEMATEC)plays an important role in U.S. ISMT makes investments for research and development far more than Japan in many universities including MIT, Rochester University, New Mexico University, and others. As seen at a meeting hosted by ISMT in January 2004 to report the accomplishments of each project from spring 2002 to the end of 2003, they regularly present and review the work conducted in each project. In Europe, there is IMEC[11] mentioned above, in Leuven, Belgium, as a base for industry-academy collaboration for the semiconductor industry.

Considering moves in U.S. and Europe, we need to promote healthy, productive industry-academy collaboration in Japan. That is, we should accumulate experience in managing the collaboration between corporations and universities in Japan based on the equal, “give and take” relationship rather than “ruler and ruled” relationship, and similar to the legally contractual relationships normally seen in U.S. and Europe. If we continuously succeed over time, we will then be able to extend the relationship to overseas universities and corporations for technology collaboration based on the “give and take” rule. Universities in Japan may mature to cover an area of the international Innovation Value Chain where the technology levels of each country are intermixed. This will result in a situation in which Japanese university production technology groups have attractive potential so that companies like Intel are interested in funding their research and development activities.

In particular, attention should be paid to how the above issues can be handled by the corporations, universities and governmental organizations involved in EUVA technology and F_2 lithography, who are expected to provide technological innovation for the next generation.

6 Conclusion

In first half of this report, Chapters 2 and 3, we reviewed recent semiconductor devices, technological trends in semiconductor microfabrication equipment and the international market share that should indicate the international competitiveness of Japanese companies; this is the background to this report. In the second half, Chapters 4 and 5, starting with the technology trends discussed in the first half of this report, we reviewed how to run industry-industry collaboration in Japan and in industry-academy collaboration in U.S. This highlighted the issues subsequently covered in this report. Finally, we made proposals to take us one step further toward better industry-academy collaboration on research and development work in Japan. In these proposals, we should:

(1) Consider the liquid immersion technology that made a breakthrough in lithographic solutions, the university in U.S. (MIT) that triggered development, even though the lithographic industry in U.S. had lost its international competitiveness. This was possible because universities in U.S. tried to identify issues and trends in frontline development work conducted by corporations worldwide and were sufficiently responsive to these issues.

(2) In other words, development fields in corporations worldwide is a crossroads of the needs of the market and the seeds of scientific knowledge, and they set technology trends while tackling frontline technical issues that become the source of new invention and discovery. Thus, university researchers involved in application research in Japan should be

engaged more deeply than ever in sharing technical issues with corporate engineers.

Here, the management and protection of IP is always an important issue. In this regard, TLOs that have been already established in universities and governmental institutions should build legally equal partnerships considering the protection of the corporation's rights as well as the rights of the university. Otherwise, corporations will not be any to universities or disclose detailed technical information. This will result in lack of progress in industry-university collaboration. In addition, corporations should disclose technical issues in frontline development to universities under the joint supervision of the IP department of the corporation and the TLO of the university, with the expectation that excellent research staff of the universities be used.

We also need to consider patent strategies to improve the efficiency of obtaining patent rights for inventions that the TLO already has. University researchers involved in industry-academy collaboration should not only aim for fundamental patents that would bring huge returns with the lowest potential for success, but should also steadily and exhaustively apply for patents for existing technologies with corporate engineers, so that there is extensive patent coverage. In addition, as patent maintenance costs are high, a strict screening process should be used for patents already applied for by the cooperation with the corporate IP department.

(3) Under agreement on the "give and take" rule between corporations and universities based on a legally equal contractual relationship that includes patented technologies, a project team should be organized by researchers and engineers with experience in developing leading-edge technologies or and. The team should pursue development steps to attain the goal of productization. This will create world-class industry-academy collaboration on research and development. This process has already been realized in corporation-corporation collaboration, and there have already been a number of accomplishments.

From this point of view, attention should be paid to the progress of EUVA, the next-next-generation lithography consortium and F_2 lithography in which universities are already participating, where industry-academy collaboration including TLOs will be tested on how well they are working. If we steadily pursue industry-university collaboration based on the equal "give and take" relationship contract common worldwide, then universities in Japan will be able to cover some aspect of the international Innovation Value Chain.

Finally, we reconfirm the scope of this article. As subtitled, this article discusses industry-university collaboration where researchers in application research groups in universities work together with researchers of corporations on joint development programs. We have investigated how to make this more effective.

Issues on industry-academy collaboration originate after the industrial revolution when contact frequency between industry and education increased. On the other hand, intellectual activity began way before the industrial revolution. People from older societies were intellectually curious, stimulated not by industry or by government, but directly by nature and society, and they voluntarily created and systemized intelligence. These people and those who need information joined to form the origin of universities. This leads us to the question of the original mission of universities along with traditions in knowledge and education. The question concerns the nature of universities, and the question is not simple enough to be answered only from the viewpoint of industry-academy collaboration. The question requires serious discussion based on facts traced back to the beginning of the university, to the industrial revolution, to the Renaissance, and to ancient Greece and the four great civilizations of the world, Egypt, Mesopotamia, Indus and China, or even the origin of humankind.

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6

Research Trends toward Intelligent Computing
— Promotion of Multidisciplinary Research in Cognitive Science and Artificial Intelligence —

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1 Introduction

The ubiquitous society is around the corner in Japan now that the nation's population of broadband subscribers has reached 15 million, allowing people to access the Internet faster and more cheaply than in any other part of the world. However, most information technology devices, which have traditionally been designed for professional users, are not easy for non-specialists to use, even at a time when these devices are widely available. Furthermore, the proliferation of the Internet has, on the one hand, given people access to large amounts of information, but, on the other hand, it has caused a deluge of information making the retrieval of the desired information difficult. Under these circumstances, an environment in which people can use computers effortlessly in their daily lives and computers that are user-friendly are strongly required. If this becomes a reality, smooth collaborative work between humans and computers will be facilitated, and intellectual productivity will improve as a result.

Studies to implement "Intelligent Computing," the concept of creating systems that support human beings in their intellectual activities and naturally interface with them have been conducted as part of research in artificial intelligence. Artificial intelligence studies aiming to develop machine intelligence on the computer began in the latter half of the 1950s, shortly after the invention of the computer. Since the intellectual capacity of artificial intelligence systems has been slow to increase, there has been criticism over research activities in this field. As the computer's processing speed increases, however, greater performance on intelligent processing has become available, allowing the commercial use of artificial intelligence. Today, the results of artificial intelligence research have been embedded in many information systems in fragments, although they are not easily recognizable as artificial intelligence technologies. In the artificial intelligence research fields, data mining using machine learning algorithms has recently been attracting attention, and studies in this area have greatly contributed to advances in security technology.

However, further enhancement of intelligent processing capability is needed because the ability of current Intelligent Computing is inferior to that of humans. To this end, researchers are facing a number of problems, the resolution of some of which may elucidate the essence of human beings. In particular, it is expected that research in cognitive science, a field that clarifies human cognitive functions, will help create new ideas for Intelligent Computing.

To make Intelligent Computing a reality, many countries, especially the U.S., have been active in implementing projects to promote multidisciplinary studies of artificial intelligence and cognitive science, recently. In Japan, on the other hand, brain research has been the center of attention, generating some results for use in cognitive science. One problem is that Japanese projects often focus on basic research and therefore lag behind their U.S. counterparts in the its applied research toward artificial intelligence.

This article describes recent research trends in artificial intelligence and cognitive science, and discusses possible measures to encourage research into Intelligent Computing, a field that appears to be slower to grow than the information technology hardware sector, which has undergone rapid progress. In this article, artificial intelligence research is including overall research activities toward the implementation of intelligent processing on computers.

2 Research trends in artificial intelligence

2-1 The history of artificial intelligence

Research into artificial intelligence began in the latter half of the 1950s with an eye toward “creating machine intelligence.” It originated through attempts by mathematicians, psychologists, and philosophers to mimic human intellectual activities by using computers. In the 1970s, researchers succeeded in describing on a computer the rules that represent expert’s knowledge and demonstrated the ability to solve problems through reasoning, without the assistance of experts. They then developed and commercialized expert systems that were able to perform simple medical diagnoses and manufacturing process failure diagnoses. However, the frame problem, where a complete description of the preconditions of intelligence rules requires an infinite number of conditions, was later discovered. For this reason, rule-based expert systems have yet to achieve performance comparable to human experts. In the 1980s, researchers sought solutions by shifting their focus to studies on data processing, particularly using neural networks from traditional research on the processing of logic and symbols. These neural network studies later led to research on the brain’s neural network functions. In the 1990s, agents, each of which has a program that autonomously move across the network to perform simple tasks, attracted great attention in the research community. They have evolved to become anthropomorphic agents, which enable computers to perform various functions instead of humans, and personalization agents (or simply personalization), a technology to collect information according to the user’s preference. In addition, there are more advanced ongoing

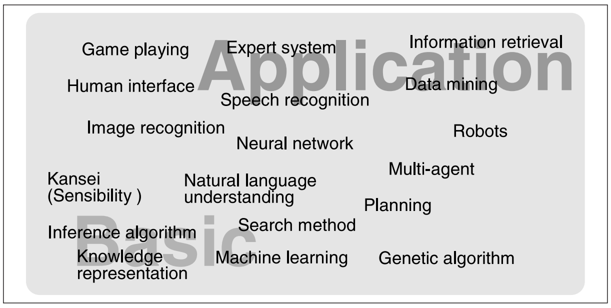
Table 1 : Historic events in artificial intelligence research

			History of the computer (reference)	
			1947	ENIAC computer
latter half of the 1950s – 60s [Emergence of artificial intelligence]	1956	Proposal of “Artificial Intelligence” (J. McCarthy)	1951	UNIVAC I commercial computer
	1965	Development of Eliza, a computer program that can interact with humans	1964	IBM 360 mainframe computer
	1967	Creation of MacHack, the knowledge-based chess program		
1970s [Expert systems (Knowledge representation as engineering approach)]	1974	MYCIN expert system (medical diagnosis)	1972	i4004 microprocessor
	1974	ABSTRIPS planning program		
	mid 1970s	Graphical user interface	1976	Apple personal computer
latter half of the 1980s [Growth of neural network research]	1982	Hopfield neural network	1981	IBM Personal Computer
	1986	Establishment of the Japanese Society for Artificial Intelligence		
1990s [Agents (Trials as distributed processing)]	1990	Start of genetic programming	1991	Windows 3.1
	1995	Situated agents (Russell)	1993	Mosaic web browser
	1995	Inauguration of the International Conference on Knowledge Discovery and Data Mining	1993	Client-Server model
latter half of the 1990s – [Data mining (Second coming of machine learning)]	1997	Victory of the chess program, DeepBlue, over a chess champion		
	1999	Proposal of the Semantic Web		
	1999	Emergence of pet robots		

projects that aim to simulate social and economic systems by running a large number of agents on a network so that each agent mimics personal behavior in a society.

The data processing capacity of the computer far exceeds that of a human being. From this perspective, artificial intelligence researchers now aim to provide "assistance for the intellectual activities of humans" rather than developing artificial intelligence to replace humans through the "creation of machine intelligence on the computer". In other words, in order to increase productivity in the intellectual activities of humans, ways of allowing computers to assist human intellectual activities and to perform tasks that humans are not good at, such as processing simple but large volumes of data or extracting significant data from a huge database, are now being the research target.

Figure 1 : Research themes in artificial intelligence



Source: Website of the Japanese Society for Artificial Intelligence

2-2 Recent research results in artificial intelligence

Research themes in the field of artificial intelligence are extensive as shown in Fiugre 1. To provide an overview of recent research trends in this area, I explain research results in the categories of game playing, agents, data mining, visual and auditory senses, and robotics.

(1) Game playing

In the research on artificial intelligence for reasoning and thinking, some researchers have been studying games in order to develop computer software that can beat human players in games such as checkers, chess, Othello, and shogi, or Japanese chess. In the U.S., the International Computer Chess Association was founded in the 1970s, and the association has been holding Computer Chess Championships. Computers successfully beat the world champion at checkers in 1994 and then at Othello and chess in 1997. In shogi, researchers believe that the ability of the computer is now equivalent to that of an amateur 5-dan player.

These game programs have a knowledge database containing large amounts of standard move sequences and best move sequences shown by professional players so that they can make inferences according to a preset strategy and decide the next move. This means that computers can now beat human beings at relatively simple games by employing inference techniques in addition to drawing on enormous databases and having high-speed processing capacity. The next challenge for researchers is to investigate the strategies of champions to develop powerful programs that can play more complicated games such as shogi and go.

(2) Agents

In the 1990s, research on agents, which are computer programs that make the rounds of different sites on a network and perform tasks independently to assist human beings, began receiving particular attention. Capable of communicating with required sites and executing simple processing tasks, an agent autonomously moves across the network and completes jobs for specific purposes. Major research themes in this area include personalization and anthropomorphic agents. The results of these research projects have been applied to schedulers and to web navigation software.

Some projects focus on "multi-agents," and these aim to design systems that enable a large number of agents to behave autonomously on a network. Possible application areas of achievements through these activities include the simulation of social or economic systems. The scheme describes the individual elements of a social or economic system as agents, allows them to operate on the network, and analyzes their behavior. This kind of project tackles unsolved difficulties such as describing agents in a manner that properly expresses the elements of a real society or economy, and describing the interaction between individual agents.

(3) Data mining

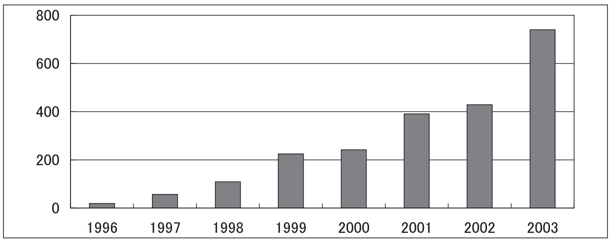
Data mining is a technology for extracting significant information from a huge set of data and has been growing as a research field since the late 1990s. Data mining uses machine learning algorithms, which have long been studied. New or improved algorithms have been proposed to meet the requirements of new application fields in data mining, including document analysis, information searching, and security.

Conventional computer security technologies such as virus detection and intrusion detection perform checks against pre-registered virus patterns or find the origins of intruders. This method, however, has the disadvantage of being unable to detect patterns that are not registered, which allows damage to occur during the time lag between the emergence of a new virus and the updating of the virus pattern file. Researchers addressed this problem by developing learning techniques that enable the flexible calculation of patterns to keep up with data changes, and they improved the ability to detect new viruses. These learning methods have proven effective in detecting network intrusions and attacks as well as computer malfunctions[1].

Another popular research area is text mining, which is a combination of data mining and natural language processing. Researchers are addressing topics such as the categorization of questionnaire sentences, reputation analysis, the automatic categorization of e-mail messages, and the categorization of purchase records; the results are in practical use as marketing tools.

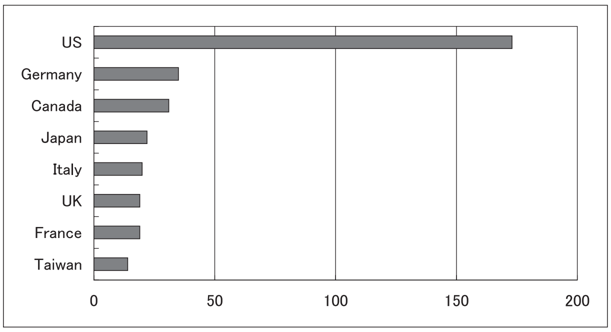
Such research efforts in the field of data mining became active in the late 1990s, particularly in the U.S., as shown in Figures 2 and 3. One achievement that prepared the way was the invention of an identification technique called the Support Vector Machine, proposed in 1995 by V. Vapnik, an American mathematician. For its excellent capability to classify unknown data, this technique is widely used as a machine learning tool. Since 1997, a data-mining contest has been held in the U.S. to encourage and speed up building the practical applications based on basic theories. In 2000, three years behind the U.S., a Japanese version of this contest, "Knowledge Discovery from Common Data Sets," was hosted by the Japanese Society for Artificial Intelligence. To secure its dominance, the U.S. is further intensifying its efforts to facilitate application-oriented basic research, as indicated by the National Science Foundation (NSF), an organization that is known as to promote basic research, planning to build a Science of Learning Center (Table 4) as a comprehensive research institution dedicated to learning, which covers a broad spectrum from basic theory to practical experiment.

Figure 2 : Change in the number of papers on data mining



Source: Based on a search of the ISI database for "Data Mining"

Figure 3 : Number of papers on data mining by country (for 2002)



Source: Based on a search of the ISI database for "Data Mining"

(4) Visual and auditory senses

Character recognition, voice recognition, and image recognition technologies are already in commercial use in suitable environments. To be usable in a wider range of environments, they need to be adaptable to varying usage conditions such as where there is ambiguous information, high ambient noise, and changes in light requiring context-based decisions or compensation by the situation. The technologies currently implemented in commercial products are in principle statistical techniques based on enormous databases. Since it is impossible to gather all data covering every possible change in the environment or the situation, or to endlessly enhance performance, extensive research is needed in areas such as multimodal systems, which use multiple modes of information for decision making, and technologies that adapt to changes in the environment.

(5) Robotics

Recently robot researchers are developing robots having visual and auditory functions. A major challenge is how to find the target for recognition in a given environment as a preparation of recognition process. From this point of view, there are a number of research themes to be addressed, including technology to identify and keep track of the human voice or the target object in a given environment.

In addition, as research into bipedal robots and nursing-care robots proliferates, the need for human-robot interaction and robots operable in people's daily lives is increasing. To allow robots to naturally communicate with humans, some researchers have begun developing robots that use nonverbal communication tools such as facial expressions and gestures. To improve current robot brains, which are still immature, breakthroughs in artificial intelligence research are expected.

2-3 Subsequent challenges in artificial intelligence research

Many achievements in artificial intelligence research are already in practical use for expert systems, text recognition, voice recognition, machine translation, data mining, information searching, and so forth. Moreover, the research results of areas such as personalization and distributed agents have already been embedded in information system software which is not easily recognizable as artificial intelligence technologies.

