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Life Sciences

Information and Communication Technologies

Environmental Sciences

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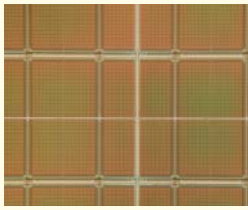



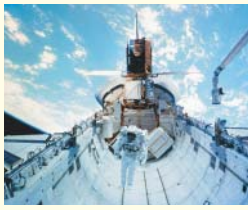

Foreword

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 such as periodical Delphi surveys.

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 Sugar Chains as the Third Biomolecule, and Post-genome Research

p.9

In this report, we deal with the functions and structure of the sugar chains, the third biomolecule that, like the first and second biomolecules, i.e., nucleic acid (DNA) and protein, has recently attracted people's attention, as well as the present states of researches and prospects of studies on the sugar chains.

Since sugar chains are involved in intercellular recognition and interaction, and play important roles in cellular network, it is expected that elucidation of the functions of sugar chains will lead to the development of strategies based on sugar chain functions for maintaining health as well as methods for preventing and treating diseases. Therefore, it can be said that the study on sugar chains represents one of the significant challenges to be dealt with in parallel with post-genome researches mainly concentrated on nucleic acids and proteins.

Studies on sugar chains in Japan have been conducted with governmental support from early on, and have been on the top world-class level. However, because of the structural complexity and diversity of sugar chains, studies on them have lagged behind those on nucleic acids or protein in spite of the recognition of the importance of such studies.

The purposes of future studies on sugar chains may include "elucidation of sugar chain structures," "elucidation of sugar chain functions," "synthesis of sugar chains" and "application of the results of studies on sugar chains to medicine." To achieve these purposes, it is anticipated that strategies for promoting such studies will be devised.

Moreover, in order for Japan to clarify the roles of sugar chains in life phenomena ahead of all other countries, it is essential to develop systems of sugar chain studies that would form the nucleus for the promotion of such studies, to tap into the collective wisdom of people not only in the world of life science but also in many other areas, and to pursue studies on sugar chains comprehensively and strategically.

(Original Japanese version: published in January 2002)

2 Trends in Research on Dementia
— Discussion Centering on Alzheimer's Disease —

p.14

Alzheimer's disease is a condition in adults characterized by disturbed memory, impaired judgement, etc. In the brain of patients with Alzheimer's disease, two characteristic pathologic changes take place, i.e., deposition of senile plaques and neurofibrillary degeneration. At the same time, death of nerve cells also occurs in the regions involved in higher-order cognitive functions such as memory and learning.

It has been believed that abnormal accumulation of two kinds of proteins (amyloid-beta protein and abnormally phosphorylated tau protein), which are rarely found in normal brains, is closely involved in the development of

Alzheimer's disease. The mechanisms of the generation of these proteins are being elucidated, and research on the relationship between the two proteins has been actively conducted.

No infallible remedy has been developed for Alzheimer's disease, and, in tandem with research on the mechanisms of the formation of the above-mentioned two proteins, development work on pharmaceutical products targeting the mechanisms has been enthusiastically done. On the other hand, effects of non-steroidal anti-inflammatory drugs (NSAIs) on Alzheimer's disease have gained the spotlight recently.

Several genes that play important roles in the development of Alzheimer's disease have been identified. Therefore, in the future, postgenome research on the disease will increasingly assume significance. In Japan too, studies on Alzheimer's disease have been aggressively conducted at the Brain Science Institute, Institute of Physical and Chemical Research (Riken), which has been established as a foundation for brain research, as well as many universities, etc. In order to facilitate progress in research on Alzheimer's disease, it is necessary to tap into the collective wisdom of people in various fields including medicine, pharmaceutical sciences and science, as well as to construct systems for appropriate collection and accessible supply of samples for research including brain tissues taken from Alzheimer's disease patients.

(Original Japanese version: published in February 2002)

3 Trends in Research and Development of Functional Foods

p.23

It has been known that foods have functions that may exert beneficial effects on the health, physical condition and mental condition of humans, and foods that are designed and processed so that they can fully exhibit such functions are generally called functional foods.

Many scientific evidences about the functional components of foods have been accumulated through studies using animal models or involving human subjects, and foods for specified health uses (FOSHU) with such approved health claims as "This product is suitable for people who want to improve gastrointestinal health" have rapidly penetrated into the Japanese marketplace. With this being the situation, consumer awareness and their interest in functional foods have greatly heightened in Japan.

In addition, many dietary supplements in the forms of tablets and capsules containing vitamins and minerals have been commercially introduced in the United States, and, in European countries, research and development of food products utilizing the concept of "probiotic" including lactic acid bacteria drinks has been actively conducted, indicating the fact that functional foods have attracted people's attention on a worldwide basis.

From now on, research and development of functional foods should be efficiently promoted while keeping in mind the following challenges to be addressed:

(i) Since the functionality of foods has been assessed based on limited scientific evidences, it may be necessary, from now on, to make continuous efforts to reinforce research techniques, including the development of biological markers, as well as to evaluate the efficacy of such foods on a massive scale and from a long-term perspective.

(ii) So far, functional foods have been designed by targeting a single disease risk

factor. However, in light of the fact that diseases are actually induced by two or more independent risk factors, it may also be necessary, in the future, to develop functional foods targeting two or more risk factors.
(iii) In order to pursue research on functional foods with the overall purpose to improve the health of the Japanese, it may be essential to develop human resources and systems that enable cooperation between the people conducting research activities aiming at the development of products and those pursuing research from the standpoints of nutritional science, medicine, etc., related to the utilization and evaluation of such products.
Furthermore, in order to secure consumers' safety, it is necessary for the authorities concerned to provide information on the risks associated with excessive intake as well as on that associated with the intake by patients with certain diseases.

(Original Japanese version: published in March 2002)

Information and Communication Technologies

4 Trends in Research and Development on Next-Generation Devices (from IEEE IEDM)

p.34

The IEEE IEDM (International Electron Devices Meeting) — one of the most authoritative meetings that serve as opportunities for presenting achievements of research into leading-edge technologies — was held from December 2 through December 5, 2001.
Japanese research achievements presented at the meeting, ranging from applications to basic research, acquired high acclaim showing Japan's true ability as a leader partly because Japan is the origin of the development of SOI devices, for which Japan has made significant achievements that shortened the realization of the research roadmap by more than 10 years, and of the carbon nanotube, whose presentation gained the highest level of attention at the meeting.
However, it is a cause of concern that Japanese studies included much fewer multinational collaborations than those by Europe and the United States, even fewer than other Asian countries. It will be extremely important for Japanese researchers to cooperate with universities, since research on leading-edge devices has reached the nano level and quantum-mechanical basics are increasingly required. Similarly, multinational collaborations will also have great significance in the field of research on leading-edge devices that will require huge research investments and resources.
In order to maintain the top position by outperforming studies on devices in the United States, Europe and Asia, who are pressing hard on Japan, it is necessary to further accelerate the cooperation between academic, business and governmental sectors, which has been promoted in Japan, and press ahead with research efforts through setting higher-standard objectives, not with the conventional cumulative approach.