Although commercialized, these technologies have their own limitations in terms of expansion. For example, statistical techniques that are dependent on databases, while being able to perform in the same environment as from where the obtained data cannot cope well with changes in the environment. Currently, artificial intelligence cannot make decisions based on various kinds of information as humans do, and researchers are seeking to narrow the gap of this ability. These researchers should advance toward a fusion between a mechanical approach, which is solely dependent on large data sets and therefore limited in potential as mentioned in the section on game research, and a human-oriented approach, which intends to learn from human strategies.

3 Research trends in cognitive science

In artificial intelligence research, described in the previous chapter, findings in cognitive science have been used as part of the human-oriented approach. The research community has high expectations to cognitive science, hoping that it will provide new ideas to overcome the limitations of mathematical and mechanical approaches for performance improvement. The sections below discuss trends in cognitive science, followed by challenges for researchers in cognitive science in pursuit of Intelligent Computing.

3-1 The history of cognitive science

To explore human cognitive mechanisms, research in cognitive science began in the 1970s by combining cognitive psychology and the computer. Psychologists, information scientists, neuroscientists, linguists, and cultural anthropologists participated in the study. Cognitive psychology is a research field explaining intellectual activity from a functional viewpoint using the mental state model and that developed within the framework of psychology mainly in the 1950s. In the 1980s, noninvasive technologies for observation of the brain activities were advanced, followed by the development of technologies to visualize observed brain activity data in the 1990s. These advances have allowed researchers to obtain a wide variety of observation data on brain activities. These data have been used to investigate which areas of the brain are responsible for cognitive function, a popular study known as brain mapping, and also referred to as cognitive neuroscience. In this area, there have been major findings on brain plasticity and interconnectivity between brain components.

Table 2 : Historic topics in cognitive science research

latter half of the 1950s Cognitive revolution in psychology	1956	Short-term memory structure (Miller)
	1956	Cognitive processes in concept formation (Brunner)
	1957	Universal grammar (Chomsky)
	1958	Cognitive filter theory (Broadbent)
1970s Emergence of cognitive science	1972	Problem-solving theory (Newell & Simon)
	1979	Establishment of the Cognitive Science Society in the U.S.
	1980	Twelve Issues for Cognitive Science (Norman)
1980s Development of noninvasive brain measurement technologies	1983	Establishment of the Japanese Cognitive Science Society
	1986	The Society of Mind (Minskey)
	1986	Proposal of cognitive engineering (Norman)
1990s Progress in cognitive neuroscience	1995	Neural network model based on neural plasticity
	1996	Bidirectional interaction of nerves in image generation
	late 1990s	Progress in brain activity imaging using computer graphics

Another mainstream research area is creating estimation models for brain information processing by using the neural network methodology employed in artificial intelligence research for simulating the brain's neural networks.

In the late 1980s, a new field in cognitive science was proposed, cognitive engineering, in an attempt to apply cognitive psychology to engineering. To increase attention to user needs in designing engineering products, researchers in this field study human-object (machine) interaction, such as interfaces and communication. They pursued an interface that humans can easily use without being aware of its presence.

3-2 Recent research results in cognitive science

Research themes in the field of cognitive science are diverse as shown in Table 3. Of the four main categories, studies related to central cognition focus on exploring the mechanisms of the sophisticated functions of the human mind. Even when researchers have access to technologies for observing brain activity, the information they have acquired on individual cognitive functions is still fragmented. With respect to the linguistic cognition category, key themes include the understanding of language, the generation of language, and communication. In the area of sensory cognition such as vision, researchers are trying to elucidate how external stimuli cause brain activity through observation of brain activity and psychological experiment. For behavioral cognition, there are research projects to observe behavior that surfaces in psychological experiments and to predict possible cognitive behavior. There are greater amounts of data available in this area since the external observation of behavior is easier than brain activity observation conducted for the study of central or sensory cognition.

Table 3 : Research themes in cognitive science

Central	thinking, learning, conception, memory
Linguistic	language, communication
Sensory	vision, affordance (environment and cognition)
Behavioral	behavior, interaction

(1) Interworking between visual and auditory senses and action

Researchers have observed that the visual cognitive function for recognizing objects involves activity not only in the visual cortex but also in the motor cortex, that means interworking exists between the visual cortex and the motor cortex. This finding, in addition to helping reveal that humans use physically memorized information when recognizing objects, has recently been encouraging the study of "embodied cognition." This interworking between vision and action is not contained in the pattern recognition mechanism of current computers, and this suggests the possibility of multimodal recognition techniques, which is an approach based on information acquired from multiple sources such as vision, hearing and physical information. Further exploration of this interworking mechanism is needed.

(2) Application of cognitive properties to products

User interfaces for information equipment have been designed to reflect in the observation results of user behavior. In addition, as information equipment proliferate, they have begun to adopt a universal design, which is a design concept to be accessible for all. While this is the case, however, the design of these devices is often prioritized by cost effectiveness rather than exploiting human cognitive characteristics. Some kinds of information equipment, for example, are equipped with a voice guidance function to ensure user accessibility. These voice guidance systems sometimes frustrate users and cause errors, suggesting the need for smarter systems that adapt to learning level of user and different usage situation. Cognitive scientists and information equipment engineers should cooperate in developing such systems.

Similarly, video conferencing systems, designed by information device engineers using cutting-edge technologies, are not sufficiently considered to cater to the needs of the user. Some researchers in cognitive science have indicated that the lack of reality of presence in video conferencing systems is attributable to the limited space information shared among participants[2]. Eye-to-eye contact and gestures do not work effectively in a small- or single-screen environment. This finding is applicable to improving user-friendliness in not only video conferencing systems but also remote control systems in general.

In the automobile field, where safe operability is emphasized, researchers have been exploring designs that consider human cognitive characteristics. For instance, they have conducted cognitive psychology experiments to study the cognitive mechanism of visual attention and discovered an inverse correlation between the depth of attention and the width of attention as well as certain characteristics of the process of shifting visual attention[3]. The relation between the depth and width of attention is reflected in guidelines for safe driving. Considering the characteristics of human vision, the finding that the process of shifting focus from distant view to near view takes longer than the reverse process has allowed researchers to point out risks associated with car navigation systems. In the area of information equipment, too, similar safety-oriented design concepts adaptable to diverse usage situations should be pursued.

(3) Designs that mirror cognitive characteristics

In much the same way that designers play an essential role in the fields of building construction and automobiles, those who design information equipment are assuming an increasingly important role. This is attributed to the increased demand for user-friendliness in information devices, which have become widely used in people's daily lives. When laying out numerous pieces of information on the Web, for example, designers should consider, in addition to appearance, cognitive aspects of the design, such as the rationality of assumed user actions and interactive capability[4].

The design process for information equipment requires the screening of user needs, design specification, and testing and evaluation of usability. An information equipment designer is expected to conduct the overall management of this process. Current information equipment are often incomplete; their appearance is good but their usability is poor, or they are attractive in their individual elements but lacking in overall design harmony. This suggests the need for integrated effort particularly in the area of interface design, which involves multiple elements such as psychology, cognitive science, human engineering, software engineering, product design, and graphic design.

3-3 Future challenges in cognitive science research

To apply cognitive science to Intelligent Computing, the utilization of findings from cognitive science research has begun, but it is not sufficient.

Knowledge of behavioral cognitive functions obtained through the study of human behavioral and cognitive mechanisms has been reflected in the design of user interfaces for some information equipment. However, these interface design activities are currently dependent on accumulated experience. The next challenge in cognitive science is achieving outcomes that can serve a wider range of purposes and further systematize cognitive properties. This requires cognitive scientists and information technologists to increase interchanges, interworking and collaboration, through which they could elucidate the essence of the cognitive properties useful for designing information devices.

Meanwhile, there is only microscopic, fragmentary understanding of the mechanisms of central and sensory cognition. Traditionally, these areas have been positioned as basic research fields and thus there has been no active effort toward application. Researchers in Intelligent Computing, however, expect new ideas to be derived from these areas, and these ideas could break through the limitations of mathematical and mechanical processing. Cognitive scientists are hopefully aware of the need for application-oriented research activities so that their results may be used for research into Intelligent Computing. At the same time, interchanges, interworking, and collaboration between the two research fields is essential. In other words, Intelligent Computing researchers should use the achievements of cognitive science on a trial basis and provide cognitive scientists with feedback on the possibilities and problems found.

4 Challenges in intelligent computing research

To realize Intelligent Computing capable of assisting the intellectual activities of human beings and of naturally interfacing with human beings, there must be a framework to ensure that advances in cognitive science are reflected in research in artificial intelligence. From this perspective, many counties are implementing projects to promote multidisciplinary studies in artificial intelligence and cognitive science. In the U.S., as shown in Tables 4 and 5, the National Science Foundation (NSF) and the Defense Advanced Research Projects Agency (DARPA) have been taking the initiative. NSF, which is offering funds for basic research activities in diverse fields, is particularly promoting joint research projects and multidisciplinary research

Table 4 : Major NSF projects related to cognitive science and artificial intelligence

Year	Project Name	Description
2001~	Cognitive Neuroscience	Research in cognitive neuroscience
2003~	Collaborative Research in Computational Neuroscience	Collaborative research in computational neuroscience
2003~	Artificial Intelligence and Cognitive Science	Multidisciplinary research in artificial intelligence and cognitive science
2003~	Human-Computer Interaction	Research in interfaces between humans and machines
2003~	Human Language and Communication	Research in new computational models for text and speech processing, as well as multi-modal communication
2004~	Science of Learning Center	Multidisiciplinary research center for machine learning, educational/psychological learning, and physiological learning

Table 5 : Major DARPA projects related to cognitive computing

Year	Project Name	Description
2001~	Augmented Cognition	Development of systems that can enhance human cognitive abilities in a stressful environment
2003~	Cognitive Information Processing Technology	Development of systems that can recognize and assist human activities
2003~	Real-World Reasoning	Development of practical inference engines
2003~	Architectures for Cognitive Information Processing	Development of computing architectures of cognitive information processing systems for real-time DoD applications

Table 6 : Competitively funded Japanese research projects related to cognitive science

Year		Project Name	Description
1997 ~ 2003	JST Basic Research Program (CREST)	a part of the "Creating the Brain" and "Understanding the Brain" projects	Development of brain-like devices / architectures and cognitive processing systems; elucidation of higher brain functions
1997 ~ 2000	Scientific Research in Priority Areas	Mind development: the mechanism of cognitive growth	Research in conceptual development, language acquisition and cognitive development
2001 ~ 2005	Scientific Research in Priority Areas	Informatics studies for the foundation of IT evolution: A03 Understanding human information processing and its applications	Investigation into dynamic interaction between perception and action, development of symbiotic systems, and realization of multimodal human-machine interaction
2002 ~ 2006	Exploratory / Fusional Development Program	Construction and elucidation of the emergence mechanism of communication through dynamic interaction	Research in the neural mechanism of action and facial expression, communication models, and the self-organizing function of neural circuits

projects. Recently, NSF has been intensifying its efforts to build comprehensive research centers that cover from basic research to applied research. In contrast, DARPA stresses systems development for demonstrations even in basic research, and requires more specific research target what is to be achieved. Each DARPA project, relatively large in scale, is administered by a program manager and is subject to a rigorous evaluation of the final results. For example, an ongoing project under the theme, "Cognitive Information Processing Technology," consists of members from 20 different organizations. Although geographically dispersed, the members work under the project leader in a virtual research institution.

European initiatives in the area of Intelligent Computing are made in the 6th Framework Program to the European Commission (EC), which addresses this field of study as 'Cognitive Systems'. The U.K. and Germany have selected cognitive science as a theme in their technology foresight activities and have begun discussing specific promotional plans. The technology foresight report[5] published in November 2003 by the Office of Science and Technology of the Department of Trade and Industry of the U.K. (OST DTI) states that interesting new signs were appearing in cognitive science and that, if coupled with artificial intelligence research, cognitive science would result in accomplishments applicable to the fields of information and communications as well as life science, thereby greatly contributing to society.

In Japan, too, a series of multidisciplinary research projects is in progress as listed in Table 6. In each of these projects, a sizable number of researchers work on a variety of themes. While these initiatives foster increased interchange between researchers from different disciplines, the project teams usually dissolve when the project finishes, leaving very few teams to form new organizations to continue activity. With an eye toward constructing world-leading research and educational institutions, Japan has been implementing the 21st Century COE Program since 2002, including the six projects selected in the area of cognitive science as listed in Table 7. These projects aim at, in addition to the promotion of multidisciplinary research, the development of creative human resources. It is expected that these projects will provide frameworks to nurture research personnel and to further develop and systematize research activities when these projects have finished, thus allowing research teams to grow into new organizations. In another initiative, Japan is encouraging brain research under the leadership of the RIKEN Brain Science Institute. This effort emphasizes basic research into the brain, including its cognitive functions.

In contrast, from the standpoint that multidisciplinary research in cognitive science and artificial intelligence will bring about results leading to practical application, the U.S. is promoting application-oriented basic research projects. In the U.S., when a project ends, it does not mean the end of the study, but rather, the start of an industry-academia collaborative effort toward commercialization. This approach is significantly different from that adopted by Japan, whose projects concentrate on basic research. Although they are potentially fruitful, the outcomes of these basic research projects have not shown major progress. There is a need for a management scheme that permits the research resources of a finished project to be effectively inherited for use in a subsequent project. In addition, it is necessary that scientists will be more aggressive to lead basic research outcome to applied research so that their projects can develop into industry-academia collaboration. The business sector, for its part, should make proactive approaches to universities, such as proposing joint research projects. Research in the information and communications sector is progressing in extremely high rate so that someone across the world are quickly taking advantage of the potential opportunities found though basic studies for practical application.

5 Conclusion

Research in Intelligent Computing to develop systems capable of assisting the intellectual activities of human beings and naturally interfacing with human beings has advanced in the area of artificial intelligence. The intelligent

Table 7 : Major centers for the 21st Century COE Program related to cognitive science

Program Title	University	Courses	Majors or Disciplines
A Strategic Research and Education Center for an Integrated Approach to Language, Brain and Cognition	Tohoku University	Graduate School of International Cultural Studies, New Industry Creation Hatchery Center, GraduateSchool of Information Sciences, Graduate School of Medicine, Medical School Hospital, Graduate School of Engineering, Graduate School of Arts and Letters	Cognitive Linguistics, Cognitive Psychology, Brain Mapping, Natural Language Processing, Linguistics, Generative Linguistics, Speech and Language Processing, Phonetics, Phonology, Neuropsychology, Neurolinguistics, Sociolinguistics, Linguistic Geography, Learning Psychology, Linguistic Anthropology, Computational Linguistics
Center for Evolutionary Cognitive Sciences	University of Tokyo	Graduate School of Arts and Sciences, Graduate School of Science, Graduate School of Humanities and Sociology, Graduate School of Agricultural and Life Sciences, University of Tokyo Hospital, Digital Museum, Information Technology Center	Human Evolution, Psycholinguistics, General Linguistic Science, Computational Linguistic Science, Cognitive Development Clinical Science
Toward an Integrated Methodology for the Study of the Mind	Keio University	Graduate School of Letters, Graduate School of Human Relations, Institute of Cultural and Linguistic Studies	Philosophy and Ethics, Aesthetics and Science Arts, History, Japanese Literature, Chinese Literature, English and American Literature, German Literature, French Literature, Library and Information Science, Psychology, Education, Institute of Cultural and Linguistic Studies
Zenjin Human Science Program (Exploration of the brain mechanisms for learning, memory, reasoning, and thinking and their application to educational technologies)	Tamagawa University	Research Institute, Graduate School for Engineering, Graduate School for Agriculture, Graduate School for Education and Letters,	Brain Science Research Center, Language and Communication Research Center
Promotion of 'Kansei' Science for Understanding the mechanism of the Mind and Heart	University of Tsukuba	Graduate School of Comprehensive Human Sciences	System Brain Science, Neural Molecular Dynamics, Behavioral Neuroscience, Psychology, Mental Disability Science, Brain-Like Information Processing Mechanics, Kansei Informatics, Art
World of Brain Computing Interwoven out of Animals and Robots	Kyushu Institute of Technology	Graduate School of Life Science and Systems Engineering	Neurophysiology, Electrochemistry, Psychology, Human Behavior, Mathematical Science, Linguistic Science, Devices, Robotics

processing capability of such systems has enhanced as the computer's processing capability has improved, and some of them have been incorporated into commercial information systems in fragments, in a manner that is not easily recognizable as artificial intelligence. However, mathematical and mechanical approaches solely dependent on the processing capacity of the computer are not sufficient for developing highly sophisticated intelligent systems.

In cognitive science, a field aiming to elucidate the mechanisms of human cognitive functions, the development of noninvasive brain observation technologies since the 1990s has brought major research advances to the mapping between cognitive function and brain activation, partially revealing the correlation between the visual/auditory senses and action. While a large part of central cognitive mechanisms, which are related to reasoning and thinking, has yet to be explained, expectations are high that this area of research will be able to propose new ideas to help overcome the limitations of mathematical and mechanical approaches in artificial intelligence research.

Traditionally, researchers in cognitive science have emphasized achievements within the framework of basic research and have not made proactive efforts toward practical application. Engineers in the information and communications sector have simply used findings in cognitive science with little interaction with cognitive scientists. The boundary between the two fields must be eliminated because new developments can be derived from such activities as addressing existing challenges in the field of information and communications in the new light of cognitive science. These efforts will lead to an application-oriented multidisciplinary research initiative. In implementing this initiative, the conventional multidisciplinary research framework must be avoided because in such a framework once a project ends, its research results disperse and stop accumulating. As a result, achievements in the project do not grow into a critical mass and further progress is inhibited. Another possible measure for multidisciplinary research promotion in cognitive science and artificial intelligence is building a research institute that recruits a sizable research staff to work on all spectrum of research from basic to application.

Recently, the U.S. has been implementing projects to encourage multidisciplinary research in the areas of cognitive science and artificial intelligence. While promoting application-oriented basic research as well as the applied research that follows, the U.S. is planning to build a center for integrating such activities to secure its position as the world leader in this field. Since research in the information and communications sector is proceeding rapidly, positive results achieved through basic research are quickly finding its application.