(Original Japanese version: published in January 2002)

5 R&D Trends in Speech Recognition / Synthesis and Natural Language Processing

— Challenges toward the Establishment of User-Friendly Human Interfaces —

p.41

Human interfaces, which are input/output technologies to allow people to operate devices, have been studied and enhanced to provide ease of use. While focusing on research on possible natural interfaces such as speech recognition/synthesis and natural language processing, this report describes the history and the current state of research as well as different approaches in Japan and the U.S. to make research projects, followed by suggestions on challenges to be addressed for advancing the research on next-generation human interfaces.

The history of research in these areas began back in the 1950s. Basic research led to some breakthroughs on which commercialization efforts were made, making these technologies available for users with some restrictions.

In the latter half of the 1990s, DARPA projects played a significant role in U.S. R&D on speech recognition. US venture firms founded based on the outcomes of the projects are now finding new applications for speech recognition technology. Here we see a problem that industry-academia collaboration and technology transfer are less common in Japan than in the U.S.

The current technologies are enable to realize voice input to word processors (dictation), and translation systems for rough and simple reading foreign-language information on the Web. However, there remain such issues as low recognition rates for daily conversation and low translation quality for complex sentences, the present technologies are insufficient for providing an easy use human interface for anyone without restriction. Amid the spread of information devices, the next-generation human interface technology is expected to solve the digital divide and to improve machines' friendliness to users even including beginners.

In order to break limitations of current technologies, there need big efforts on research to make a new model of sound processing, recognition processing and language processing. With the growing global trend in basic researches depend more on universities' effort than business enterprises' effort, an expectation for universities basic research outcomes is increasing. To allow them to carry out research projects on the basis of risky but innovative ideas, the culture should be changed where fair competition and evaluation are ensured, and those failed are more tolerated and encouraged to make another endeavor.

(Original Japanese version: published in March 2002)

Environmental Sciences

6 Trends in Technologies to Combat Contaminated Soil Environments

p.49

Measures to combat soil environment pollution also have many difficult aspects technically in comparison with air and water pollution, and their enactment into law also had been lagging behind. In recent years, there have been many instances where soil contamination has been proven in soil surveys attendant to the redevelopment and sale of land, and in independent surveys by businesses based on ISO14001, and the government is currently advancing discussions concerning the establishment of laws to combat soil contamination.

Looking at the current state of technologies to combat soil environment contamination, technologies gaining popularity as permanent countermeasures include landfill disposal at final disposal sites and solidification by cement, etc., for heavy metals; soil vapor extraction for volatile organic compounds; and adhesion of active carbon by pumping-up of groundwater.

Considering the restrictions due to the shortage of final disposal places, and that it is conceivable that cases requiring purification will increase hereafter, technologies that treat soil contamination on site and at low cost need to be considered with great importance in terms of establishing the direction of future technological development. Furthermore, since action is also being sought on wide-area, low density pollution caused by environmental hormones, the importance of establishing bioremediation and other biological treatment technologies is considerable. What is more, Asian countries are also facing soil environment problems, and from the perspective of international contribution, the research and development of these countermeasure technologies should be positioned as policy and promoted.

(Original Japanese version: published in March 2002)

Science and Technology Policy

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The Trend of the R&D Policy in the U. S.

— Transition of priority areas in the R&D budget allocation of the federal government —

p.57

In this January, President Bush signed all the appropriation bills for fiscal 2002 (from October 2001 to September 2002), and, subsequently, the government budget for fiscal 2002 was approved. The budgets of the DOE and the NSF, of which rates of increase from the previous year were minus in the President's Budget Message for fiscal 2002, were finally increased due to a larger R&D budget as support measures for the occurrence of the simultaneous multiple terrorist attacks against the U. S., with the entire budget then reaching $102.9 billion (which increased by 12.5% from the previous year).

According to the Budget Message for fiscal 2003 (from October 2002 to September 2003) announced this February, the entire R&D budget will reach $111.8 billion (an increase of 8.7% from the previous year), and the R&D budgets of the DOD and the NIH, which account for about 3/4 of the entire budget, will be increased significantly in particular. Fiscal 2003 is the last year of the NIH's budget doubling 5-year campaign, which was started from fiscal 1999, and the targeted amount for the NIH was achieved in the Budget Message. Furthermore, it is expected that both the President and Congress will actively support R&D, accepting a red ink balance in the national finance, and the governmental R&D budget will increase in general with the attachment of importance to R&D for countermeasures against terrorisms and R&D to boost the economy.

(Original Japanese version: published in February 2002)

8

Trends in French Science, Technology, and Innovation Policy

— The MINATEC Industry-Academia-Government Nanotechnology Innovation Center Project —

p.64

In recent years, Europe has joined the United States and Japan as an active base for nanotechnology research and development. Among the Europeans, France determined its basic science and technology policy within an interministerial committee on science and technology created in July 1998 and chaired by then-Prime Minister Lionel Jospin. In October, the National Science Council was formed with representatives of industry, academia, and government. Since then, France has seen rapid development of an emphasis on research fields and budgeting, large-scale reforms of its public research institutions, and researchers starting businesses.

The MINATEC joint industry-academia-government project in the Grenoble area, where many public research institutes are concentrated, is especially meaningful because it is a microcosm of these shifts in science and technology and innovation policies.

In this project, research backed by the nanoscience of such national laboratories as CNRS (National Center for Scientific Research) and CEA-LETI (Atomic Energy Commission-Electronics and Information Technology Laboratory) is carried out in highly advanced nanotechnology fields including carbon nanotubes, MEMS, and nanobiology. The project aims for the lead in a wide array of fields involving microtechnology and nanotechnology. In microelectronics, a field with current applications, the project has also formed alliances with IMEC in Europe and SEMATEC in the USA to research advanced semiconductor technology.

In the operation of this project, policies are steadily being implemented to form a base for research by loosening the restrictions preventing national laboratory researchers from doing other work or starting companies, by utilizing international researchers, by seeking foreign direct investment (FDI), by forming alliances and partnerships with research institutions in other countries, and by providing tax incentives for private-sector corporate research and development. Rather than merely building a center for joint research, a dynamic system where emphasis is placed on motivation that will naturally give rise to industry-academia-government cooperation is being constructed.

The key is that industry-academia-government cooperation is not an end in itself. It is a means of promoting research and development through a dynamic system that naturally leads to such cooperation.

(Original Japanese version: published in March 2002)

1

Sugar Chains as the Third Biomolecule, and Post-genome Researches

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1.1 Introduction

In recent years, the sugar chains, the third biomolecule, has been attracting people's attention like the first and second biomolecules, i.e., nucleic acid (DNA) and protein.