Japan has not been successful in embodying or applying excellent new concepts found through basic research to engineering. Another discouraging element of Japanese research initiatives is that multidisciplinary research teams usually dissolve once the project ends, reducing the opportunity for the results to be further studied and developed. Japan should consider a program of constructing a research center dedicated to cognitive science and artificial intelligence, while seeking more the flexible operation of research organizations in universities by, for example, adopting a 'scrap-and-build' approach. Yet another weakness of Japan is its lack of effort in linking basic research with applied research. Possible solutions by the government are to increase incentives to promote interchange between basic and application initiatives and to encourage application-oriented basic research activities. In the meantime, the business sector should also make proactive approaches to universities, such as proposing joint research projects, to facilitate the commercialization of potentially fruitful findings.

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7

Trends and Issues in Computing Curriculums

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1 Introduction — Introduction to issue

Most activities, whether industrial, public, academic research or everyday life, rely on the technical advances of software.

Software production in Japan totals approximately 20 trillion yen per year. It produces extensive ripple effects in various industries, because of its high growth and sheer scale. More than 10,000 university students receive computing-related professional training every year. Skills that these students acquire are also important from the standpoint of the competitiveness of Japanese industries.

Technological advances over the past ten years have produced environmental concerns, especially involving software production. Accordingly, there is a gap between the content of education offered at universities and the realities of industries.

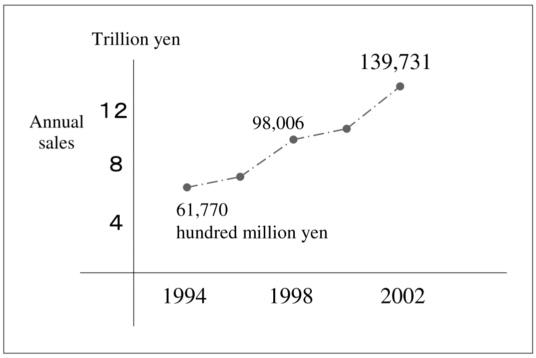
This article investigates the present state of the model curriculum adopted by information processing-related faculties and departments such as the Computer Science Department in order to analyze the above issue. This report also explains the present circumstances surrounding the industrial world and the educational institutes of Japan and the US, with a specific focus on the field of software engineering, the significance of which has greatly increased in recent years. Finally, recommendations for a technology policy are presented.

2 Present position of software industry

This section provides data that indicate a quantitative expansion of software production. According to statistics from the "Survey of Selected Service Industries of 2003 (information service business version)" released by the Ministry of Economy, Trade and Industry, the amount of sales in the information service business obtained during the fiscal year 2003 was approximately 14 trillion yen. The number of employees showed roughly the same pattern as the annual sales to reach 570,000 as of the fiscal year 2003. Figre 1 shows the annual sales in the field of information service for the past ten years.

Software can be divided broadly into (i) business software, (ii) package software, (iii) embedded software and (iv) game software. Business software represents the development of so called ERP(Enterprise Resource Planning) software used, for example, for production

Figure 1 : Change of annual sales by information service business



Source: Prepared by the author based on statistics released by the Ministry of Economy, Trade and Industry.

or sales management. Package software often describes the development of software components used for selected businesses. A software development service that provides prepackaged applications that are adjusted for client companies' operations is also included in this category. Software (i) to (iv) are in the order of production value.

Who are target customers for software development and other services? One survey shows that customers are from a wide area of industry, with the service industry accounting for 22.4% of all customers, the finance industry for 18.4%, the manufacturing industry for 13.6%, the government and other public offices/prefectural and city governments for 12.8%, the telecommunications industry for 7.8% and other businesses for 7.7%.

Other software products are not included in the above statistics. For example, software is often developed when a new production line is introduced at a manufacturing premise. Such software is not included in the above statistics. Engine control software and other embedded software are also excluded. Software that does not fall under the category of "information service business" is estimated at a few trillion yen. If such software is included, Japanese software production is estimated at approximately 20 trillion yen.

In fact, the development of custom-made software to meet various needs of client companies constitute substantial portion of software production of approximately 20 trillion yen, accounting for nearly 80% of total software production. To support the future software production industry, more than 10,000 students receive processing training at universities or graduate schools every year.

3 Significant changes in information technology and software

This section considers qualitative changes in software production. As discussed in the previous section, software production expanded as client-server information systems that integrate Internet and Web-based technologies spread into the core business of companies and various other social activities.

"Information processing" power that we enjoy in our daily life has dramatically increased over the past ten years. In 1977, the average processing rate for average modern personal computers was 100 MHz in clock frequency, which has increased to a few GHz today. In addition, about 9.2% of households had Internet access by the end of 1997. By the end of 2002, only five years later, the number of Internet users reached 54.2% and became the majority[2]. Processing rates for average access lines increased from a few or dozens of Kbps to dozens of Mbps during the same period. If information-processing power can be calculated by multiplying the processing rate by the volume of communication, it has increased by tens of thousands of times during the previous five years. In addition, this tremendous processing power has spread widely from laboratories into households and offices. Today, software plays increasingly important roles in social activities, due to increases in information processing power.

For example, tailor-made therapy is considered important in the field of medical technology today. In order to put it into practice, it is necessary to establish a system that enables distribution, use, and management of a huge amount of patient personal information. Without using the Internet and Web-based technologies, as well as a large-scale database and safe information exchange networks, there would be no tailor-made therapy.

Another example is "electronic shops" that offer product information through Web sites. A growing number of companies are introducing business-oriented package software such as ERP (Enterprise Resource Planning), CRM (Customer Relationship Management) and SCM (Supply Chain Management) for information management. These software packages also run on the client server system using Web-based technologies.

4 US response

Information processing-related educational organizations in North America responded quickly to such changes in technological trends.

This section briefly explains developments in North America.

Initially, information processing-related disciplinary was considered "computer science" derived from mathematics and electrical engineering. "Software engineering" has always been considered a part of computer science, and therefore a growing gap has developed between a career path and the acquired knowledge of graduates who majored in software engineering. Consequently, claims were made that computer science and software engineering should be treated separately as an independent subject[7,8].

In the US and Canada, active discussions have been pursued concerning the positioning of computer science and peripheral engineering subjects and the role of the curriculum since the second half of the 1990's. Today, the "engineering aspect" is becoming more important in average computing education.

4-1 Model curriculum

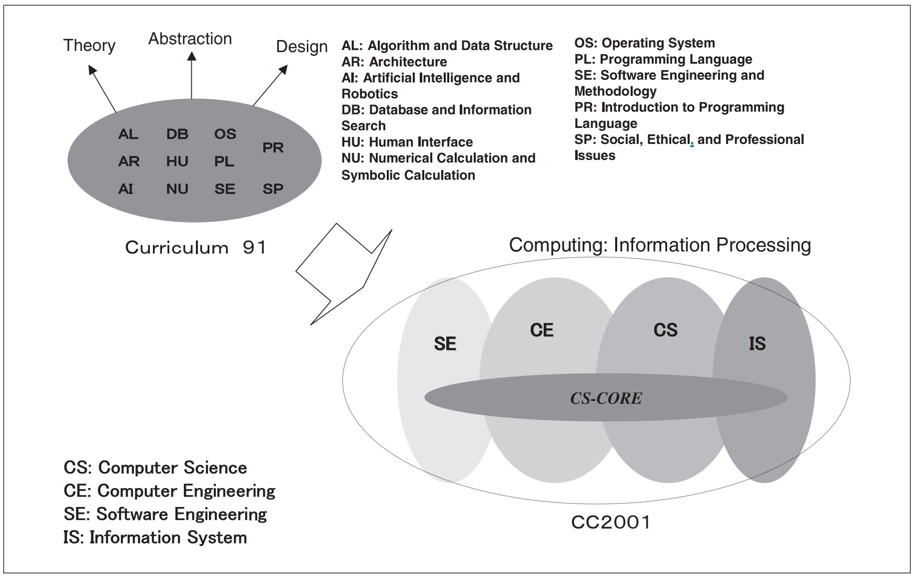
The following is an outline of the model curriculum. ACM (Association for Computing Machinery) and IEEE/CS (The Institution of Electrical and Electronics Engineers, Inc./Computer Society) are the world's biggest society in the field of computer and in the field of electrical and electronics engineering, respectively. Since the 1960's, they have developed a few model curriculums together. After several attempts, CC1991 was developed in 1991. In 2001, ten years after the development of CC1991, the latest model curriculum CC2001 (Computing Curriculum 2001) was developed.

CC2001 divides computing[*1] clearly into four disciplines, CS (Computer Science), CE (Computer Engineering), SE (Software Engineering) and IS (Information System). CS provides a mathematical background into information processing such as algorithm and data structure. CE aims to use computers for numerical calculations, graphics, and other technical purposes. IS handles relationships between information processing systems and corporate and economic activities. Finally, SE aims to acquire skills required for software production.

CC2001 consists of a group of subject components that belong to each of the sub-fields. Components of the curriculum depend on the direction of an educational institute. Figure 2 shows changes in curriculum at the time of transfer from "Curriculum 91" to "CC2001" in a conceptual way. CS is positioned as a "core" for all four disciplines.

CC2001 stipulates that CE and SE belong to engineering, and CS and IS to science. In the context of CC2001, "engineering" and "science" differ from what the "faculty of engineering" and the "faculty of science" represent in Japan. These words seem to imply "technology and skill" and

Figure 2 : Conceptual diagram of curriculum transition - from "Curriculum 91" to "CC2001"



Source: Prepared by the author based on References[3].

"science and research", respectively.

4-2 Human resources required in industry

Based on the technological changes, the model curriculum CC2001 investigated human resources that would be in greater demand in connection with information processing. The investigation revealed that human resources are expected to possess specific skills, as shown in Table 1. For example, skills that fall under the category of 1 to 3 of Table 1 are essential for designing and building a client-server system described above. The category 5 points out the importance of providing information technology education at an early age.

In order to respond to the need for developing such human resources, the content of computing education at universities was determined. Table 2 shows new items that cannot be found in previous model curriculums. This table promotes a greater understanding of the growing importance of a relationship between information processing and the corporate activities in social life, as well as a relationship between information processing and information infrastructure that constitutes social infrastructures. It was difficult to acquire these skills in the framework of previous model curriculums.

Table 2 : Items included in a curriculum due to technologica changes in the second half of 1990's

A	World Wide Web and its application
B	Networking technology, with TCP/IP based ones in particular
C	Graphics and multimedia
D	Embedded system
E	Relational database
F	Interoperability
G	Object-oriented programming
H	Use of sophisticated application programmer interface (APIs)
I	Human - computer interaction
J	Software safety
K	Safety and encoding method
L	Application area

Source: Prepared by the author based on References[12].

Table 1 : Human resources to be in greater demand at the time of technological change

1	Programmer who is familiar with multipurpose type relational database systems and multipurpose enterprise resource planning package software in particular.
2	Programmer and designer with experience in object-oriented and Java languages.
3	Experts in Web and electronic commerce.
4	Network designer.
5	High school teachers, instructors who teaches information at vocational technical schools or undergraduate programs at universities.
6	Manager and project leader.

Source: Prepared by the author based on References[12].

4-3 Example of advanced software engineering education

In the US and Canada, undergraduate education are generally devoted to "engineering" or practical education, and graduate schools focus on providing "science" education. The faculty of "computer science" and that of "computing" accept more students than other faculties. In addition, graduates of these faculties have more choices for disciplines when they proceed to graduate schools. These factors encourage students to apply an acquired knowledge of and skills for information processing to many different fields.

Information processing-related faculties in US and Canada are often called the "Faculty of Computer Science." Students study CS as a core subject in the Faculty of Computer Science, and then proceed to a graduate school to become a researcher in the CS discipline. That is the typical career path for the graduates of the Faculty of Computer Science. As software plays an increasingly important role in industrial activities, there is a new career possibility. Students who study software engineering, for example, begin their career by managing and operating a project to develop enterprise resource planning software, before rising to the position of CIO[9].

The following is an example of education practice in the discipline of advanced software engineering in the US. Objectives of the discipline of software engineering are design and production of software. For that purpose, it is important to cultivate knowledge of software engineering by providing courses for “software life cycle and process model,” “examination of requirements, rapid prototyping,” and “knowledge of tools for modeling, test and product control,” in addition to programming exercises.

Carnegie Mellon University provides the first example[10]. Carnegie Mellon established its SEI (Software Engineering Institute), which was financed by the Department of Defense. SEI conducts practical research and provides many practical educational programs to professionals. For example, in exercises called “pair programming”, an implementer and verifier of functions work together to develop a program. As there is a growing demand for the quality of programs, performance verification-oriented production is considered an advanced skill.

Carnegie Mellon collaborates with companies to provide various practical seminars. In these seminars, students analyze actual business demand and develop software design specifications. They then perform programming based on a developed specification. It is as though students are undertaking a “virtual contract” to develop software to meet the requirements of companies. Students also practice various techniques such as PSP/TSP, reengineering and RUP (Rational Unified Process/UML)[10].

The Georgia Institute of Technology presents another example, as it established the “College of Computing” in 1990. The new college was established parallel to the “College of Engineering” and the “College of Science.” This indicates that the Georgia Institute of Technology places an emphasis on education in the information processing discipline. The institution is ranked high recently in the third-party university evaluation[11].

A more advanced educational content would enable students to acquire a more advanced design theory. Recently, various new concept have been introduced into software design theory. Among them are the “Spiral Model Method” and the “Agile Method.” The “Spiral Model Method” provides a continual opportunity to ensure adherence to user requirements, while the “Agile Method” (agile is defined as speedy) aims for a reduction in overall process time. Lectures on these design theories are an extension of training to acquire practical software production skills.

In short, the leading school in US makes positive efforts to provide education in order to respond to technological evolution as a leader in this field.

5 History of computing education in Japan

This section traces the history of information processing education in Japan. The first electronic calculator was invented in the 1940’s. The second half of the 1950’s saw the expansion of academic disciplines such as control, communication, calculator, and applied mathematics. Individual universities began developing a new educational system in an attempt to respond to such changes.

In 1959, Kyoto University set up the Department of Mathematical Science and Engineering under the Faculty of Engineering. This was the beginning of a curriculum for information processing in Japan. Its establishment was aimed at “developing researchers and engineers who have a comprehensive perspective of not only common areas but also boarder areas for individual disciplines, in order to overcome difficulties of the division of disciplines into specialized subfields of science and technology and contribute to the dramatic growth of learning and industry.” Kyoto University also launched the Department of Computer Science in 1970. The two departments were later merged into the Department of Informatics and Mathematical Science.

The University of Tokyo set up the Department of Counting Engineering in 1962 when it restructured the Department of Applied Physics. This was the first attempt to provide computing education at the University of Tokyo. In 1970, a research facility was established under the School of Science, which later evolved into the Department of Information Science.

In the advent of information society, there was a growing awareness of the importance of information study and education. During this period, many universities set up new departments. For example, the Faculty of Science at the Tokyo Institute of Technology opened the Department of Information Science. The University of Electro-Communications and Yamanashi University set up the Department of Computing Machinery under the Faculty of Engineering, respectively. In the 1980's, many universities set up a faculty or department of computer science in succession to respond to the call for developing more engineers with expertise in information processing. Since then, many universities have opened unique faculties and departments, including the Faculty of Business and Information Administration (Tama University, 1989) aimed at combining the discipline of social science and that of information processing, the School of Computer Science and Engineering that focuses on computer science (the University of Aizu, 1993), the Faculty of Software and Information, which is software oriented (Iwate Prefectural University, 1998).

Meanwhile, the issue of what should be taught in the context of information processing was debated as needed[5]. An examination was conducted along with the model curriculum developed by ACM, upon which each university introduced an educational curriculum that reflects the results of the examination. In recent years, J97 was developed in 1997, based on CC1991 developed in 1991[16]. This was not the result of explosive growth in Internet use or the emergence of the Web in the middle of the 1990's. Presently, Information Processing Society of Japan is developing a new model based on CC2001, with an eye to proposing a new model in the spring of 2005.

Today, a large number of students receive information processing education. According to the Association of Computing Schools in Japan [4], a total of 130 faculties and departments provide information processing programs across the country (the association has 274 members at present in 2004, including graduate schools). According to an estimate, more than 10,000 students graduate from undergraduate and postgraduate courses every year.

6 Analysis of issues

When discussing the frustration of the software industry from its viewpoint, the main complaint is that today's university education does not enable people to put theory into practice. Some may hold different views. However, it cannot be denied that in general, there is a gap between the outcome of computing education and the needs of the industry. The following is an analysis of these circumstances.

6-1 Characteristics of computing education in Japan

Despite "dramatic" technological changes in the field of information processing in recent years, universities took measures that are "gradual" to respond to the changes and the need for a new model curriculum.

Such reluctance stems from the way a new faculty or department was formed. The Faculty of Engineering consists of major industries of the mid 20th century such as Civil Engineering, Machinery, Electricity, and Chemistry. Therefore, universities "increased the enrollment limit" or "asked for a budget increase." This was mostly seen in the Department of Electrical Engineering when they set up the information-processing related departments.

In Japan, undergraduate students are allowed to belong to a laboratory when they reached their final year. This is one of the major characteristics the Faculty of Engineering is operating in Japan. Research activity based education is available for only senior students and in a guild like atmosphere after three years of preparatory education. This is probably because the Faculty of Engineering at national universities first introduced a credit system that encourages students to go into subdivided research disciplines based on the research oriented course structure. Individual laboratories that comprise an education system tend to show an interest in a specific research area only. Furthermore, research-oriented universities tend to evaluate instructors based on their research papers. This probably made it difficult for a university to make concerted efforts to implement business education or pursue newly evolved of education areas.

Reform of the education system is not simple for newly created universities with the aim of pursuing original research areas. Even after the deregulation of official requirements for the establishment of a college called the establishment of broad outline ("Taikouka" in Japanese) in 1991, newly created universities are required to adhere to the same curriculum until the first group of students graduate, and ensure that educational contents, presented to students at school entry, will be in place until their graduation. Although these requirements are essential to guarantee a right to receive education that is based on a certain philosophy, they can be a disadvantage when universities respond to technological evolution.

In general, these requirements make it difficult for a university curriculum to reflect the needs of industry.

6-2 Need to promote "engineering" education

In Japan, criteria for "skills" that must be achieved are not as clear as that in the US. Some may argue that "it does not matter if we do not meet the criteria for "skills" adopted in the US, as long as a quality education is provided." However, people who are engaged in software production are increasingly required to acquire skills that comply with the international standard, under the concept of the software as a product.