Most nucleic acids and proteins have many parts that are commonly found in almost all animal species, so it can be said that studies on those biomolecules are longitudinal types in terms of the evolutionary process of all species of animals. On the other hand, considering the fact that the structures and functions of sugar chains not only differ among different animal species but also vary even in the same species in accordance with organs, tissues or types of cells, it can be said that studies on sugar chains are cross-sectional types, in terms of the evolutionary process, aiming to clarify fundamental mechanisms underlying the biodiversity.

Therefore, it can be said that the study on sugar chains represents one of the significant challenges to be dealt with in parallel with the post-genome researches mainly concentrated on nucleic acids and proteins.

This article discusses the current state of studies on the functions and structures of sugar chains, and the future prospect of sugar chain studies.

1.2 What is the sugar chain like?

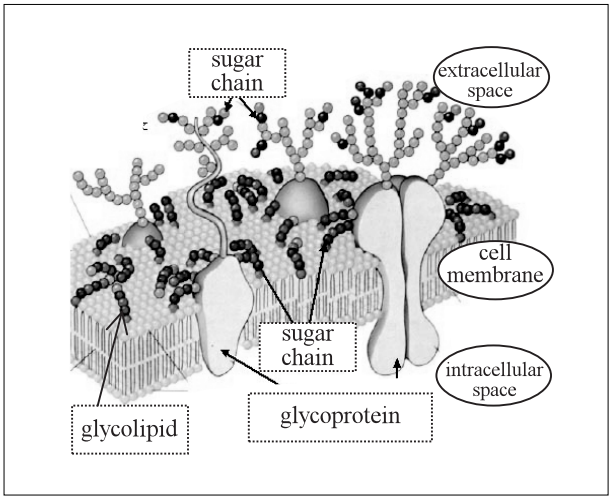
The human body is a huge cellular network consisting of about 60 trillion cells, and all of which have many sugar-chain molecules on their surfaces (Figure 1). ABO blood types, for example, are dependent on the antigenic properties of sugar chains on cell surfaces.

Sugar chains are involved in intercellular recognition and interaction, and play important roles in cellular network. Therefore, disturbance of cellular networks will result in the occurrence of, for example, cancer, chronic diseases, infectious diseases, senile changes, abnormalities in the immune system, brain, development, etc.

For example, cancerization of cells is known to be associated with structural changes of sugar chains. In addition, it is also known that pathogens such as Vibrio cholerae and influenza virus invade and infect host cells by recognizing specific sugar chains on cell surfaces and binding to them.

It is expected that the results of studies on sugar chain functions will be applied to various areas. For example, elucidation of sugar chain functions is expected to lead to the development of pharmaceutical and food products based on new theories, and contribute to the prevention and treatment of diseases.

Figure 1: Sugar chains on the cell membrane



Source: Press release issued by RIKEN (the Institute of Physical and Chemical Research) on November 20, 2001.

Table 1: Structure of components of organisms

Component	Constituent chain molecule	Basic unit of structure (chain)	Modes of binding between basic units
Nucleic acid	polynucleotide chain	nucleotide	phosphodiester bond
Protein	polypeptide chain	amino acid	peptide bond
Glucide	sugar chain (oligosaccharide chain, polysaccharide chain)	monosaccharide	glycosidic bond

Source: Authors' compilation based on the report (1990) on "Strategies for promoting comprehensive research and development in terms of the establishment of foundations of glycotechnology" (Request for advice No. 14) submitted by the Council on Avionic and Electric Technologies.

1.3 Structure of sugar chains

Major components of living organisms other than water include nucleic acid, protein, glucide and lipid. Fundamental data on the structures of nucleic acid, protein and glucide are shown in Table 1.

Sugar chains have bonded covalently with proteins and lipids in living organisms. About 60% of the proteins that makes up the bodies of living organisms takes the form of glycoprotein, which is produced through the covalent bonds of sugar chains with proteins.

Such sugar chains are often composed of two or more kinds of glucides. The human body contains 9 kinds of glucides, and they form various patterns of monosaccharide sequence. For example, for two molecules of a monosaccharide, 1,116 patterns of sequence can be created, and for three molecules of a monosaccharide, 119,736 patterns can be achieved.

In addition, when allowing not only for the sequence of monosaccharides in a sugar chain, but also for the manner(s) and site(s) of bonding of monosaccharides in a sugar chain, length and manner(s) of branching of a sugar chain, conformational structure of a sugar chain, etc., it can be easily conceivable that sugar chains assume far more complex structures as compared with nucleic acids (DNA) and proteins. Therefore, structures of sugar chains contain a wider variety of biological information than those of nucleic acids (DNA) and proteins.

However, because of the structural complexity and diversity of sugar chains, studies on them have lagged behind those on nucleic acids or protein, in spite of the recognition of the importance of such studies.

1.4 Current state of sugar chain studies in Japan

Figure 2 shows the major themes of sugar chain studies, which have been conducted with governmental support in Japan.

With the support given by government agencies, sugar chain studies in Japan have been on the top world-class level. For example, among the 110 sugar chain-related genes that have been discovered up until now in the world, 54 genes were identified in Japan.