In 1998, the "agreement to recognize equivalence of accredited engineering educational programs leading to an engineering degree" which is also called the "Washington Accord" was signed. Based on the Washington Accord, JABEE (Japan Accreditation Board for Engineering Education) plans to examine and accredit programs in engineering education in line with international standards. The Committees to Develop Curriculum for Information Processing Education, a work group of Information Processing Society of Japan also believes that the introduction of the accreditation system based on third-party evaluation or international standards will bridge the gap between social needs and educational contents in the field of information processing. For that purpose, educational institutes need to strengthen software engineering education, if they place importance on the enhancement of computing education from a standpoint of the software industry. In return for the effort to strengthen software engineering education, educational institutes can build up their market competitiveness.

However, there are many obstacles to overcome for implementation of accreditation. Experts believe that under present circumstances, none of the faculties or departments of Japanese educational institutes will successfully meet the screening criteria of ABET (The Accreditation Board for Engineering and Technology) for accreditation in the field of software engineering. This is not the matter of quality of education at Japanese universities. Rather, this is attributed to the fact that there is a difference in educational systems between the US and Japan.

It is not appropriate to rely solely on accreditation as a way to enhance the contents of curriculum. Accreditation should be conducted at the final stage in a series of efforts to match educational contents to technological evolution. For that purpose, educational institutes must make systematic efforts to respond to changes, while addressing curriculum issues.

7 Recommendation to the management of undergraduate-level computing education

This section recommends measures that need to be done in order to enhance the discipline of "Software Engineering," in view of the previous discussions and present circumstances of computing education at the undergraduate level in Japan.

From the standpoint of adapting to the US style of engineer education, it is necessary to implement a third-party evaluation to uncover how Japanese universities are meeting the criteria of the existing model curriculums. In order to conduct third-party evaluation, it is essential to modify the educational content, which may not be favored by universities. Firstly, such a problem should be alleviated.

Japanese universities tend to attach a special importance to the number of theses presented at academic societies, when they evaluate the performance of instructors. Under the circumstances, it is necessary to introduce specific incentives for instructors so that they can work towards the implementation of business-oriented education. For example, the accreditation criteria of JABEE question if there is an incentive structure that recognizes the achievement of instructors, which would provide information for making an important employment decision such as that on the offer of lifetime employment. Educational institutes can take various measures such as employment policy change, introduction of fixed-term system, reexamination of retirement age, and an introduction of greater flexibility in observing the fixed number of instructors.

It is also good to provide an opportunity to instructors, who are willing to provide practical education, to participate in practical training so that they can experience software development tools that are used in the business environment. The “programming exercise” may have two completely different scopes of practice, if one provides Pascal language exercises for understanding an algorithm, and the other aims to teach how to design an input/output interface for the Web use that is based on a Java authoring tool. Private training institutions offer a variety of programs in relation to the “IT skill standard” that is highly valued in the industry. Universities can introduce new educational content, if they send instructors to these courses. In that respect, policy support would be effective.

Enhancement of teaching materials is also important. For example, a video library can be created by recording practical lectures by business people and provided through the University of the Air Foundation. It is possible to promote the use of these videos at universities. Universities can also outsource their courses. Among them are the courses that teach the basic principle and operational procedures of network facilities, and the usage of database systems. However, educational content that emphasize the efficiency or that are too business-oriented, may not seem compatible with the intrinsic values of university education. Therefore, it is preferable that certain guidelines will be developed before the introduction of measures that are aimed at facilitating implementation of the guidelines.

To reinforce the incentives for students who receive education, it would be effective to provide courses that lead to a qualification. A relationship between qualifications such as that for data processing specialist, professional engineer, and assistant professional engineer, and curriculum, or IT skill standard and curriculum should be examined first. Then, a relationship between job descriptions and examination subjects must be explained in a straightforward manner. Academic societies can play a major role in this respect.

In the meantime, the industry must treat graduates with certain qualifications well in terms of salary, depending on their qualification status. Many of the information service related companies provide extra benefits to employees who are qualified as a data processing specialist, depending on the qualification they hold. This makes it important for universities to be aware of the possibility of market principles interfering with the selection of disciplines by undergraduate students.

The present education system at engineering universities, which allows senior students to engage in a research project, is unique to Japan. It should be cherished because of its long tradition. When it comes to accreditation, due consideration must be given to this aspect of university education. On that basis, a private company and individual laboratory can introduce a year-round internship program collectively for those working on a graduate thesis. The internship program has a great advantage for the industry, because they have access to students with certain skills who could be a reliable candidate for their opening positions. If it is difficult for individual companies to implement an internship program, an industry organization should coordinate effort to develop a cooperative framework to launch the “Internship Center” or other schemes.

8 Conclusion

In the Meiji era, fledgling Japanese engineering education was modeled after Britain. After the end of World War II, it has evolved, using examples from the US system. Japanese manufacturing industry's success in the second half of the 20th century owes, in a large part, to students who studied "engineering" at universities, and who are superior in terms of quantity and quality to their overseas counterparts.

Expansion and dispersion of information processing technologies, and changes involved in terms of quantity and quality of software production represent dramatic changes that took place over the past ten years or so. Having faced such technological changes, there is a growing awareness, both nationally and internationally, that production capacity and quality of software are important for national competitiveness. Given this factor, it is imperative to increase the proportion of practical education that is leaning towards the industry and to improve the quality of education, in order to pursue the technology policy.

Notes

***1** In the context of the curriculum in Japan, the word "computing" is usually translated "Johogaku (Information Science)". This paper also uses "Joho Shori (Information Processing)" as translation for "computing" depending on the circumstances.

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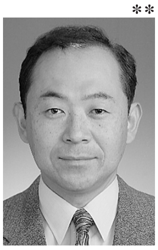
8

Trends in Japanese Zero Emission Systems that Lead the World
— Creation of Recycling Systems Centering on Materials Industries —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1 Introduction

"Zero emission" has been a key concept in converting a variety of technological systems in an effort to create a sound material-cycle society. This particular concept, first proposed by the United Nations University in 1994, was put into practice as part of the program to "reconstruct socioeconomic systems toward sustainable development." There, "zero emission" is defined as an "effort to create recycling-based industrial systems producing no waste, by restructuring the production processes of all industries and developing new industrial clusters in which all waste is recycled as materials."

In other words, "zero emission" is a system design concept that enables the recycling of waste among various processes, plants, businesses and areas. It organically links the "veins" (waste stream) with the "arteries" (material stream for production), creating new industrial clusters. At the same time, waste from certain industries is used as materials by other industries in a cascade manner to minimize the generation of waste. Properly speaking, "zero emission" does not refer to the total elimination of waste, but to the minimization of waste. Meanwhile, investments have been made in the creation of zero-emission systems and their business models in Japan, which in turn are producing a variety of recycling frameworks, ranging from small-scale regional systems to large-scale nationwide systems. In particular, systems primarily implemented by materials industries (e.g., the steel, cement and non-ferrous metal smelting industries) are worth noting; they have developed into unique recycling systems.

"The Qualitative Assessment and Analysis of the Contribution of Science and Technology to the National Economy, Society and Life[1]," a survey jointly conducted by the National Institute of Science and Technology Policy (NISTEP) and Mitsubishi Research Institute, Inc. (MRI), suggests that waste-disposal and recycling technologies have a significant impact on the economy and public life. In fact, the public and private sectors have been engaged in joint research programs to develop waste-recycling systems, which have significantly contributed to creating today's technological systems of Japan. Of recycling systems that center on materials industries and individual element technologies, the gasification melting technology has made rapid headway, with the industrial sector playing a leading role in its design and development. The adoption of new environmental regulations and other regulatory measures have also served as an incentive. For example, increasingly stringent regulations on dioxin emissions have prompted the development of gasification melting technology, while government subsidies to municipalities have encouraged the introduction of expensive processes. Support measures including subsidies have thus made an indirect contribution to technological development by plant manufacturers. The gasification melting technology, which was originally imported from abroad, can be considered a technology[2] that has made a great leap forward in Japan[1].

2 Status of zero emission initiatives at home and abroad

Terms referring to “zero emission business models” vary from country to country. The “Eco Industrial Park (EIP)” is one. The President’s Council for Sustainable Development (PCSD) of the U.S. defines EIP as follows:

“EIP is a community composed of companies in the manufacturing and service industries, each of which pursue common interests and maximize its individual profits by jointly managing resources such as the environment, energy, water and other materials. EIP is designed to improve the economic performance of its member companies, while minimizing their environmental load.” With PCSD established, the US government decided to promote EIP projects on nationwide scale, designating four EIP demonstration sites. In addition, an initiative for eco-friendly regional development is underway in more than 10 sites across the country[3]. Table 1 shows frequently quoted examples of overseas EIP projects. An overview of the Kalundborg project, a typical EIP project, is shown in Figure 1.

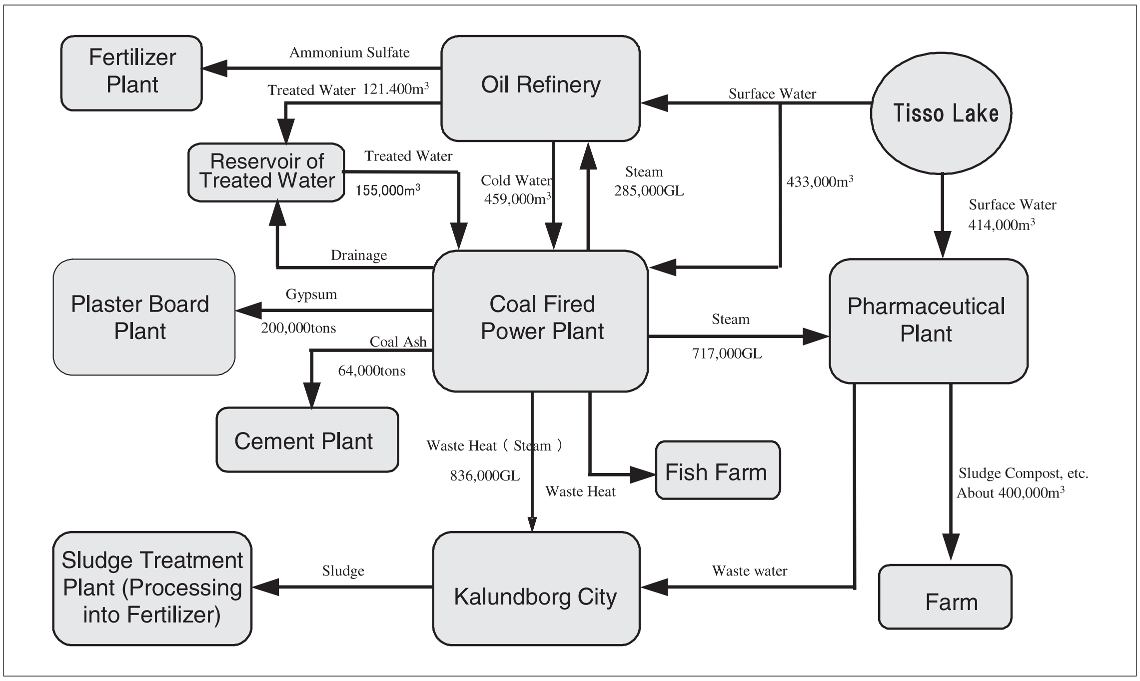
In line with the “zero emission” concept, meanwhile, several zero emission industrial parks have already been set up in Japan, with more awaiting development. The government subsidizes the construction of zero emission facilities in a total of 18 “eco towns” designated as of April 2003[4]. Figure 2[5] shows the areas

Table 1 : Overseas zero emission systems

Location	Overview
Kalundborg (Denmark)	A municipality and five major companies in the fields of power generation, plaster board, pharmaceuticals, oil refining and soil improvement form a network, through which each member company utilizes waste generated by other companies. The system was launched about 30 years ago, and 19 projects are currently underway.
Fairfield Ecological Business Park (US)	Industrial and municipal waste is recycled within the region, e.g., sludge from sewage treatment plants is processed into compost, parts from scrapped cars are recycled, and food residual is processed into feed.
Gulf of Mexico (Mexico)	A total of 21 companies are discussing the reciprocal trade of their byproducts, e.g., the recycling of steel slag as cement materials and the reuse of auto shredder residual by steel plants.
Montreal (Canada)	A total of 15 companies are discussing the reciprocal trade of their byproducts, e.g., the reuse of caustic soda and sodium sulfate by paper mills.

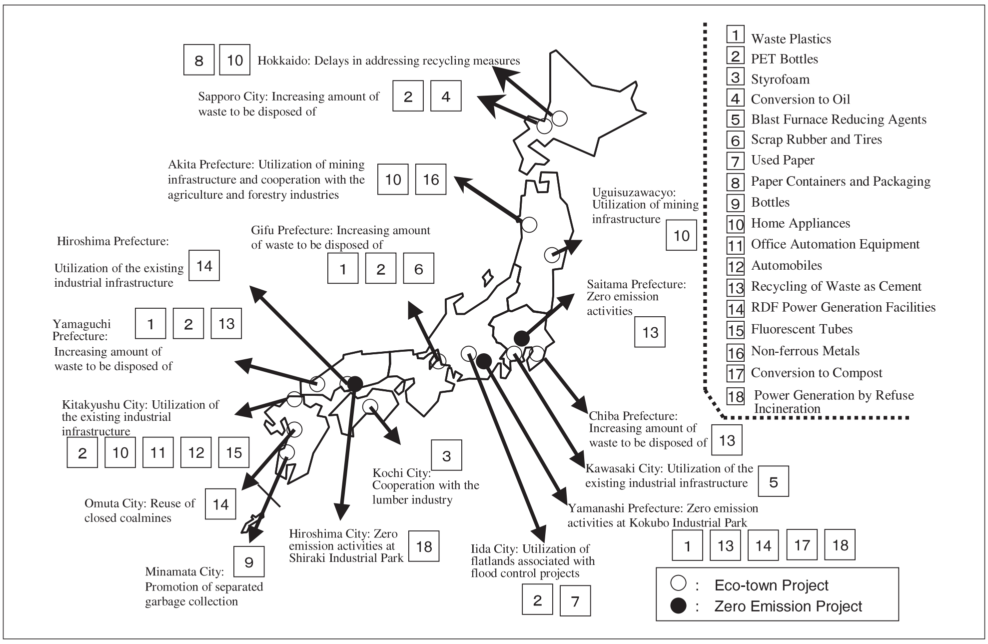
Source: Website of each project, etc.

Figure 1 : Industrial symbiosis at Kalundborg



John R.Ehrenfeld and Marian R.Chertow 2001

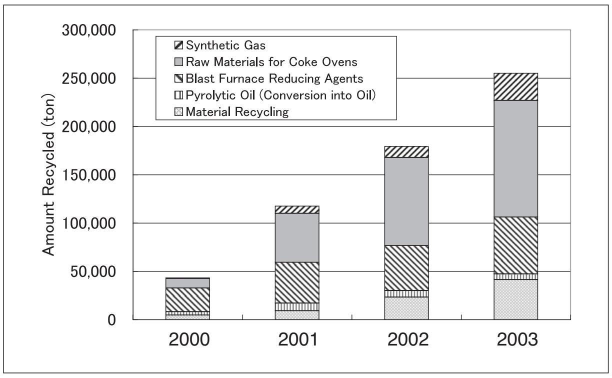
Figure 2 : “Zero emission” regional recycling projects (as of 2001)



Source: Report prepared by the National Institute for Environment Studies (The 2002 Research on the Global Environment)

designated as “eco towns” and regional zero emission projects coordinated by municipalities. In terms of relevance to the subject of this article (namely, materials industries), non-ferrous metal smelting operation in Akita Prefecture and systems that center on cement production in Saitama Prefecture, etc. merit particular attention.

Figure 3 : Amount of packaging plastics recycled[5]



3 Status of the creation zero emission systems in materials industries

3-1 The steel industry

While steel manufactures have contributed to recycling initiatives as users (electric furnace maker) of iron and steel scrap, they are now branching out into the recycling of plastic materials in response to the enforcement of the Packaging Recycling Law, an eye-opening trend. Figure 3[6] shows the amount of packaging plastics (i.e., plastics other than PET bottles, which municipalities recovered in compliance with the law) recycled as of fiscal 2003. About 70% of the packaging plastics recycled (250,000tons) in fiscal 2003 are attributable to the steel industry, which use them as fuel for coke ovens and blast furnaces. The steel industry has an annual capacity to recycle about five million tons of waste plastics[7] (the total amount of waste plastics is estimated at 10 million tons a year, almost half of which is currently disposed of).

In instituting the law, “material recycling” and the “conversion of waste plastics into oil” were prioritized over other alternatives on technological grounds. The recycling of waste plastics by the steel industry, however, turned out to be “feedstock recycling.” Because of its technological credibility and capacity to recycle waste plastics, it did not take long before the steel industry took center stage in waste plastic recycling. By contrast, the conversion of waste plastics into oil, which was initially considered a promising alternative, has found limited applications to date.

Recycling packaging plastics has yet to be implemented in other countries except Germany, where they are recycled as blast furnace reducing agents in compliance with the directives relevant to packaging recycling.

3-2 The cement industry

The cement industry has been a major user of a variety of waste and byproducts (coal ash, waste oil, reclaimed oil, scrap tires, slag, byproduct gypsum, etc.), which are used as raw materials or fuel for cement production. The unit consumption of waste and byproducts in cement production increased from 295 kg/ton in 1998 to 361 kg/ton in 2002[8]; it is expected to reach 400 kg/ton in 2010. Table 2[9] shows the breakdown of waste and byproducts by source and descriptions, and Table 3[9], the actual amount of waste and byproducts recycled in recent years. As these charts suggest, large-scale cement plants have the potential to quickly change the waste stream in the areas in which they operate. The industry's recent recycling efforts include "eco cement," which uses ash from municipal waste incinerators as raw materials. The cement industry stands prepared to use other waste materials such as used pachinko machines, garbage and hazardous waste (polluted soil, specified CFCs, etc.). Indeed, a new plan is underway to use a massive amount of illegally dumped waste found on the border between Aomori Prefecture and Iwate Prefecture. Japan leads the world in the co-incineration of waste in cement kilns (in terms of the scale of operations and the proportion of received waste in its total production), a recycling effort that is attracting

Table 2 : Sources and descriptions of waste and byproducts recycled by the cement industry[8]

Sector	Source (Industries, Facilities)	Descriptions of Waste and Byproducts	Usage in Cement Production
Private Businesses	Steel	Blast Furnace Slag (Granulated), Blast Furnace Slag (Slow Cooled), Flay Ash	Raw materials/Admixtures
	Electricity	Coal Ash, Waste Crude Oil Flue Gas Desulfurization Gypsum	Raw materials /Fuels/Admixtures
			Admixtures
	Non-ferrous Metal	Slag, Sludge, Foundry Sand, Gypsum	Raw materials/Admixtures
	Chemical	Waste Plastics, Gypsum, Sludge	Raw materials/Fuels/Admixtures
	Automobile	Foundry Sand, Paint Residue, Scrap Tires	Raw materials/Fuels
	Oil	Waste Clay, Waste Oil, Waste Catalysts, Sludge, Oil Coke	Raw materials /Fuels
	Construction	Waste Gypsum, Boards, Tatami Mats	Raw materials
	Construction Material	Board Chips, Sludge	Raw materials
	Paper & Pulp	Sludge, Ash	Raw materials
	Printing	Waste Plastics, Ash	Raw materials /Fuels
	Agriculture	Waste Plastics	Fuels
	Fisheries	Shells, Entrails	Raw materials /Fuels
	Food	Waste China Clay, Waste Plastics, Distilled Spirit, Deposits, Coffee Sludge, Brewer Grain, Waste Juice	Raw materials /Fuels
	Electronics & Electric	Waste Plastics, Waste Toner, Sludge, CFCs	Raw materials / Fuels /degradation processing
	Leisure	Used Pachinko Machines	Raw materials /Fuels
Municipalities	Water Treatment Plants	Sludge Derived from Water Treatment	Raw materials
	Sewage Treatment Plants	Sewage Sludge	Raw materials /Fuels
	Refuse Incineration Plants	Ash, Soot and Dust	Raw materials
	Other	Municipal Waste (Garbage), CFCs	Raw materials/Fuels
			Degradation processing

attention at home and abroad.

3-3 Non-ferrous metal smelting industry

The non-ferrous metal smelting industry could be another major user of waste in the future. The industry, which has been recycling car batteries, is beginning to use a variety of waste materials including metal resources, e.g., automobile shredder residue (ASR) generated in the course of car recycling, the circuit boards of used home appliances, and fly ash from municipal waste melting plants. Figure 4[10] shows the breakdown of waste materials received by 10 major waste-disposal and recycling companies; the first pie chart represents waste purchased as recyclable materials, while the other represents waste collected at cost to its producers. As these charts show, the industry is using various waste materials including metal resources to recover copper, lead, zinc, precious metals (gold, silver, platinum), etc.

A comparison with the results in fiscal 1999 reveals that the amount of recyclable materials was stable, while that of waste materials collected for intermediate treatment increased by more than 30%[10]. Specifically, ASR increased due to tightened landfill regulations for ASR (1996), and so did used home appliances (printed circuit boards, flint glass, etc.), with the Home Appliance Recycling Law in place. Sludge and contaminated soil also showed an upturn. Incidentally, a non-ferrous metal smelting plant of the “eco-town” project in Akita Prefecture is a “designated recycling plant” under the Home Appliance Recycling Law, serving as a recycling hub of waste home appliances in the Tohoku region.

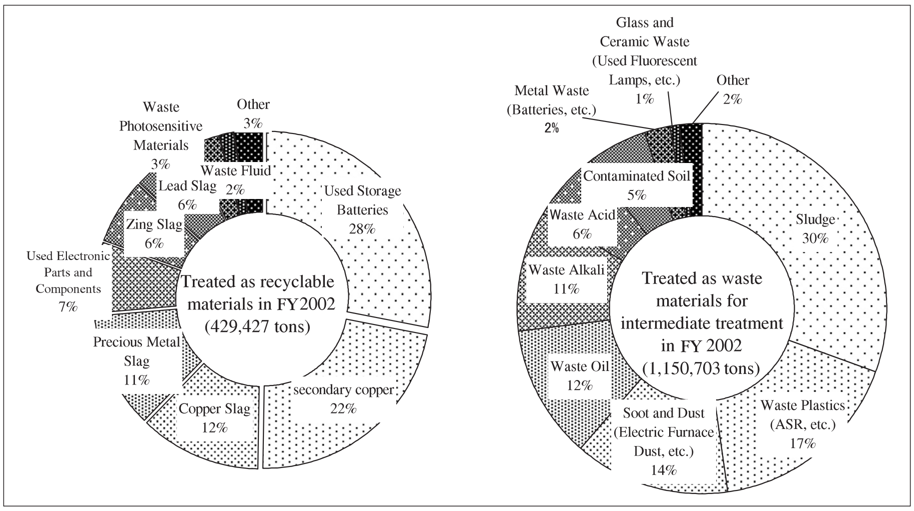
Table 3 : Amount of waste and byproducts recycled by the cement industry[8]

	FY2000	FY2001	FY2002
Blast Furnace Slug	12,162	11,915	10,474
Coal Ash	5,145	5,822	6,320
Byproduct Gypsum	2,643	2,568	2,556
Sludge	1,906	2,235	2,286
Non-ferrous Slag	1,500	1,236	1,039
Steel Making Slag	795	935	803
Burnt Residue, Soot and Dust	734	943	874
Slag Heap	675	574	522
Foundry Sand	477	492	507
Scrap Tires	323	284	253
Reclaimed Oil	239	204	252
Waste Oil	120	149	100
Waste China Clay	106	82	97
Waste Plastics	102	171	211
Other	433	450	942
Total	27,359	28,061	27,238
Total Cement Production	82,373	79,119	75,479
Unit Consumption	332	355	361

Unit: 1,000 tons for waste, byproducts and cement production; kg/ton for unit consumption

Source: Cement Handbook

Figure 4 : Recycling of waste, etc. by the non-ferrous metal smelting industry (FY2002)



4 Japanese state-of-the-art zero emission systems

4-1 Economic advantages

One of the reasons that zero emission systems have developed so extensively in materials industries lies in their substantial contribution to reducing initial investment by taking advantage of existing facilities such as blast furnaces, cement kilns and non-ferrous metal smelting furnaces. The waste disposal licensing system, through which waste disposal fees can be charged, has also served as an incentive. Previously, a number of constraints (the need to obtain a license in accordance with the Waste Management Law, etc.) hampered the recycling and treatment of waste materials, sometimes forcing materials manufacturers to purchase waste as “raw materials.” With the licensing system in place, however, waste disposal has become a profitable business. While the production of and demand for industrial materials are declining, materials industries appear to be shifting from being “arterial industries” that produce industrial materials to “venous industries” that recover waste materials.

In addition, government support measures including subsidies are playing a part in promoting zero emission systems. In particular, the Ministry of Health, Labor and Welfare, the Ministry of Economy, Trade and Industry, the Ministry of Education, Culture, Sports, Science and Technology and the Ministry of Environment provided research and development funds to materials manufacturers in the 1990s when grave problems such as dioxin treatment and the final disposal of waste materials loomed large[1], to expand the category of waste, produce high-quality slag, and improve power generation efficiency. Recycling facilities to be set up in designated “eco-towns” are also subsidized, an arrangement that encourages the construction of new facilities.

4-2 Effects of individual recycling laws

A series of recycling laws instituted or to be instituted in response to Extended Producer Responsibility (the Packaging Recycling Law, the Home Appliance Recycling Law, the Construction material Recycling Law, the Food Recycling Law and the Automobile Recycling Law) are also essential in establishing the current zero emission systems. Of packaging plastics recovered by municipalities in accordance with the Packaging Recycling Law, a major part of “other plastics” (excluding PET bottles) is recycled as blast furnace reducing agents and coke materials. With the Home Appliance Recycling Law in place, meanwhile, an increasing amount of circuit boards and other waste materials are recycled by non-ferrous metal smelting plants, regardless of whether they are designated as “recycling plants” or not under the law. The Automobile Recycling Law and the Construction Material Recycling Law are expected to promote the recycling of ASR, with the latter recycled as wood chips for paper manufacturing. As mentioned earlier, the cement industry is no exception to this trend, recycling scrap tires and wood voluntarily, not under specific recycling laws.

The existing recycling laws mandate the recycling of waste materials, while specific laws such as the Packaging Recycling Law and the Home Appliance Recycling Law stipulate that manufacturers and waste producers bear the costs of recycling, which together constitute a system that ensures reasonable profits for those involved in the recycling business.

4-3 Technological factors: technological credibility and great potential for recycling

Both industrial materials production and waste disposal involve high-temperature processes (above 1,000 degrees Celsius), which is the reason that waste disposal has developed so extensively through the zero emission systems of materials industries. With their proven high-temperature processes and advanced emission control systems, materials industries ensure the safe disposal of waste materials with varying properties, some of which contain hazardous substances, a great advantage in waste recycling.

Another advantage is the capacity to recycle waste; they have the potential to consume a massive amount of waste materials, with their industrial processes fully utilized on a nationwide basis.

5 Direction of research and development in zero emission systems and dissemination of Japanese models

Zero emission systems centering on materials industries, however, have yet to contribute to waste disposal in other countries, although some pilot projects are underway. Japan leads the world in terms of the amount and variety of waste recycled through the systems. Indeed, Japanese zero emission systems are yielding practical results, materials industries being the driving force. This is a noteworthy trend that suggests the possibility of their being business models applicable to other countries.

In order to further develop such Japanese business models, new recycling technologies should be developed (in addition to waste recycling through existing industrial processes) by incorporating some sort of qualitative conversion processes. The following section provides two excellent examples of such processes: the waste melting process, and the process of gasifying and recycling waste plastics as chemical raw materials

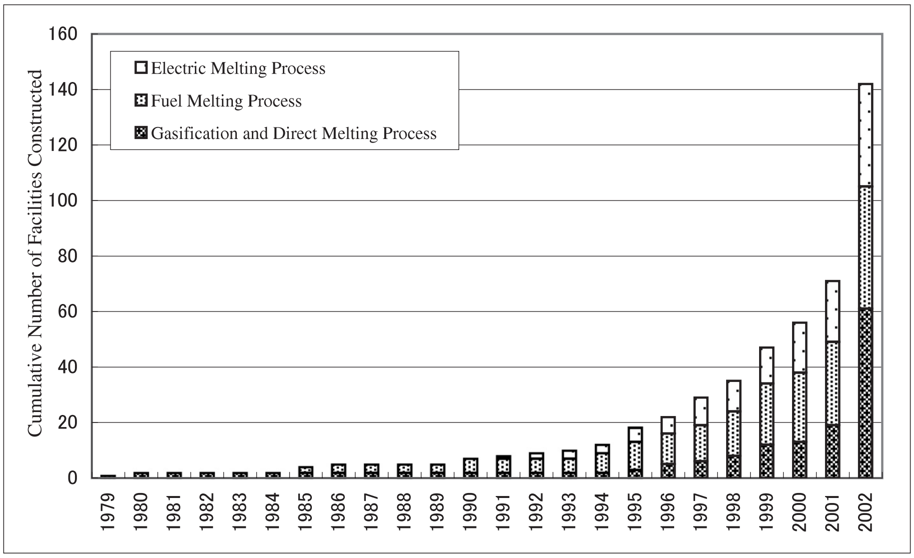
5-1 Coupling of waste melting process and non-ferrous metal smelting process[12]

The non-ferrous metal smelting industry is recycling an increasing amount of fly ash originating from municipal waste melting furnaces. The fly ash, which usually contains high concentrations of copper, lead, zinc, etc, can be recycled as quality raw materials. This coupling of materials industries and the waste melting process is unique to Japan, and hence could be a Japanese model applicable to many other countries.

Waste melting furnaces, which have contributed significantly to establishing this system, are increasing in number because of dioxin issues and a shortage of landfill space, with the Law Concerning Special Measures against Dioxins and incentives such as government subsidies playing a major role. Figure 5[11] shows the number of melting furnaces constructed in the past, which doubled year-on-year in 2002 in response to the full-scale implementation of measures against dioxins in December 2002.

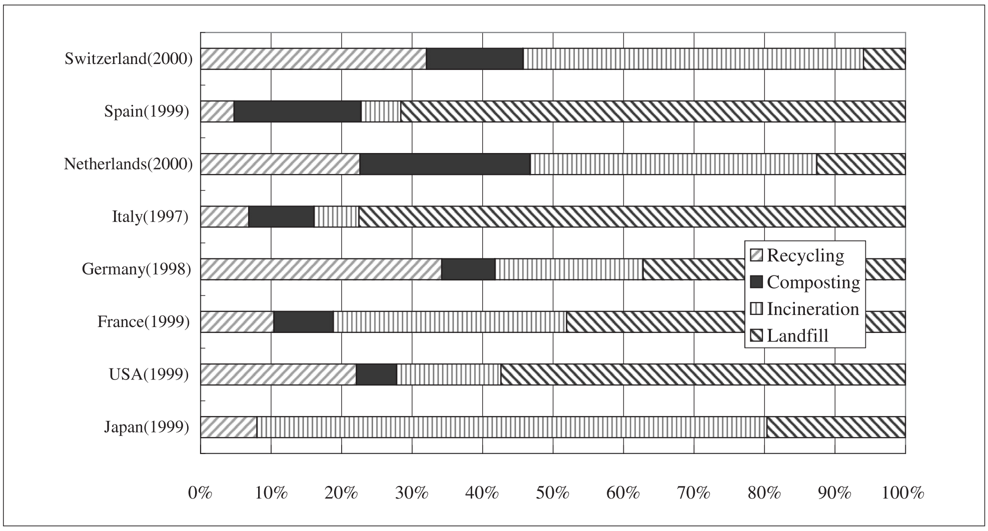
This situation is unique to Japan. Figure 6[12] shows the status of municipal waste disposal in major countries. Although the data is somewhat out of date, it shows a general trend where countries with limited land opt for incineration and recycling to minimize landfill. This is

Figure 5 : Number of melting furnaces constructed[11]



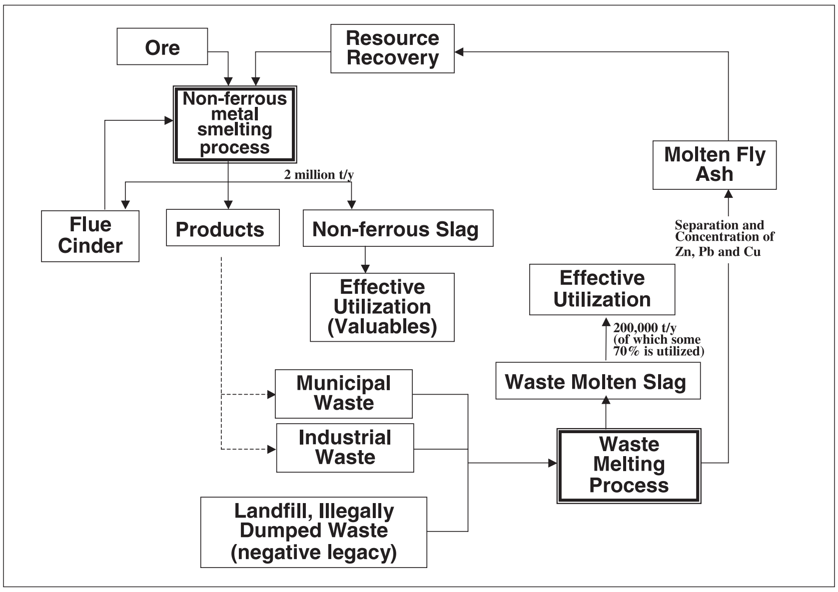
Source: A survey conducted by the National Institute for Environmental Studies in 2003

Figure6 : Municipal waste disposal in major countries



Source: OECD Environmental Data Compendium 2002

Figure 7 : Zero emission system combining the waste melting process with the non-ferrous metal smelting process



particularly true in Japan where as much as 40 million tons of waste is incinerated a year, the world's largest amount. With this situation as a backdrop, the waste melting process is increasingly popular in Japan. While many related technologies were first introduced from Europe, Japan now leads the world in the quality of its waste melting system as well as in its expertise in operating the system. Two waste melting systems are in place: an ash melting system where electric or fuel furnaces melt the ash from waste combustion, and a gasification melting system where waste is gasified for melting purposes. The development of the latter has been a subject of competition across the world, and Japan predominates in the number of gasification melting facilities in operation[13]. In fact, plant construction companies in Japan invest rather excessively in the research and development of the gasification melting process, boasting one of the best technological resources in this particular field.

Figure 7 shows the process of a system in place. The waste melting process, originally designed for waste disposal, also functions as a process for separating and concentrating metals. It is thus considered a qualitative conversion technology that establishes linkage with the non-ferrous metal smelting process. What is particularly intriguing in this chart is the way metals are recycled; buried municipal waste is recovered to extend landfill life and then fed to melting furnaces to produce slag and fly ash. The Ministry of Environment subsidizes facilities adopting this system, which is in a way an attempt to eliminate the "negative legacy of the past," promoting the recycling of metal resources in the years to come. With this system fully developed, waste landfill sites could turn into "urban mines" for the non-ferrous metal smelting industry.

A massive amount of industrial waste illegally dumped on the island of Teshima is now being recovered and disposed of at melting facilities set up on an adjacent island (Naoshima), fly ash from which is being recycled at a non-ferrous metal smelting plant located nearby. This process also deserves attention as a means to incorporate the "negative legacy" into the recycling of metal resources.

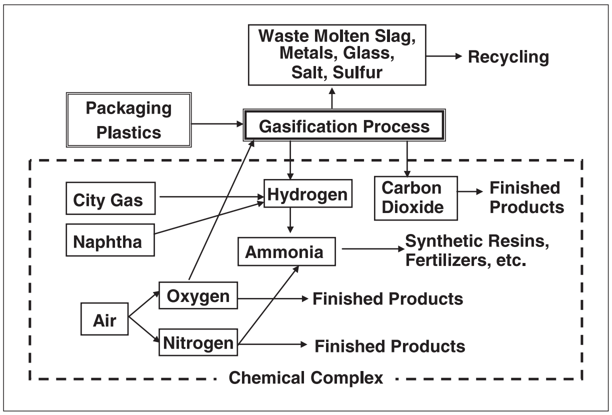
The disposal of municipal waste has a solid management base, as it is part of the public services. For municipalities, meanwhile, it makes economic sense to have the non-ferrous metal smelting industry recycle fly ash from the melting furnace, previously disposed of at landfill sites, even at their cost, which is a win-win arrangement since the industry is entitled to charge disposal fees.