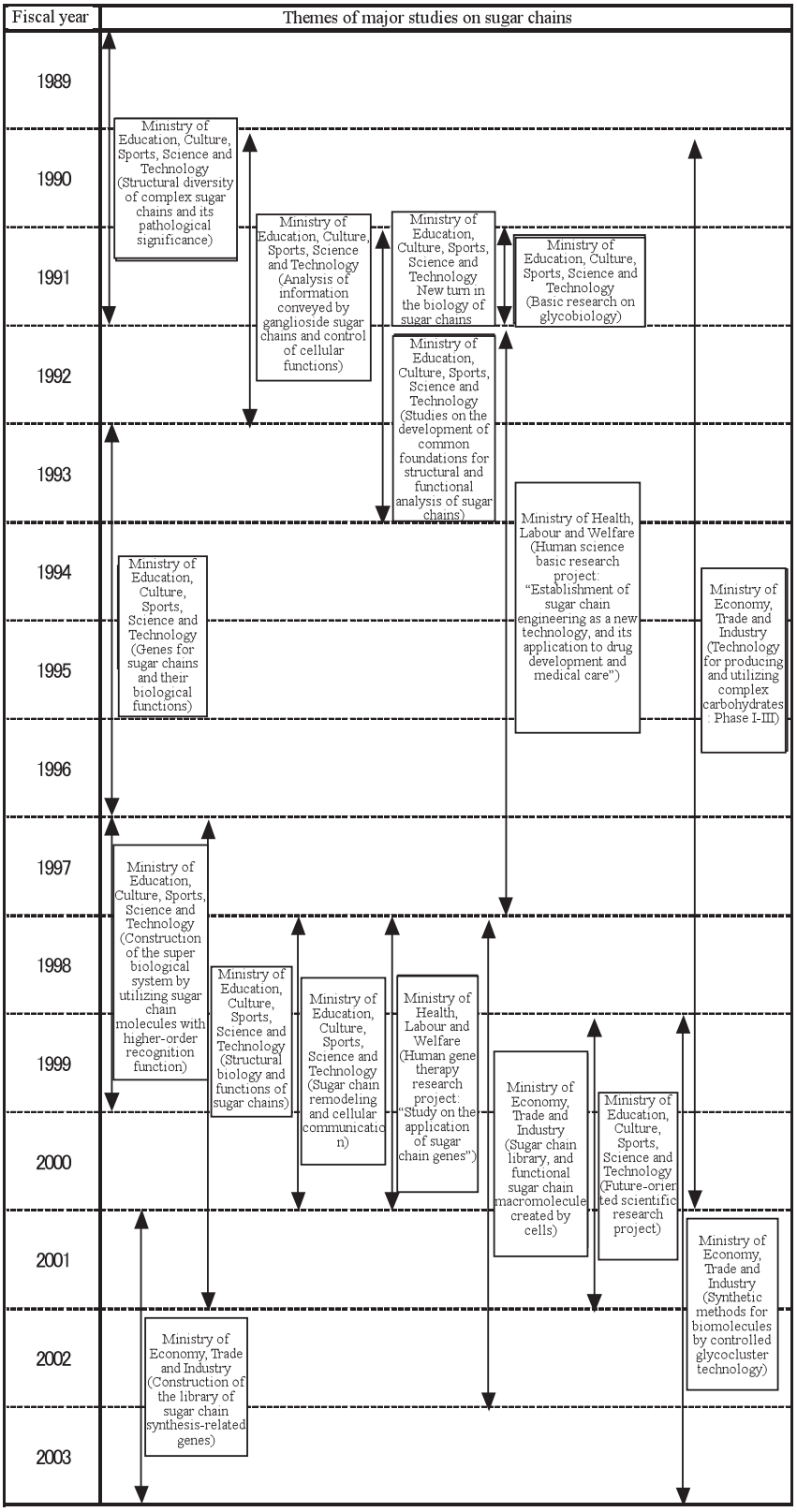
In fiscal year 2001, the Ministry of Economy, Trade and Industry started the program of the "construction of sugar chain synthesis-related genes library" as one of the "study programs for the foundations on which to do biotechnology research targeted at the maintenance and promotion of public health" and submitted a 500 million-yen fiscal 2001 budget request. The program aims to accomplish the cloning of about 300 genes for enzymes essentially involved in sugar chain synthesis as well as to conduct functional analysis of those genes to construct a functional database of them.

Furthermore, the Institute of Physical and Chemical Research (RIKEN) decided to include the "study on super-biomolecular system research" in the second-generation frontier research systems in October 1999. Under the project, RIKEN has pursued studies in the field of integrated sugar chain biology to clarify, for example, the contribution of sugar chain recognition and the mechanism of expression of sugar chain-related genes by the cells in the immune and nervous systems.

At present, it is earnestly hoped that automated sugar chain sequencers and automatic

synthesizers of selected sugar chains will be developed that may form the technological foundations of future studies on sugar chains. However, many challenges are to be addressed before the development of such technologies because of, for example, the highly complex structures of sugar chains and the difficulty of the extraction of sugar chains that sparsely exist intracellularly.

Figure 2: Themes of sugar chain studies in Japan



Source: Authors' compilation by making reference to the materials provided by Yoshitaka Nagai, director of the Mitsubishi Kagaku Institute of Life Sciences.

1.5 Future prospects of sugar chain studies

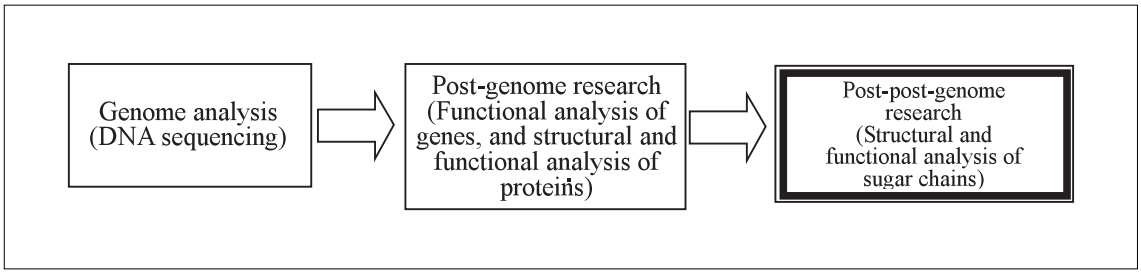
The study on sugar chains can be regarded as a category of the post-post-genome research following the post-genome researches that were pursued with gene function analysis as well as functional and structural analysis of proteins as the core (Figure 3).

A conceptual illustration of future prospects of sugar chain studies is given in Figure 4. Future studies on sugar chains can be roughly classified into 4 categories including "studies targeted at the elucidation of sugar chain structures," "studies targeted at the elucidation of sugar chain functions," "studies targeted at sugar chain synthesis" and "studies targeted at the application of the results to medicine."

Such studies on sugar chains are expected, for example, to lead to the elucidation of the mechanisms underlying fundamental life phenomena or become able to be applied to medicine through work in cooperation with researchers in other fields of life science.