In most countries, domestic waste containing a variety of materials is handled and disposed of by municipalities, many of which opt for landfill. The EU Landfill Directive, however, banned waste disposal at landfill sites, except for waste converted into inorganic forms through treatment such as incineration, a measure to extend landfill life in EU member states with limited land. While the recent movement in European countries towards recycling waste materials is irreversible, they appear to have no other options but to promote waste incineration, as is the case in Japan. The Japanese zero emission system shown in Figure 7, therefore, has the potential to be a model system that is compatible with the waste management policies of European countries.

5-2 Coupling of chemical complexes and the process of gasifying waste plastics to produce chemical raw materials

Another qualitative conversion alternative concerns the coupling between chemical complexes and the process of gasifying waste plastics to produce chemical raw materials. Figure 8 shows an outline of this system, i.e., packaging plastics are gasified to recover hydrogen, which is then fed to chemical complexes to produce ammonia, etc. Chemical complexes separate oxygen and nitrogen, which are base materials for various products, from the air, using some of the oxygen for the gasification process, and the nitrogen for producing ammonia by reaction with hydrogen derived from the process. Ammonia is used to produce items such as synthetic fibers and chemical fertilizers. The byproducts of the process (slag, metals, glass, salt, sulfur, etc.) are also recycled. In this case, the gasification process functions as a qualitative conversion process that establishes a linkage with chemical complexes.

Figure 8 : Zero emission system combining the gasification process of packaging plastics with chemical complexes



Source: Brochure of Showa Denko K.K.

The gasification process developed rapidly, accounting for some 10% of the total amount of packaging materials recycled in 2002 (see Figure 3), with a waste supply and profits ensured by the Packaging Recycling Law. Subsidies for gasification facilities to be constructed in designated "eco towns" has also worked as a great incentive.

These two systems are designed to recycle mixed waste materials with complex properties at existing industrial facilities through qualitative conversion processes (based on pyrolysis gasification and melting technologies); they are expected to be the main alternatives in creating zero emission systems in the future. The process shown in Figure 8 can be applied not only to waste plastics but also to other types of mixed waste materials (biomass, etc.) that can be gasified. Indeed, commercial facilities are already in operation in Chiba Prefecture, and setting up new facilities in Mizushima is planned. While the development of the process of gasifying waste plastics to produce chemical raw materials is attracting attention worldwide, Japan has a proven record in its commercial operation[13].

The major factors in the development of the two systems are: a stable waste supply ensured by laws and regulations; disposal fees chargeable to waste producers; engagement of the public sector; subsidies for the construction of new facilities, which solidify the management bases of waste-disposal and recycling companies. The socioeconomic system supporting these systems, coupled with the technologies involved, could be a Japanese model applicable to other countries. In particular, waste management is likely to be a major concern for East Asian countries including China, whose infrastructures and materials industries are rapidly developing. The Japanese models introduced in this article have the potential to become widespread in these countries, assuming that they adopt and enforce the appropriate environmental regulations.

6

Towards the creation of Japanese zero emission systems

The original concept of "zero emission systems" is to create chains (linkages) among various industries. The Japanese zero emission systems that center on materials industries are virtually hub-based systems creating linkages between materials industries and other industries. As is the case with ecosystems, a loss of diversity may undermine these zero emission systems. In other words, the systems may fail once materials industries are unable to accept waste materials. Japanese zero emission systems, however, are expected to remain stable over the short and medium term as they are supported by legislation and have substantial economic advantages, as mentioned earlier.

In the meantime, over-emphasis on recycling efforts seems to have created blind spots in the systems. The aspect of "safety and security," namely the safety of products originating from zero emission processes is one. Specifically, the safety standards for recycled cement (produced in kilns using waste as raw materials) and byproduct slag (originating from the non-ferrous metal smelting process) could become a bottleneck when discussed on the grounds of environmental JIS and the criteria for specified goods under the Green Purchasing Law because conservative substances (heavy metals, etc.) derived from waste materials may remain or accumulate in products. In the non-ferrous metal smelting process, for example, impurities such as hazardous metals concentrate in slag as the purity of the finished product increases. Being commercial items, non-ferrous slag has been exempt from the Waste Management Law, and hence traded as general commodities, safety requirements for which are non-existent. While there has been a growing awareness of the safety of recycled products, the application of the safety standards for waste materials to recycled products could change what have been considered "products" to "waste," resulting in a situation where industrial plants can no longer recycle waste in their production processes.

A systematic concept of the safety standards for general commodities, recycled products and waste materials should thus be created immediately so that they are recognized and accepted by society, including consumers. To disseminate Japanese business models to the world, moreover, the systematization of these safety standards needs to be discussed in the context of harmonizing international standards. The topics mentioned above are the biggest challenge in establishing Japanese zero emission systems.

Whether to prioritize "reducing," "reusing" or "recycling," and whether to prioritize "recycling" or "material recycling," should also be rationally discussed, taking into account the life cycle of each practice.

Whatever the case, Japanese zero emission systems, which are linked with the hub-based processes of materials industries through the qualitative conversion of waste materials, as well as socioeconomic conditions that support the systems and their element technologies (new qualitative conversion alternatives including pyrolysis gasification and melting technologies), could be exemplary models of industrial systems, if all the challenges are properly met. It is thus recommended that the government promote research and development activities and encourage technological transfer in the field of “zero emission,” focusing on the global market.

Acknowledgements

We would like to thank everyone who provided invaluable support in creating this article, particularly Mr. Kenji Takahashi (manager of the Environmental Technology Division, the Planning Department, Takuma Co., Ltd.), Mr. Seiichi Abe (director of the Recycle Engineering Division, Kubota Corporation) and Mr. Kanehiro Monzen (The Japan Mining Industry Association).

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9

Structure Maintenance Technology and Risk Based Maintenance (RBM)

SHIGEMITSU KIHARA *(Affiliated Fellow)*

1 Background

In Japan, confidence in safety has been shaken recently by events such as the occurrence of major industrial accidents and the falsification of inspection records. As a mature society, Japan possesses a vast amount of social and industrial infrastructure assets. The time has come for such assets to be carefully maintained and utilized. Under these circumstances, the urgent tasks are a detailed analysis of the reasons for the outbreak of numerous problems despite Japan's strict regulations and the preparation of maintenance technology to keep a safe and secure society.

The deterioration of the structures that comprise the social and industrial infrastructure, declining numbers of preservation-related engineers, inadequate transmission of techniques to new generations, and outdated regulations have been pointed out as causes of problems such as those mentioned above. At the same time, increasingly harsh international competition necessitates cost cutting and efficient plant operation in all manufacturing industries. In other words, it is extremely important that technologies be developed, personnel be trained, and policies be prepared to maintain aging facilities at low cost without compromising safety.

Under these circumstances, recently attention is being paid to the maintenance management method called "risk based maintenance" (RBM), which began in Europe and the USA and utilizes risk (the probability of failure multiplied by the amount of consequence that would be caused by failure) as its standard. Under the RBM method, risk is quantified in order to determine priority for maintenance. Because it reduces unnecessary inspections and prioritizes investment where risk is greater, it is a highly rational method. Since a safe and secure society can be defined as one in which the risk to any structure is below a acceptable level, it is expected that RBM will be established in Japan as well.

In addition, because extending the longevity of social and industrial infrastructure will bring about a massive reduction in garbage, establishing methods for the long-term, safe utilization of existing infrastructure is an urgent task from the point of view of environmental protection as well.

2 The current state of technology related to structure maintenance

Most existing structures utilize concrete and steel as their primary materials. To state the concept another way, a structure that is operated safely is one that is operated without breaking down. When structures fail during use, they do so according to the specific fracture mechanisms of concrete and steel. We have a long history of utilizing those structural materials and many cases of their failure, so it is correct to say that their fracture mechanisms are fully understood.

2-1 Fracture mechanisms

Below I will describe the known fracture mechanisms of concrete and steel.

(1) Concrete fracture

Concrete fracture during use occurs through the mechanisms shown in Table 1, when its

Table 1 : Overview of concrete deterioration mechanisms

Deterioration mechanism	Overview
Carbonation	Concrete bonding declines mainly through the penetration of atmospheric carbon dioxide and rain, causing rebar corrosion and generating cracks in the concrete through expanding rust.
Salt injury	Chloride ions from salt water, etc., penetrate the concrete, causing rebar corrosion and generating cracks in the concrete through expanding rust.
Frost damage	The freezing of moisture within the concrete causes expansion, generating cracks.
Alkali aggregate reaction	If chloride ions are included at the time of manufacture (through use of sea sand, etc.), they react with the aggregate over time, decreasing concrete bonding, causing rebar corrosion, and generating cracks in the concrete through expanding rust.
Chemical erosion	When used in environments where the concrete contacts chemicals, penetration of corrosive materials causes decreased concrete strength and rebar corrosion.
Fatigue	Repeated loads generate cracks in the concrete.

Table 2 : Overview of steel fracture mechanisms

Fracture mechanism		Overview
Fatigue		Loads that would not cause fractures if they were static can bring about fractures if they are repeated. This is called “fatigue fracture.” Because fatigue will not occur below a certain level of stress (the fatigue limit) , designs ordinarily are made under the stress that would bring about fatigue. However, unexpected concentrated stresses and so on may cause fatigue. This is the most common of the fracture mechanisms for ferrous materials.
Corrosion	General Corrosion	A uniform surface is contacted by a uniform corrosive agent (chemicals, etc.) and corrosion proceeds uniformly (thinning phenomenon), so corrosion is easy to detect.
	Local corrosion (pitting)	Corrosion proceeds locally through discontinuity in surface shape, non-uniform flow of corrosive agents, etc., so corrosion towards the depth (pitting) is swift. Detection is difficult.
	Stress corrosion cracking (SCC)	Corrosion proceeds in the form of cracks under stress, so cracks develop swiftly. This is the most dangerous corrosion phenomenon. SCC of stainless steel under chloride ions is the best-known type.
Creep		Metal materials that will not distort or fracture under load conditions at normal temperature will distort and fracture over time when above certain temperatures. This is called “creep” (or “creep fracture”).
Brittle fractures and corrosion damage caused by deterioration characteristic of materials		At high temperature, the atoms of metal materials move, causing structural changes and degrading the characteristics of the material. After material characteristics have been degraded, fractures may occur even under use conditions met until that point. For example: • Brittle fracture through degraded toughness (tempering, creep embrittlement, 475°C embrittlement, sigma phase embrittlement) following use at high temperature for a specific period. • Corrosion damage through degradation of corrosion resistance (sensitizing, etc.).

strength declines (deteriorates) and it breaks down or flakes under the cyclic load, impact, or earthquake.

(2) Steel fracture

Fracture during use of steel occurs as shown in Table 2.

2-2 Life prediction

Regarding known fracture mechanisms, if fractures can be predicted (when and where they will occur), safe operation is possible. Research and development has been carried out on technology for predicting life based on each type of fracture mechanism.

Among the fracture mechanisms of concrete and steel, prediction (life assessment) of creep for steel is the most advanced. Because creep is inevitable in boilers, turbines, and other equipment used at high temperatures, they are designed to permit it. Life assessments are continually performed while they are in use, thus making life assessment technology indispensable. Life prediction research regarding creep fracture is thus the most advanced. On the other hand, designs attempt to avoid fatigue and corrosion, and research emphasis is placed on methods to prevent their initiation. Life assessment methods regarding fatigue and corrosion are therefore not sufficiently established.

Below I will describe an example of creep life assessment for heating tubes in fossil-fuel power generation boilers. Figure 1 shows the progress of deformation (creep curve) over time of steel boiler tube under a fixed load at high temperature, finally resulting in rupture. The photographs in the chart show the internal structural changes of the materials as creep deformation progresses. Life prediction is to learn what stage of its entire life a member has reached by non-destructive methods. The chart shows how measuring the amount of distortion and the degree of structural change in the steel boiler tube enables us to know its position in its life cycle. Although direct measurement of the amount and degree of distortion of a steel tube is impossible except in special cases, the tube’s surface can be ground to observe structural change and ultrasonic can be used to detect voids and microcracks. Methods to assess the life of steel boiler tubes through other parameters (material hardness, precipitation characteristics, electric resistance, etc.) are currently being developed. The Ministry of Economy, Trade and Industry’s guidelines for extending the time between periodic inspection of boilers suggests that the inspection period may be extended from two years to four years if detailed prediction through any of the methods shown in Figure 2 confirm sufficient life.

Figure 1 : Schematic of development of creep damage in Cr-Mo steel

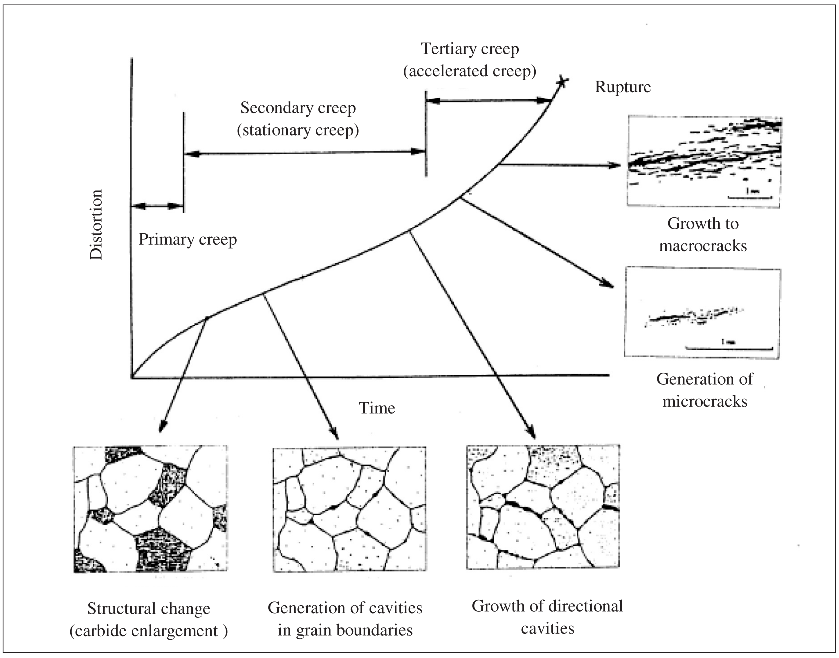


Figure 2 : Non-destructive creep damage assessment methods indicated by guidelines

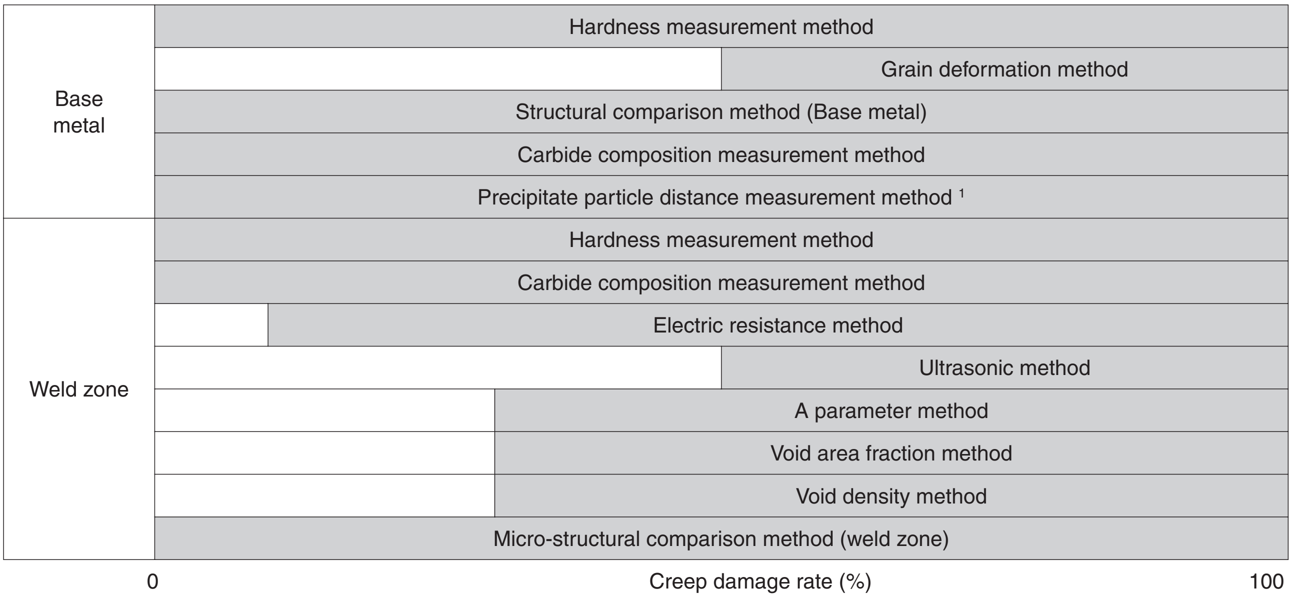
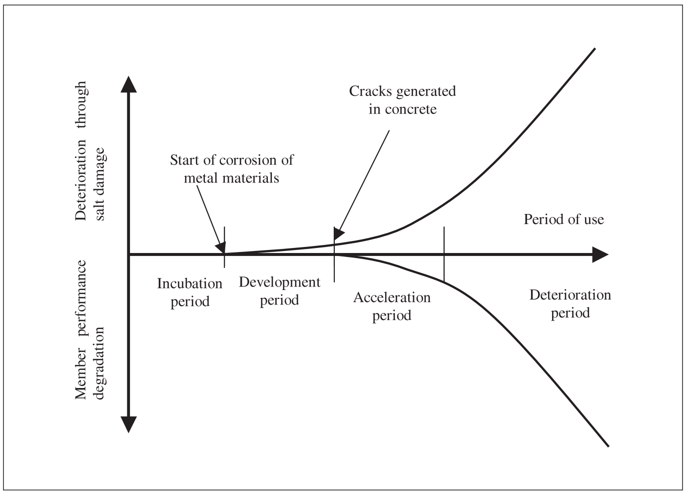


Figure 3 : Model of the process of deterioration due to salt injury



Fossil-fuel power generation boilers are the most advanced example of the use of life assessment methods for preservation and the rational extension of life. Life diagnosis for steel structures in general is quite advanced, but it is desirable that rational preservation be implemented in all social and industrial infrastructure through the establishment of life assessment policies.

Concrete structures are designed with a higher safety factor than steel structures, and with the exception of earthquakes, there are no cases of failure due to deterioration under normal use. Because there is therefore little need for life assessment, research remains inadequate. Figure 3[1] provides a schematic of the process of deterioration through salt injury. The deterioration process is understood qualitatively, but a method to measure the degree of deterioration has yet to be developed. With the number of concrete structures 50 years of age or older to increase in the near future, research and development on life prediction technology is greatly needed.

2-3 Non-technical issues

(1) Human resources responsible for preservation

Safe operation has been made possible by skilled engineers working in design and maintenance. During the period of high economic growth in Japan in the latter half of 1960s, there was a boom in the construction of all types of plants. Many outstanding engineers were involved in their construction, gaining valuable on-site knowledge and experience. Subsequently, they engaged in the maintenance of those plants and supported their safe operation as experts. In research as well, building materials research reached its peak in the 1970s, with many researchers engaged not only in materials development but also research on the fracture mechanisms mentioned above. That led to progress both in explaining mechanisms and in the development of prediction technologies. In recent years, however, plant construction has declined drastically and construction materials development has plateaued. On-site engineers lack opportunities to gain experience, and structural materials research is very quiet. Furthermore, advancing computer measurement and control are leading to the rationalization of sites, and the number of maintenance engineers is declining.

(2) Globalization

In the past, all Japanese social and industrial infrastructure has been designed and built in Japan using domestically manufactured materials. In recent years, however, as the wave of globalization has overtaken Japan, the introduction of foreign products (including materials) is advancing. Most products manufactured in Japan have quality near the upper limits of standards, but those manufactured overseas vary much more widely in quality and include some at minimum standards. For Japan, which has been used to uniformly high-quality products, the safe maintenance of variable products requires a new set of responses.

Specifically, establishment of a database of standards and quality for foreign products is desirable.

3 Recent trends in preservation in Japan and abroad

Japan's nuclear power generation facility maintenance standards were implemented in October 2003. In the past, all defects detected through the inspection in power generation facilities were required to be repaired. Under the new maintenance standards, however, the development of defects over a certain amount of time is predicted, and if the degree of degradation of structural strength meets the safety standards the facility can be operated as is. Actual assessment must meet the Codes for Nuclear Power Generation Facilities (Rules on Fitness-for-Service for Nuclear Power Plants) of the Japan Society of Mechanical Engineers. Detailed analysis is required, but in light of the ill effects of repair welding of tiny flaws (generation of residual stress, etc.), the maintenance standards enable more rational and highly reliable maintenance of nuclear power generation facilities.

In light of that trend, risk based maintenance (RBM; see next section for details), a maintenance management method that uses risk (the probability of failure multiplied by the amount of consequence that would be caused by failure) as its standard, is garnering attention[2].

The establishment of RBM methods requires broad-based research and development related to maintenance, and is drawing great interest from industry and academia. The High Pressure Institute of Japan (HPI) began an RBM research committee three years ago. The maintenance subcommittee of the equipment materials committee of the Society of Chemical Engineers, Japan, is studying RBM. The Engineering Advancement Association of Japan (ENAA) has undertaken a two year project of "feasibility study on the development of RBM methods for optimal maintenance of mechanical systems[3]" beginning in 2003 under contract with Foundation System Research & Development Institute of Japan. Beginning in 2004, the ENAA began a government-commissioned project on "development of advanced maintenance systems for extending the life of industrial and social capital structures." In fiscal 2004, the Japan Society for the Promotion of Science established a leadership research and development committee on "risk-based preservation technologies for chemical plants."

Overseas, the American Petroleum Institute (API) published guidelines for risk-based inspection (RBI)[4,5] in oil refineries and promotes the spread of RBI. The American Society of Mechanical Engineers (ASME) also publishes RBI guidelines for various types of plants[6]. Europe as a whole is promoting the RIMAP (Risk Based Inspection and Maintenance Procedure for European Industries) project.

In those ways, interest in RBM is deep in industry, academia, and government in Japan, and in Europe and the United States, organizational research and development is progressing.

In addition, in October 2003 Japan Society of Maintenology was formed with Professor Miya of Keio University as Chair by users of preservation technology mainly in nuclear power plants. In 2001, the National Institute for Materials Science began a five-year project on "research concerning the development of material risk information platform for safe use of materials." The Japan Science and Technology Agency began its five-year Failure Knowledge Database project in 2001 to gather case studies of failure in various types of plants. The National Institute for Materials Science has been creating data sheets on creep and fatigue for over 30 years, compiling one of the world's best databases.

From the above, we can see that knowledge of the importance of maintenance is now growing in industry, academia, and government, and that Japan's technological potential is sufficiently high in comparison with Europe and the United States.

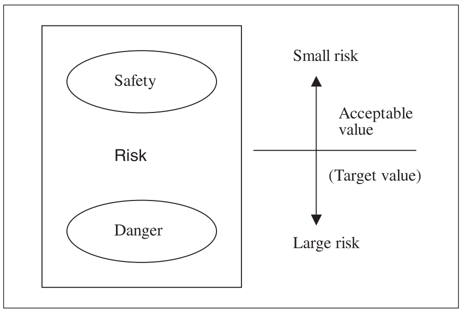
4 Overview of risk based maintenance (RBM)

As shown in Figure 4[7], risk incorporates both safety and danger. When risk is lower, safety is higher; when risk is higher, danger is higher. Until now, absolute safety has been required in Japan, but the line between safety and danger is often obscure. In the concept of risk management, the line between danger and safety is drawn at the level of acceptable risk. People from a variety of fields contribute to the determination of acceptable risk, enabling a broad consensus on danger and safety to be reached. Concretely, risk is expressed as the product of “the probability that failure will occur” and “the amount of consequence that would be caused by the failure.”

The RBM method began in Europe and the United States, and some application of it has begun in Japan as well[8]. The method is rational because it indexes risk and uses it to set maintenance priorities, thus reducing unnecessary inspections and prioritizing investment where risk is high. As mentioned in Section 2, existing technology has elements that can determine where failure is likely (probability), but it is also necessary to determine what damage would be caused by failure. With risk as the standard, emphasis is placed on necessary maintenance, enabling highly reliable maintenance at low cost.

Figure 5 shows an example of the RBM process and necessary development areas. The process is as follows.

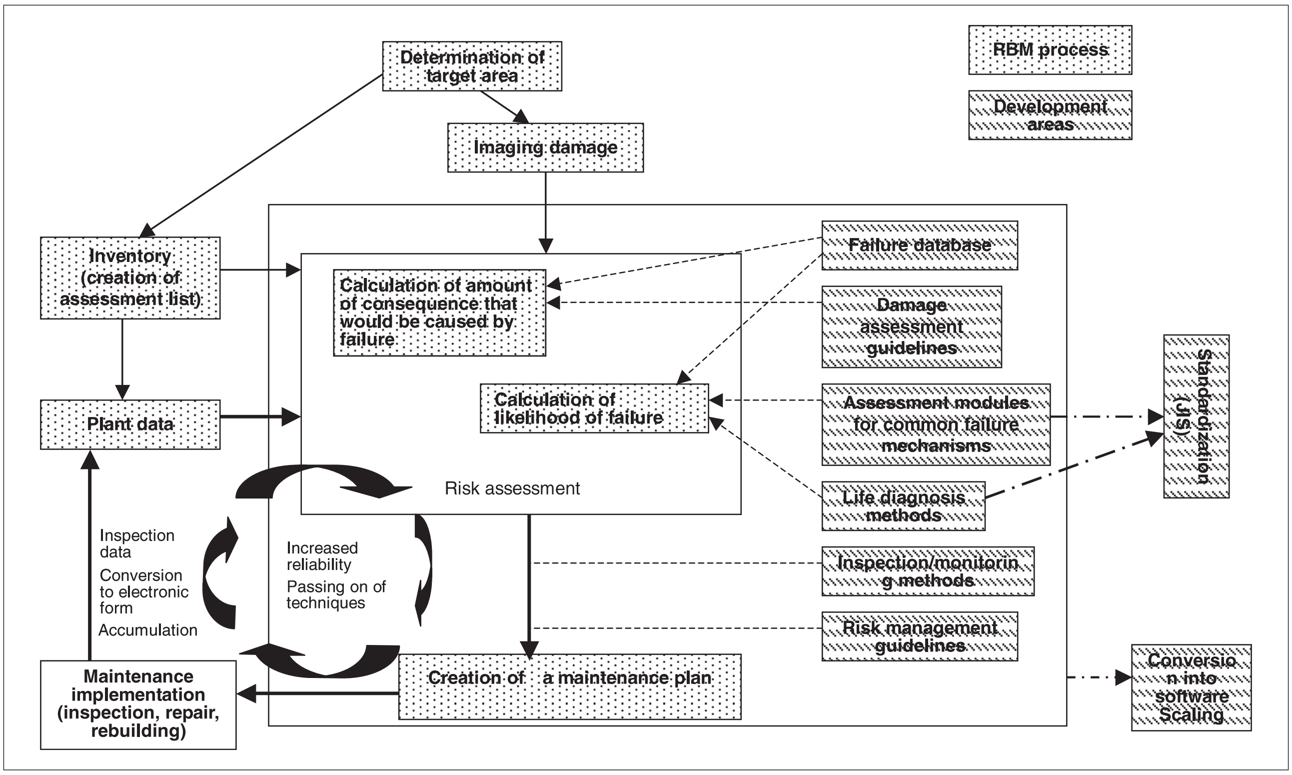
Figure 4 : The concept of “risk”



(1) Preparation

- Determination of target area: determination (by manager) of the extent of RBM application (entire plant, specific equipment, etc.).
- Imaging damage: imaginary of the possible human, economic, and environmental damage that could be caused within the target area.
- Inventory (creation of assessment list): the target area is classified, with the smallest parts to be assessed (assessment units) listed. Failure mechanisms to be concerned with for each part are established.
- Plant data collection and input: data such

Figure 5 : Example of the RBM process and necessary development areas



as design parameters, operating history, and inspection results are collected and processed.

(2) Assessment

- Risk assessment: “the amount of consequence that would be caused by failure” and the “likelihood of failure” are calculated separately, and as shown in Figure 6[9], plotted in a risk matrix. Figure 6 shows a semi-quantitative method, with each property expressed in four levels (it need not be 4×4).

  In addition, if calculation is detailed, likelihood of failure can be expressed as probability and amount of harm as money. Results of the risk ranking are reflected in the inspection categories in the next inspection and in repairs in the maintenance plan, and so on. In this case, four categories of risk levels have been determined.
- Calculation of amount of consequence that would be caused by failure: the amount of human and economic damage that would be caused by failure is calculated. If the process liquid is explosive, toxic, or polluting, detailed analysis with thermal or fluid analysis technology is used to determine the amount that would be released and the extent of its spread and calculate the amount of damage.
- Calculation of likelihood of failure: Probability of failure from past cases, life assessment, effectiveness of inspection, severity of operation, management circumstances, and so on are used to calculate the likelihood of failure within a given time period.

(3) Maintenance planning and implementation

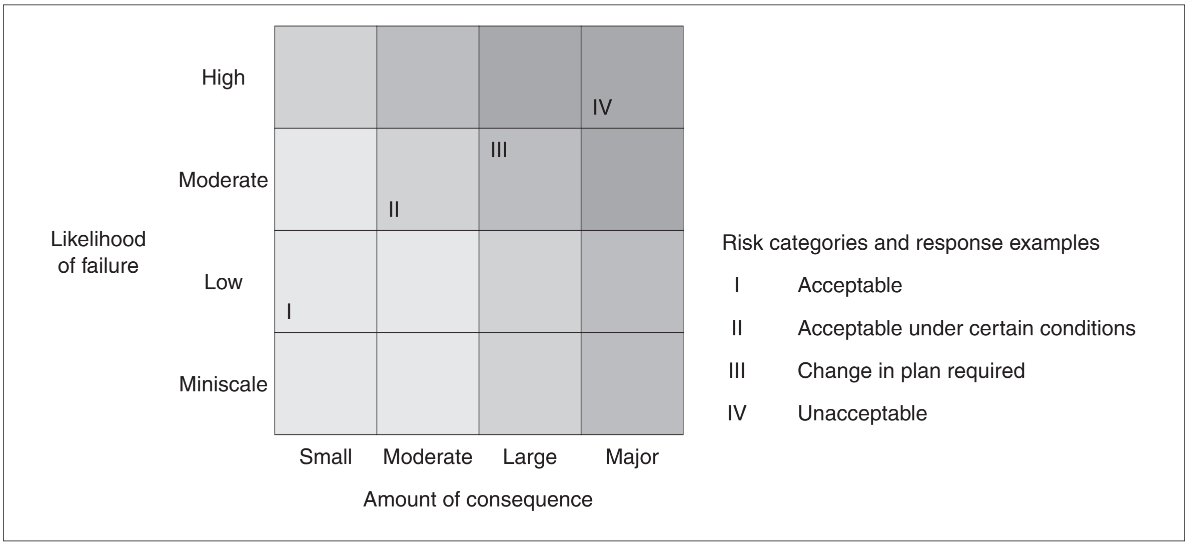
- Creation of a maintenance plan: As a result of the risk assessment, a maintenance plan that includes measures to lower risk in high risk areas is created. Risk-lowering measures may include more effective inspection methods, implementation of monitoring, improved operating conditions, and steps to lessen possible harm.
- Maintenance implementation: Maintenance is implemented in accordance with the plan above.

Data gathered through maintenance is fed back as plant data and reflected in the next round of maintenance. As this is repeated and data is accumulated and processed, reliability improves. Another result is the conversion of the data to electronic form and the passing on of techniques.

The development categories required for the establishment of RBM are as follows:

- Failure database: cases of failure from various plants are collected and sorted. The database is used to calculate consequence and likelihood of failure.
- Damage assessment guidelines: guidelines for the calculation of consequence and likelihood

Figure 6 : Risk ranking matrix and response examples



Risk categories and response examples

I	Acceptable
II	Acceptable under certain conditions
III	Change in plan required
IV	Unacceptable

of failure.

- Assessment modules for common failure mechanisms: methods to assess sensitivity to failure through each fracture mechanism.
- Life diagnosis methods: various life diagnosis methods are sorted and impact on risk is assessed.
- Inspection/monitoring methods: development of inspection/monitoring methods to reduce risk and assessment of their impact.
- Risk management guidelines: guidelines regarding methods to reduce risk.
- Code: assessment modules for common failure mechanisms, life diagnosis methods, and so on are coded for easy general use.
- Standardizing the RBM process and converting it into software: the RBM process is standardized and converted into software for easy general use.

Because risk can be expressed quantitatively (in term of money), the value of investment in maintenance can be calculated and used as information in making management decisions. In financial engineering and other forms of advanced asset management, a quantitative risk value can be utilized as important data. Furthermore, large-scale plants such as power generating stations must share ideas regarding safety with the general public can use acceptable risk standards as a tool to speak objectively to the public. For those reasons as well, risk-based management methods are garnering attention from a wide range of people.

To implement RBM methods as described above, almost all the categories in Section 5 below, "The optimal future of maintenance," are necessary. Progress in RBM research will lead the future of maintenance in the correct direction.

5 The optimal future of maintenance

For Japan, which must maintain and use its vast social and industrial infrastructure with care, the following is necessary.

(1) To more accurately predict failure, life prediction technology should be improved through the application of advanced sensing technology.

(2) To create an environment in which a broad range of people, including the lay public, can discuss the safe operation of structures from a common perspective. It is absolutely necessary that the results of long years of research into understanding of fracture mechanisms and life prediction technology should become common sense.

In concrete terms, the following is proposed.

- To disseminate the idea of risk as the standard for a generally shared perspective on safety.
- To disseminate technologies already established such as life assessment methods by standardizing them and converting them into PC software.

(3) Vitalization of maintenance technology fields.

- Maintenance technology requires a broad range of fields. Primary amongst them are mature fields such as, strength of materials, metals science, thermodynamics, and fluid dynamics. Currently in Japan, research and development and education are insufficient in those fields. Regarding the training of maintenance engineers as well, universities should spotlight research and education in such fields.
- A certification system for maintenance engineers should be established.

(4) Frameworks for responding to globalization (the advancing adoption of imported products) must be developed.

- Information on worldwide materials characteristics, materials standards, cases of failure, and so on should be collected in easy-to-use databases.

6 Conclusion

Based on the above, I propose the following science and technology policies.

(1) Among maintenance technologies, life prediction methods, risk assessment

methods (soft), and maintenance related (failure case studies, materials characteristics, etc.) databases should be highly accessible, and assessment standards must be based on broad consensus. Furthermore, the responsibility of maintaining the majority of social infrastructure belongs to the national government. Therefore, the government should invest research and development funds to develop maintenance technologies. At present, using national government funds to drive research in RBM, which is drawing the joint attention of industry, government, and academia, would be effective. Funds should be invested in academic societies and other public institutions, and committees should be established to develop techniques and standards.

(2) Maintenance integrates engineering fields such as structural materials sciences like materials strength and ferrous materials with thermo-dynamics and fluid mechanics. Those engineering fields are mature, and their attraction as research fields is weak and student interest is also low. Nevertheless, they are vital engineering fields if structures are to be maintained safely.

Taking them from the new perspective of safety, those engineering fields can be seen as a new R&D/academic field including social science fields such as safety science and financial engineering for asset value assessment. In Europe and the United States as well, maintenance is not systematized. It should be organized into an academic discipline, with graduate school majors in maintenance science and maintenance technology research centers that draw a broad range of personnel from Japan and abroad and promote education in the field.

(3) Government and the private sector should work together to prepare maintenance-related standards and to implement the setting and revising of standards in accordance with technical progress. Standards that stimulate the rationalization of maintenance should be welcome during the current trend towards deregulation.