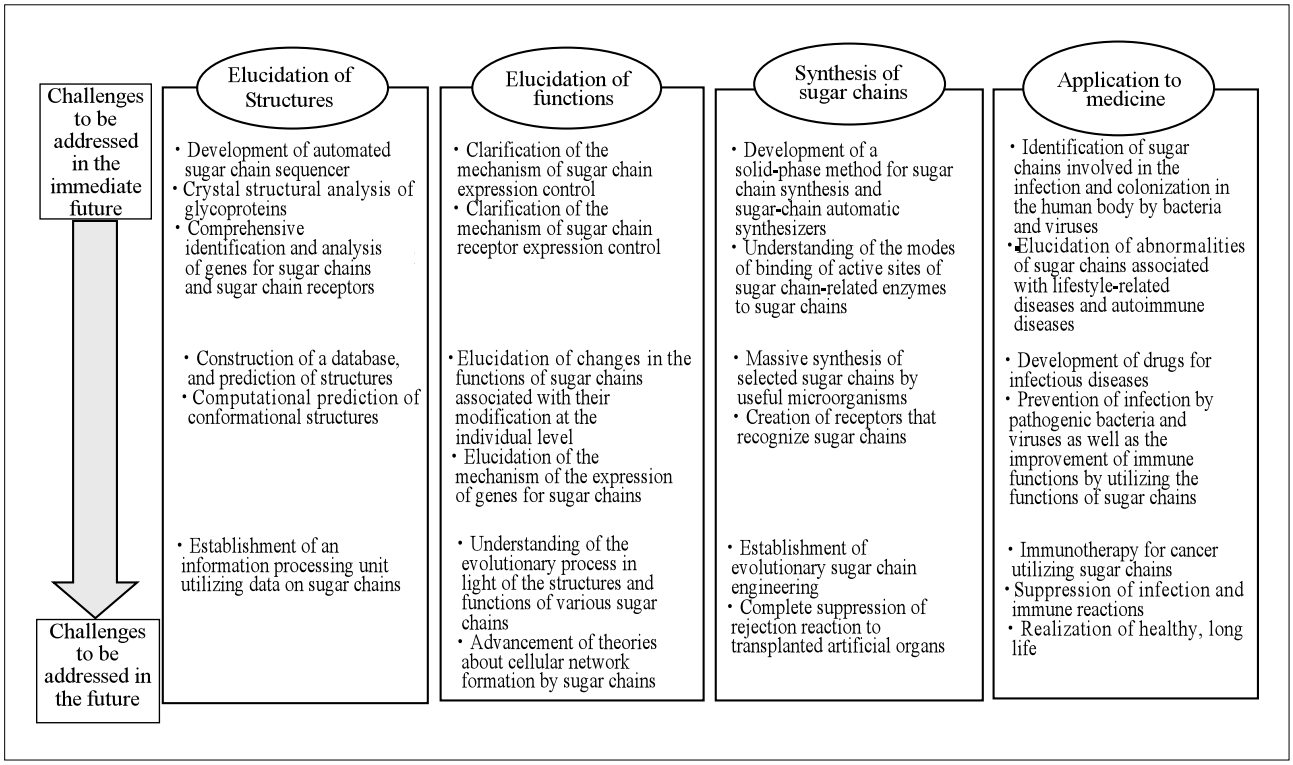
In the United States, efforts to promote sugar chain studies have been undertaken. For example, the National Science Foundation (NSF) held a workshop under the theme "Frontiers in Glycoscience" in May 2000. The report on this workshop points out that sugar chain studies in Japan are in an advanced state, and refers to the

Figure 3: Sugar chain studies as the post-post-genome research



Source: Authors' own compilation

Figure 4: Future prospects of sugar chain studies



Source: Authors' compilation by making reference to the materials provided by Yoshitaka Nagai, director of the Mitsubishi Kagaku Institute of Life Science

necessity of establishing programs and providing financial support for the purpose of promoting joint research in the United States by people in different academic fields (chemists and biologists), and summarizes the suggestions made in the workshop, for example, that construction of sugar chain-related databases in the United States should be promoted. In addition, the National Institute of Health (NIH) announced that it would start a project for promoting sugar chain studies on a 5-year budget of 4.4 billion dollars. Therefore, it can be said that, also in the United States, increasingly earnest efforts have been made to foster research on sugar chains.

1.6 Conclusion — suggestions for the promotion of sugar chain studies —

Recently, government support has been provided mainly for challenges to be dealt with in this era of post-genome research including the functional analysis of genes as well as the structural and functional analysis of proteins. Since studies on sugar chains may represent one of the important categories of post-post-genome research, which should be pursued from the present time when post-genome research is being carried forward, promotion of the employment of the following strategies is desired:

- **Recruitment of competent personnel from a wide variety of academic areas**
  Studies on sugar chains are accompanied by difficulties arising from their structural complexity and diversity. Hence, sugar chain studies need to be pursued comprehensively and strategically by tapping into the collective knowledge of people not only in the areas of biology, such as molecular biology and cell biology, but also by those in other various academic areas including chemistry, physics, engineering and agriculture.
- **Development of research systems**
  Studies on sugar chains in Japan have been on the top world-class level. In order not only to maintain the current level of research into the future, but also to elucidate the roles of sugar chains in life phenomena before any other countries, it may be effective to establish research systems under which world-class personnel can be assembled. It can be expected that products of sugar chain research will synergistically facilitate advancement in post-genome research.
- **Conceptual designs of the future direction for the promotion of sugar chain studies**
  Figure 4 entitled "Future prospects of sugar chain studies" is a conceptual drawing of the future direction for the promotion of sugar chain studies. It is expected that strategies for promoting sugar chain studies will be devised aiming to attain these goals.

Acknowledgements
This article summarizes the contents of the lecture delivered by Yoshitaka Nagai, director of the Mitsubishi Kagaku Institute of Life Science under the theme "Sugar chains as the third biomolecule, and post-genome research" at the National Institute of Science and Technology Policy (NISTEP) on June 27, 2001. We are deeply grateful to Mr. Yoshitaka Nagai who, on the occasion of the making of this article, willingly provided us with guidance and related materials.

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2

Trends in Research on Dementia
— Discussion Centering on Alzheimer's Disease —

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2.1 Introduction

In these days when declining birth rates and graying are reported to be ongoing in Japan, many people desire not only to live a long life but also to spend their old days in good health. In this increasingly graying society, we might be obliged to not only receive care but also administer care to someone. According to the report on the "Basic Investigation of National Life" in 1998, published by the Ministry of Health, Labor and Welfare, about 81% (one million people) of the roughly 1.24 million Japanese citizens requiring care at home is represented by people aged 65 years or older. Furthermore, about 53% of the people who are administering care to those aged 65 years or older requiring at-home care is constituted by the elderly aged 60 years or more.

Under these circumstances, dementia has become a grave concern to many people. According to the "Report on Special Investigation of the Actual Conditions and Health of the Elderly" in 1997, published by the Tokyo metropolitan government, about 4% of the elderly aged 65 years or more living at home have developed dementia. Furthermore, according to the report on the "Projected future population of Japan" in 1997, published by the National Institute of Population and Social Security Research, Ministry of Health, Labor and Welfare, the number of elderly people with dementia in Japan reached 1.56 million in 2000, which is expected to increase sharply to 2.26 million in 2010, and further to 2.92 million in 2020.

Against this backdrop, in the Phase Two Technology Master Plan (adopted at the Cabinet meeting held in March 2001), elucidation of the mechanism of brain aging and suppression of nervous system diseases were selected as strategic challenges to be addressed with high priority in order to tackle national and social problems.

In the 7th Technology Foresight, whose results were published by the National Institute of Science and Technology Policy, survey of the current state of research on Alzheimer's disease, a common type of dementia, was conducted and the outlook for the challenges to be addressed through research on the disease was given. The challenges mentioned and year when each of those challenges is expected to be accomplished is as follows:

- "Elucidation of the mechanism of development of Alzheimer's disease"..... 2014
- "Inhibition of the progression of Alzheimer's disease"..... 2017
- "Development of therapy that completely cures Alzheimer's disease"..... 2020

Under circumstances where the Japanese government has taken various measures to cope with problems arising in this graying Japanese society such as the provision of nursing care services and establishment of facilities for nursing care, to what extent has research targeting the suppression of Alzheimer's disease been pursued?