(4) With the number of maintenance engineers decreasing, the quality of those few engineers must be ensured by national government policy that actively encourages maintenance-related academic associations to set qualification standards for maintenance engineers.

The modernization and rationalization of maintenance through the implementation of RBM as described above will also have the following propagation effects, and should be achieved promptly.

- Maintenance costs are expected to tie up corporate management in the future, but the quantification of risk and maintenance costs may become an important tool for management decision making. A new academic field fusing management engineering with maintenance science may open.
- Establishing maintenance techniques will bring about the safe extension of facilities and equipment life, resulting in a significant reduction in industrial waste.
- The establishment and implementation of maintenance techniques will result in their reflection in the design and production of new structures. This may lead to the development of risk-base engineering that will establish optimal designs for structure life[10,11].
- It is projected that when neighboring countries inevitably face the same situation after years from now, Japan can take a leadership role and its maintenance businesses can develop abroad.

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10

Science and Technology Policy Trends in the United States
— Report on the AAAS Annual Forum on Science and Technology Policy —

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1 Introduction

On April 22 and 23, 2004, the American Association for the Advancement of Science (AAAS) held its Annual Forum on Science and Technology Policy. The Annual Forums have been held each spring since 1976 in Washington D. C. as meetings to discuss science and technology policy. This year's forum was the 29th.

The themes of the Annual Forums are chosen from policy issues, such as funding, currently facing the US science and technology community. The forums are held after the Federal Government announces its budget for the coming fiscal year, when Congressional debate is heating up. The forums thus take place at an appropriate time for those concerned to express criticism of or support for the proposed budget, for government officials to explain policy, and for those concerned to debate the issues among themselves.

This year over 500 people attended, including government officials such as John H. Marburger, III, Director of Office of Science and Technology Policy; members of Congress such as Senator Tom Daschle (D); heads of university research departments; analysts from relevant think tanks; lobbyists from scientific associations; and foreign experts on science and technology policy. Topics discussed included the following:

- Outlook for the Federal Government's FY 2005 research and development (R&D) budget
- The impacts of post-terrorism security policies on US science
- US competitiveness in the face of informatization and globalization

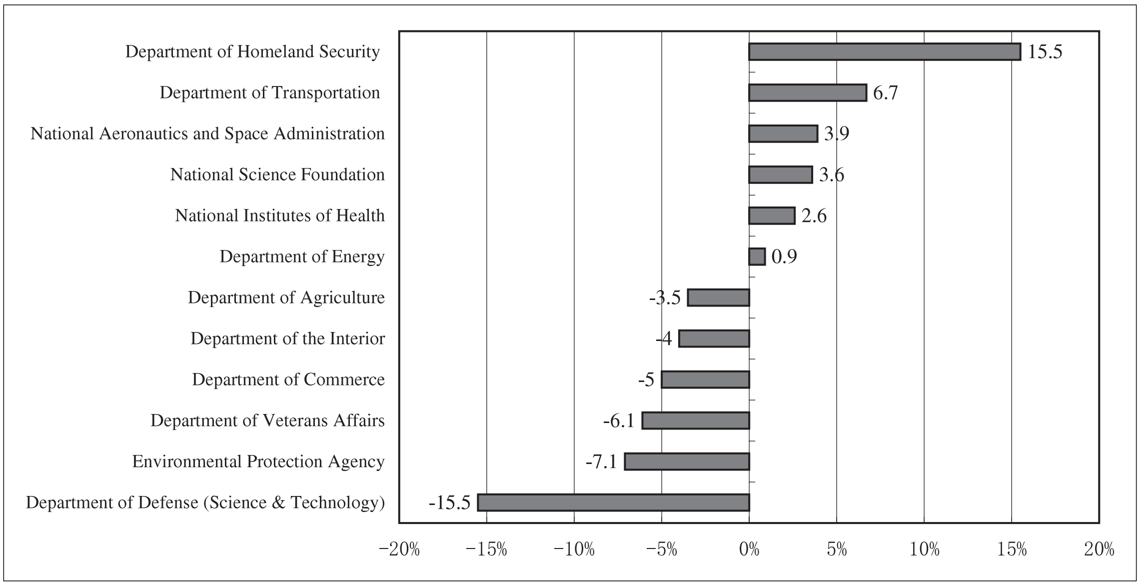
This article will provide an overview of major topics discussed at the Annual Forum[1].

2 Outlook for the Federal Government's FY 2005 R&D budget

Released by the Bush Administration on February 2, 2004, the proposed US federal budget for FY 2005 is $2.4 trillion. The federal budget for research and development is $132 billion. Broken down further, 57 percent (about $75 billion) of that is for defense R&D, while the remaining 43 percent (about $57 billion) goes to non-defense R&D. Compared with the previous fiscal year, the budgets for both defense and non-defense R&D increase, but the rate of increase was greater in the defense sector (4.3 percent overall, 5.9 percent for defense, and 2.3 percent for non-defense).

Figure 1 shows the FY 2005 R&D budget requests of various government agencies in comparison with their FY 2004 budgets. The budget for sectors related to national security is clearly increasing under the Bush Administration. In particular, the proposed R&D budget for the Department of Homeland Security is $1.2 billion, a 15 percent increase over the previous fiscal year. Meanwhile, most of the increase in the Department of Defense R&D budget is allocated to the development of missile defense systems, and the budget for science and technology such

Figure 1 : Comparison of FY 2005 government agency budget proposals with FY 2004 budgets



Source: Prepared by the author based on Annual Forum materials: “Kei Koizumi, AAAS, The Federal Investment in R&D in FY 2005 and Beyond.”

as basic and applied research has decreased sharply. The Bush Administration’s priorities are i) defense, ii) homeland security, and iii) the economy, and while the federal government’s R&D budget reflects those priorities as well, budget increases are going mainly to defense and homeland security.

Kei Koizumi, director of the AAAS R&D Budget and Policy Program said that if the federal R&D budget proceeds in accordance with the Bush Administration’s deficit-reduction plan (reducing the deficit to half the FY 2004 level over the next five years), the following would occur in the next five years:

- The defense R&D budget, for the Department of Homeland Security, etc., will continue increasing.
- With the exception of NASA, the non-defense R&D budget will decrease by 5 to 15 percent from fiscal 2004 levels.

The increase in NASA’s budget would come from the New Vision for Space Exploration Program (comprising the development of a crew exploration vehicle, plans for manned Moon expeditions, and concepts for future exploration) announced by President George W. Bush in January.

Opinion is divided on the Bush Administration’s science and technology policy. In his keynote address, presidential advisor Marburger stated that under the current Administration not only national defense related R&D budgets but also budgets for non-defense R&D aimed at long-term economic development are showing sustainable growth. He also emphasized the establishment of a new advisory board on biosecurity in the US Department of Health and Human Services as an example of cooperation between the government and the scientific community. On the other hand, in his own address, Senator Daschle claimed that although the government has a duty to ensure that scientists can freely carry out research with sufficient resources, the current Administration is neglecting that duty. In addition, he alleged that two members were removed from the President’s Council on Bioethics because they actively engage in human embryo research, and that the Administration pressures and twists scientific analysis to obtain the results it wants.

3 The Impacts of post-terrorism security policies on US science

Regarding the impacts of post-terrorism national security on US science, discussion centered on biosecurity and visa issues.

The terrorist incidents using anthrax in 2001 gave rise to an awareness that technology for biological manipulation developed to improve health and other new discoveries could be used in malignant ways that could pose a threat to national security. In accordance with this concept, the Public Health Security and Bioterrorism Preparedness and Response Act of 2002 was established. The law requires the registration of institutions that handle designated pathogens and toxins and background checks on individuals who handle them.

Furthermore, during the current fiscal year, a new advisory board on biosecurity was established in the US Department of Health and Human Services. The National Science Advisory Board for Biosecurity creates policy to prevent biological research from being used in terrorism and provides advice and guidance to government agencies and research institutions.

In addition, as a concrete example of national security policies having negative results, it was pointed out that grants-in-aid and contracts for non-US citizens are being limited and that cases of the publication of research results being restricted are increasing. Visa problems are lessening the desire of students and fellows from overseas to study in the US, and the number of students entering doctoral programs at Massachusetts Institute of Technology has declined since 2003.

As a result, the following concerns and ways of addressing them were discussed

- The outward flow of scientists due to excessive restrictions on non-US researchers
- The influence of strengthened government oversight of joint research on relationships with joint researchers abroad
- The influence of difficulties securing outstanding students and fellows from abroad and their impact on science and technology and US leadership

A glimpse of the large shadow national security issues have been casting on US science since the terrorism of 2001 was provided.

4 US competitiveness in the face of informatization and globalization: The rise of China

The forum showed awareness of advancing technology outsourcing to India and China as informatization and globalization progress. The fact that, unemployment among information technicians and the accompanying declines in competitiveness and wages, was cited as short-term effects of outsourcing. A survey by the Computing Research Association (CRA) that found that young Americans are aware of this trend and that fewer people are entering bachelor’s degree programs in computer science was presented. It was also pointed out that long-term effects would include structural changes in employment and impact on military dominance and national security.

In addition, while Japan was seen as an economic competitor in the past, a majority now sees China in that role. In particular, it was pointed out that the technological development model underlying high Chinese growth differs from that of Japan (i.e., Japan: high prices, high wages, advanced technology, industrial policy, and so on; China: low prices, low wages, advanced technology, an active entrepreneurial spirit, and so on).

China has utilized its low-cost manufacturing ability as the basis for high economic growth, but now its ability to innovate is also growing rapidly. Underlying that growing ability is China’ s characteristic expanding access to overseas research activities through overseas-Chinese scientists and students from China studying abroad. It was further pointed out that US visa issues, linked with China’s call-back policy, result in outstanding Chinese scientists returning home and further contributing to China’s production strength.

Georgia Institute of Technology professor Diana Hicks presented various data showing the rise of China. According to her data, gross national expenditures on research and development (GERD) for Singapore and China increased rapidly between 1991 and 2001, when it reached 2.5 to 3 times the 1995 level. China's 2001 GERD was $57 billion, about half that of Japan. Looking at the number Chinese receiving doctorates between 1986 and 1999, the 1999 figure was an astonishing 54 times as great as that of 1986. In absolute terms, the figure is at the same level as Japan in 1998 (about 6,500). In addition, China also published 4 times as many papers in 1999 as in 1986.

Most of the data presented by Professor Hicks showed the US and Japan still leading in absolute terms, but on the other hand they show China rapidly increasing its presence.

5 New directions for R&D: cognitive science

One could also sense that "research on the mind" or "cognitive science" continues to come to the fore as a new direction for research and development.

Senator Daschle also stated that understanding how human beings learn, remember, think, and communicate and how to apply those to areas such as education, safety, and security can be an important direction for research following the Human Genome Project.

Discussion also took place on the concept of NBIC technologies and how NBIC will impact society and ethics.

NBIC is a concept integrating nanotechnology, biotechnology, information technology, and cognitive science. Examples given included the development of technology such as interface between human being and sensors and biochips that connect neurons with electrodes.

By linking the four science and technology sectors mentioned above, NBIC opens the possibility of improving human beings physically, mentally, and socially. Ethical issues and security cannot be ignored in the development of this field. The forum showed an awareness that if NBIC is to be accepted by society, obtaining a consensus on ethics including ethicists, technology transfers that preserve the creativity and originality of the four technologies, and help with their fusion are necessary.

6 Conclusion

This year's Annual Forum was held a year after the war in Iraq, and it provided a glimpse of the large shadow cast over US science by security issues since the terrorism of 2001. That shadow takes forms such as difficulty in securing budgets for non-defense R&D, visa issues, and issues concerning oversight of life sciences research laboratories. In particular, the US scientific community feels a strong sense of crisis because non-defense R&D budget decreases in the next five years due to financial issues and the tendency to put priority on anti-terrorism policy.

China was the focus of much attention and awareness as a powerful economic rival of the United States. Although the US and Japan maintain their leads in areas such as overall R&D funding and papers published, China's presence is rapidly increasing. Japan's presence is in relative decline.

In addition, "research on the mind" or "cognitive science" continued to come to the fore as the next major topic of research and development. Currently there are no national-level projects on cognitive science in the United States, but it is possible that a national project on the subject will be carried out in conjunction with fields such as nanotechnology, information technology, and biotechnology. It is necessary to watch for future developments.

Finally, a few thoughts from the author on having attended the Annual Forum. The Annual Forums are timed to follow the opening of full-fledged Congressional debate on the proposed budget for the coming fiscal year. Persons on the front lines of science and technology policy in various sectors gather in a single venue and vigorously debate various points of contention regarding science and technology policy. This is something that cannot be experienced in Japan. Attending the Annual Forum was extremely valuable as a means of learning the science and technology policy issues of the United States. I sensed that it would be highly meaningful if Japan would also hold this kind of forum to openly debate science and technology policy and dispense information about its S&T policies to other countries.

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About SCIENCE AND TECHNOLOGY FORESIGHT CENTER

It is essential to enhance survey functions that underpin policy formulation in order for the science and technology administrative organizations, with MEXT and other ministries under the general supervision of the Council for Science and Technology Policy, Cabinet Office (CSTP), to develop strategic science and technology policy.

NISTEP has established the Science and Technology Foresight Center (STFC) with the aim to strengthen survey functions about trends of important science and technology field. The mission is to provide timely and detailed information about the latest science and technology trends both in Japan and overseas, comprehensive analysis of these trends, and reliable predictions of future science and technology directions to policy makers.

Beneath the Director are five units, each of which conducts surveys of trends in their respective science and technology fields. STFC conducts surveys and analyses from a broad range of perspectives, including the future outlook for society.

The research results will form a basic reference database for MEXT, CSTP, and other ministries. STFC makes them widely available to private companies, organizations outside the administrative departments, mass media, etc. on NISTEP website.

The following are major activities:

1. Collection and analysis of information on science and technology trends through expert network

— STFC builds an information network linking about 3000 experts of various science and technology fields in the industrial, academic and government sectors. They are in the front line or have advanced knowledge in their fields.

— Through the network, STFC collects information in various science and technology fields via the Internet, analyzes trends both in Japan and overseas, identifies important R&D activities, and prospects the future directions. STFC also collects information on its own terms from vast resources.

— Collected information is regularly reported to MEXT and CSTP. Furthermore, STFC compiles the chief points of this information as topics for “Science and Technology Trends” (monthly report).

2. Research into trends in major science and technology fields

— Targeting the vital subjects for science and technology progress, STFC analyzes its trends deeply, and helps administrative departments to set priority in policy formulating.

— STFC publishes the research results as feature articles for "Science Technology Trends" (monthly report).

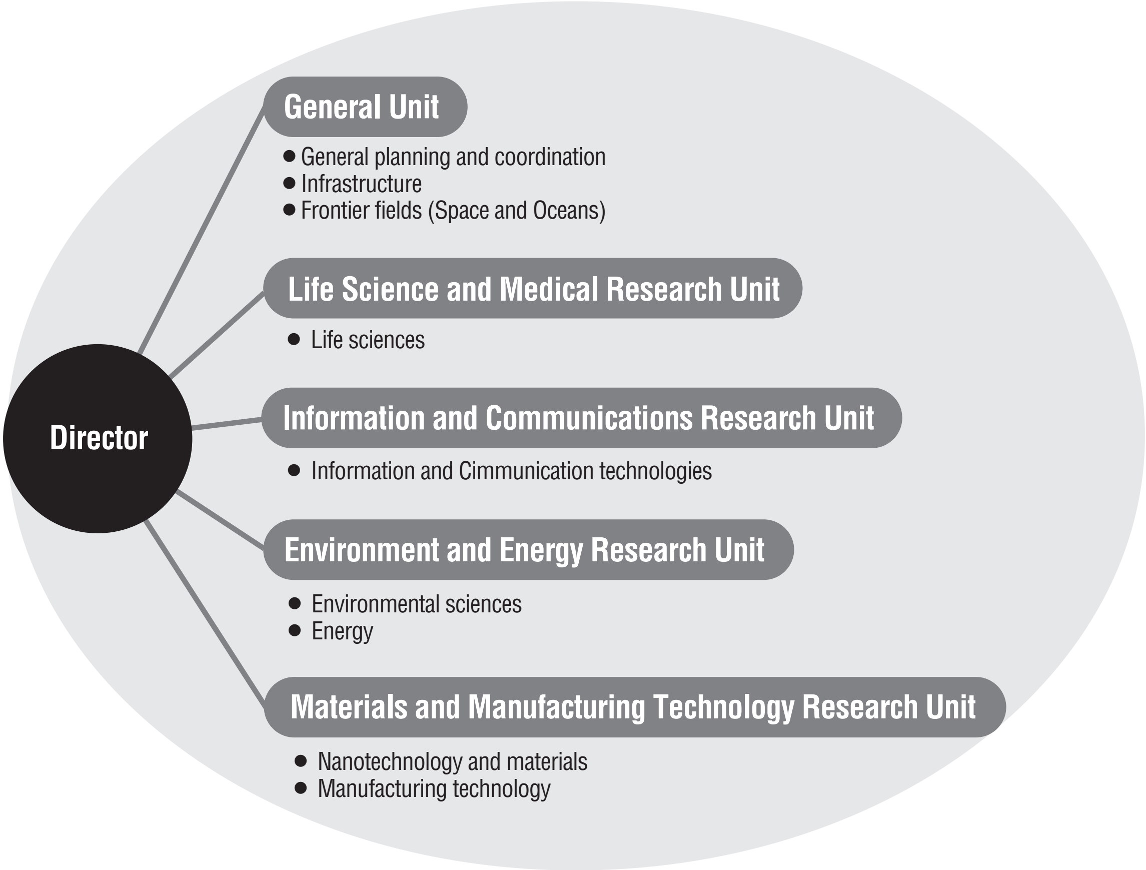
3. Technology foresight and S&T benchmarking survey

— STFC conducts technology foresight survey every five years to grasp the direction of technological development in coming 30 years with the cooperation of experts in various fields.

— STFC benchmarks Japan's current and future position in key technologies of various fields with those of the U.S and major European nations.

— The research results are published as NISTEP report.

Organization of the Science and Technology Foresight Center



＊Units comprise permanent staff and visiting reseachers (non-permanent staff)
＊The Center's organization and responsible are reviewed as required

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