In order to find the answer to this question, we invited Professor Takeshi Iwatsubo, Graduate School of Pharmaceutical Sciences, Faculty of Pharmaceutical Sciences, University of Tokyo to have him deliver a lecture about recent trends in research on dementia, especially on Alzheimer's disease, at the Institute of Policy for Science and Technology on December 11, 2001, and wrote this article as the summary of the contents of his

lecture while incorporating the data from our study.

This report discusses the "General description of dementia (section 2.2), "Characteristics of Alzheimer's disease" (section 2.3), "Current state of research on the mechanism of Alzheimer's disease development" (section 2.4), "Current state of development work on pharmaceutical products for Alzheimer's disease" (section 2.5), and "Strategies for promoting research on Alzheimer's disease in Japan" (section 2.6), and, in the last section, gives a summary of "Challenges to be addressed through research on Alzheimer's disease" (section 2.7).

2.2 General description of dementia

Dementia is a disorder of memory and intelligence (judgement, cognitive function, etc.) in adults. With aging, people become more forgetful but can live a normal life as a member of society if they still have normal judgement, etc. On the other hand, patients with dementia have not only memory disturbance but also intelligence disorder, so they cannot live a normal life as a member of society. In most cases, dementia occurs when nerve cells in a certain region of the brain are damaged from some cause and are lost.

Dementia can be classified into various groups including senile dementia, dementia caused by abnormality of proteins, etc. (e.g., Alzheimer's disease), that following the onset of cerebrovascular disease (cerebrovascular dementia), that associated with the displacement of a part of the brain (displacement of neurovascular structures), that caused by brain tumors, etc., as well as due to infectious diseases including prion disease, etc.

The two most common types of dementia are Alzheimer's disease and cerebrovascular dementia.

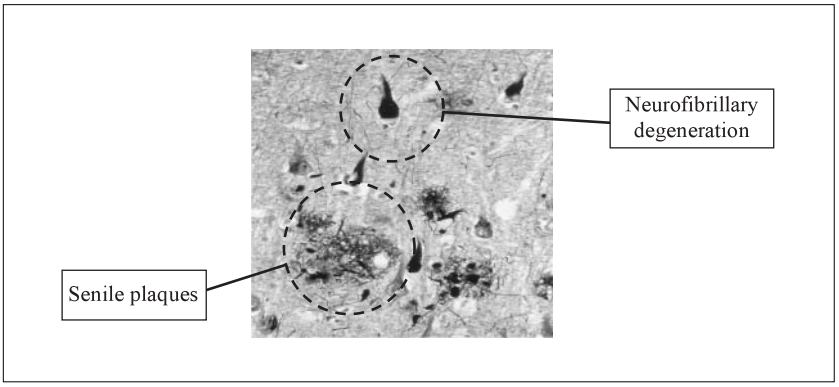
2.3 Characteristics of Alzheimer's disease

Dementia is diagnosed by step-by-step elimination of other diagnoses, which are conceivable in light of the patients' clinical history, as well as findings from physical examination or from diagnostic imaging, etc. However, in the last ten some odd years, studies on Alzheimer's disease have greatly advanced and produced a variety of scientific evidences.

The first report on a patient with Alzheimer's disease (AD) was made by Alois Alzheimer in 1906. The patient died at the age of 51. During autopsy, marked cerebral atrophy (shrinkage of the brain) was observed, and many granular structures and degenerated nerve cells with thick tangled fibrils were seen mainly in the cerebral cortex.

Principal symptoms of Alzheimer's disease include progressive and irreversible dementia, particularly memory disorder, orientation disturbance (impairment in the ability to recognize one's surroundings and their temporal and spatial relationship to oneself), as well as impaired judgement. In the brain of patients with Alzheimer's disease, characteristic histo-pathological changes are noted such as marked cerebral atrophy, as well as deposition of senile

Figure 1: Senile plaques and neurofibrillary degeneration



Brain tissue sample taken from a patient with Alzheimer's disease was stained using a special staining technique.

Source: Materials provided by Professor Takeshi Iwatsubo

plaques (Figure 1) and tangled bundles of fibers called neurofibrillary tangles (Figure 1) due to the accumulation of abnormal proteins. Other brain changes in people with Alzheimer's disease include death and loss of nerve cells (neuronal loss) in areas of the brain (cerebral neocortex and hippocampus) that are vital to higher-order cognitive functions such as memory and learning.

The senile plaque is histopathological change observed only in patients with Alzheimer's disease or Down's syndrome, or the elderly, while neurofibrillary degeneration is associated with various diseases. During the course of Alzheimer's disease, senile plaques appear at the earlier stage, and neurofibrillary degeneration takes place at the advanced stage of the disease.

After the first report by Dr. Alois Alzheimer, studies on these structures started. Electron microscopic studies and subsequent immunohistochemical studies have provided clues for clarifying the causes of the accumulation of abnormal proteins. Currently, the mechanism of the development of Alzheimer's disease is well on the way to becoming elucidated by studies also adopting molecular biological techniques.

A certain type of Alzheimer's disease (familial Alzheimer's disease) has been found to occur in specific families. Molecular generic studies in such families have yielded many significant findings. In around the early 1990s, patients with Alzheimer's disease were found to have mutation on genes from a protein called amyloid beta. In parallel with studies on such genes, research on causative agents of neurofibrillary degeneration (see section 2.4.3) had been pursued. Then, researchers trying to elucidate the causative agents of Alzheimer's disease had competed fiercely to identify the major constituents of the two histopathologically abnormal structures, i.e., senile plaques and neurofibrillary tangles. At present, based on the results of many studies, the theory that accumulation of amyloid beta is deeply involved in the development of Alzheimer's disease has gained strong support. On the other hand, it has been reported that the major constituent of neurofibrillary tangles seems to play a significant role in inducing nerve cell death.

2.4 Current state of research on the mechanism of Alzheimer's disease development

2.4.1 Major molecules involved in the deposition of senile plaques

Deposition of senile plaques, one of the characteristic histopathological findings seen in the brain of Alzheimer's disease patients, results from the extracellular accumulation of amyloid beta protein (Aβ), which is a protein rarely seen in normal brains. Generally speaking, amyloid refers to the bundle of protein fibrils. Amyloid is barely soluble and is apt to clump (aggregation) and accumulate. The letter "β" in the name of amyloid β, which appears in the brains of Alzheimer's disease patients, is derived from the fact that the protein has a characteristic conformational structure called β sheet. This β sheet structure contributes to the protein's predisposition to aggregate.

Aβ is processed from the amyloid β precursor protein (APP) (Figure 2). The role of APP, which is expressed in all organs and tissues of the body, has not been fully elucidated as of yet.

In the processing of Aβ, two enzymes, i.e., β and γ secretases, are involved; β secretase works first, and then γ secretase.

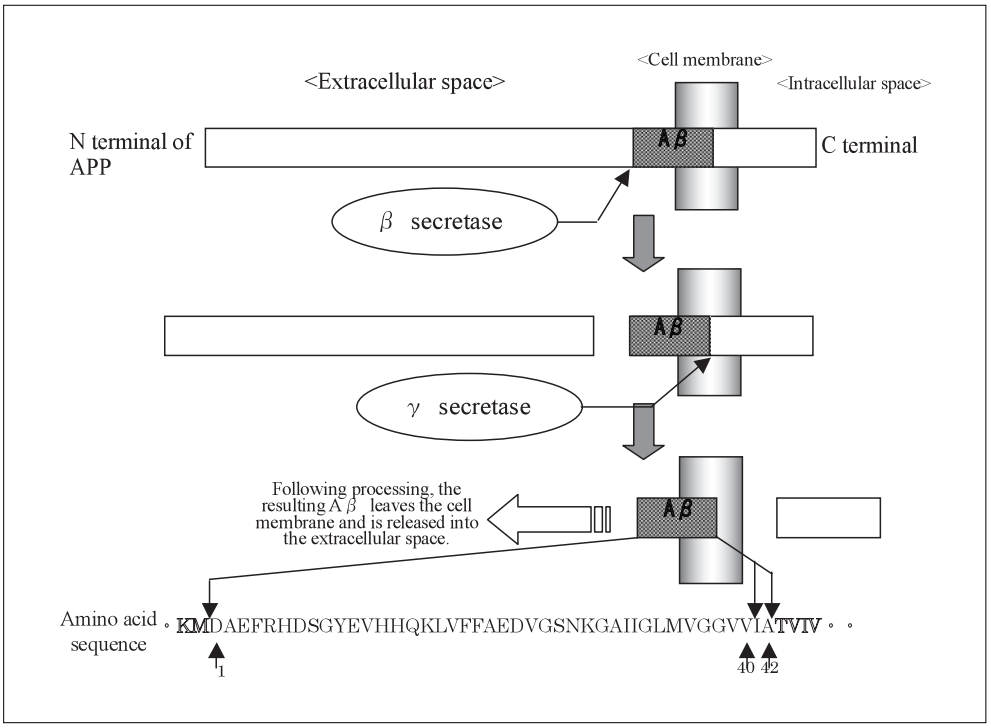
Aβ can be classified into two groups including Aβ40 and Aβ42 according to the number of constituent amino acids. Aβ42 has a stronger tendency to aggregate one another as compared with Aβ40. In addition, Aβ42 is closely involved in the formation and distribution of senile plaques.

2.4.2 Molecules involved in the degradation of Aß

In the human body, Aβ is steadily generated under normal conditions. However, under normal metabolic conditions, Aβ is thought to be rapidly degraded following its generation before it aggregates or accumulates. In studies on non-familial, sporadic Alzheimer's disease, it has been reported that decreased degradation of Aβ may lead to its accumulation.

While the mechanism of the degradation of Aβ has not been clarified, Japanese researchers recently

Figure 2: Processing from APP into Aß



reported new findings with regard to the mechanism. Nishimichi et al. at the Brain Science Institute, the Institute of Physical and Chemical Research has published an article entitled "Identification of the Metabolic Pathway involved in the Decrease of Aβ42 Predominantly Expressed in the Brain Tissue" in the journal Nature Medicine in 2000, which suggests for the first time that an enzyme called "neprilysin" is involved in the degradation of Aβ. Subsequently, in 2001, Nishimichi et al. published an article entitled "Control of Cerebral Metabolism of Aβ by neprilysin" in the journal Science. In the study reported in this article, he demonstrated that Aβ increases in the brain of neprilysin-knockout mice (mice whose genes for neprilysin are knocked out by genetic engineering) , showing that neprilysin is involved in the degradation of Aβ.

2.4.3 Mechanism of the development of neurofibrillary degeneration

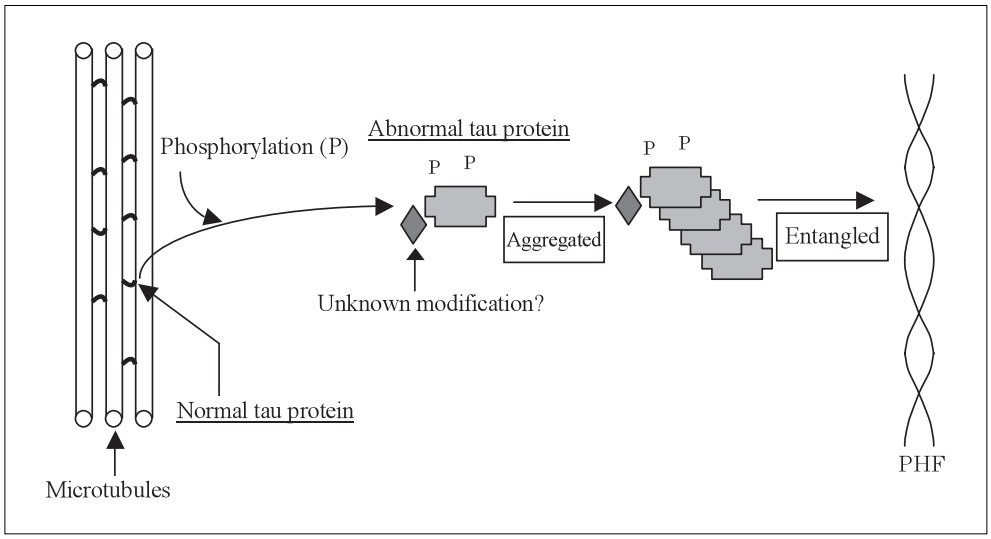
In addition to senile plaques, neurofibrillary tangles are characteristically seen in patients with Alzheimer's disease. As is the case with senile plaques, neurofibrillary degeneration is caused by the accumulation of abnormal proteins.

Neurofibrillary tangles are abnormal fibrous structures and are composed mainly of paired helical filaments (PHF) consisting of two helical proteins. In contrast to Aβ which forms senile plaques extracellularly, PHF is accumulated in nerve cells. Figure 3 shows the process of PHF generation. In nerve cells, there is an organelle called microtubule, whose major functions are to maintain cytoskeleton and transport substances intracellularly. Tau protein is a substance whose function is to place microtubules in a specific direction and at regular spatial intervals to stabilize them. When the tau protein is hyper-phosphorylated for some reason or another, it will leave the microtubule, and hyperphosphorylated tau proteins are believed to aggregate to form PHF. Moreover, it is speculated that PHFs also aggregate one another and accumulate in nerve cells, leading to neurofibrillary degeneration.

2.4.4 Challenges to be addressed through future research

With regard to the mechanism of the development of Alzheimer's disease, observational findings strongly support the hypothesis that onset of the disease is first triggered by the accumulation of Aβ, which is followed by the accumulation of hyperphosphorylated tau proteins, resulting in nerve cell death. Currently, investigation on the pathway from the accumulation of Aβ to the accumulation of hyperphosphorylated tau proteins is being actively conducted. In a recent

Figure 3: Normal tau protein and abnormal tau protein



Source: Authors' compilation by making reference to the materials provided by Professor Iwatsubo.

study using genetically engineered mice, it was reported that a certain relationship was actually noted between Aβ and hyperphosphorylated tau protein.

In addition, research on the mechanism of excessive phosphorylation of tau protein has also been performed. Such research will evolve into that aiming to find the mechanism through which development of Alzheimer's disease can be inhibited.

Furthermore, many studies on the ultimate mechanism of nerve cell death are also in progress. There are some diseases other than Alzheimer's disease, which are caused by excessive phosphorylation. herefore, it is expected that elucidation of the mechanism of the excessive phosphorylation will lead to advances in studies not only on Alzheimer's disease but also on some other diseases.

Concerning familial Alzheimer's disease, results of studies have indicated that there still exist Alzheimer's disease susceptibility genes, which have not been found so far, and the competition to identify such genes is becoming increasingly fierce.

2.5 Current state of development work on pharmaceutical products for Alzheimer's disease

No infallible remedy has been developed for Alzheimer's disease. Since therapeutic drugs for Alzheimer's disease with higher efficacy could produce large profits, research and development aiming at introducing such a drug into the market has been very actively conducted with the involvement of many companies. On the other hand, it is also important to develop prophylaxes, because histopathological changes in the brains of Alzheimer's disease patients have already become irreversible at the time when clinical symptoms of the disease appear.

The following paragraphs in this section briefly introduce major drugs currently used in the treatment of Alzheimer's disease, or are under research and development, as well as the current state of major studies targeting the development of therapeutic drugs.

2.5.1 Drugs for Alzheimer's disease

Currently, not many drugs are used in the treatment of Alzheimer's disease, and the drugs prescribed to patients with the disease are mostly represented by antipsychotic agents, anti-depressants, antianxiety agents, hypnotic drugs, etc., targeting symptoms associated with the disease including depression.

Donepezil hydrochloride (trade name: Aricept) is the only drug so far to have gained marketing approval in Japan for use in improving symptoms specifically seen in patients with Alzheimer's disease (approved in November 1999). It has been shown that acetylcholine, a neurotransmitter associated with memory, etc., decreases in the brains of patients with Alzheimer's disease.

Donepezil hydrochloride is an acetylcholinesterase inhibitor that interferes with the degradation of acetylcholine in the synapse to increase available acetylcholine. The drug can delay the progression of early-stage Alzheimer's disease to a certain degree.

2.5.2 Studies on therapies focusing on the accumulation of Aß

Aβ is thought to be closely involved in the development of Alzheimer's disease. At present, studies on the following five therapies aiming to inhibit the accumulation of Aβ are in progress:

Firstly, reports have been made on studies on "vaccine therapy" (administration of a segment of the Aβ peptide): Alzheimer's disease model mice in which APP is overexpressed were immunized with Aβ, leading to the generation of antibodies, which prevented the accumulation of Aβ within the mouse brain and even markedly decreased existing Aβ deposits, known as plaques. Secondly, results of studies on "antibody therapy" (passive immunization with antibody administration specific to the Aβ peptide) have also been reported. Studies on these two therapies have advanced rapidly and clinical studies on these therapies are underway in the United States. However, concerning the vaccine therapy, new problems to be tackled have arisen recently, including adverse reactions of the central nervous system.

Thirdly, several nonsteroidal anti-inflammatory drugs (NSAIDs) including indomethacin and ibuprofen have been reported to exert effects in the treatment of Alzheimer's disease. In addition, in studies using Alzheimer's disease model mice orally given NSAIDs and experiments using cultured cells, generation and accumulation of Aβ have been reported to decrease. While the mechanism of inhibition of Aβ generation and accumulation by NSAIDs are being clarified, further investigation is required.

Fourthly, studies on gamma-secretase inhibitors specifically targeting gamma secretase have been conducted. In experiments using Alzheimer's disease model mice, gamma secretase inhibitors have been reported to be effective in, for example, inhibiting the accumulation of Aβ. It is expected that gamma secretase inhibitors can be a class of the next-generation drugs, which are effective in preventing the onset and inhibiting the progression of Alzheimer's disease, and clinical studies on some gamma secretase inhibitors have started in the United States. However, gamma secretase has been found to have substrates other than APP, and there is a possibility that gamma secretase-mediated reaction with APP might be disturbed by such substrates, so there remain problems to be resolved before gamma secretase inhibitors are brought to the market as therapeutic drugs for Alzheimer's disease.

Lastly, studies focusing on beta secretase have been actively conducted recently. It has been reported that knockout mice missing genes for beta-secretase do not seem to exhibit any abnormality in general, and that accumulation of Aβ is not seen in the brains of such mice. Many pharmaceutical companies are reportedly competing fiercely to develop gamma secretase inhibitors as therapeutic drugs for Alzheimer's disease, but most of the results of studies they conducted have not been published. Introduction of gamma secretase inhibitors to the market requires further advances in research.

2.5.3 Studies on biochemical markers

Studies have also been performed on specific biochemical markers of Alzheimer's disease. As in the cases of other diseases whose severity or risk can be known from the results of blood tests including the quantitative evaluation of blood sugar and serum cholesterol, risk or stage of Alzheimer's disease might be known from the results of examination on specific biochemical markers, which may possibly lead to the prevention or delay of onset of the disease through adequate prophylactic treatment. Currently, studies are being pursued on the relationship between the level of Aβ or excessively phosphorylated tau protein in cerebrospinal fluid taken from Alzheimer's disease patients and the stage of Alzheimer's disease. However, many problems should be addressed before the utilization of such relationship for diagnosing the disease in that invasiveness of cerebrospinal fluid sampling is so high and that utilization of the levels of Aβ and excessively phosphorylated tau protein require data sampling not only from

patients with the disease but also from people without the disease. Up to this time, no specific molecular markers have been found other than Aβ42 and hyperphosphorylated tau protein in cerebrospinal fluid. Under such current realities, many problems have to be tackled before the preclinical diagnosis of Alzheimer's disease becomes utilizable in actual clinical practice, including the exploration of new molecular markers, determination of reference values and the development of less invasive diagnostic techniques.

2.5.4 Development of new materials for diagnostic imaging with PET

With regard to measures to investigate cerebral histopathological changes in living patients, development work is proceeding to develop techniques for detecting the distribution and the amount of Aβ in senile plaques and neurofibrillary tangles in the brain with the use of PET (positron emission tomography). The first isotope probe for use in such PET examination has been reportedly developed. Currently, fierce competition is being intensified to develop better isotope probes, which can pass through the blood-brain barrier and are specifically bound to Aβ for the intended time with unbound probes going out of the brain rapidly. The PET examination using such isotope probes will serve as a very useful technique in the diagnosis of MCI (mild cognitive impairment) discussed in the following section as well as in future preclinical diagnosis of Alzheimer's disease.

2.5.5 Methods for diagnosing very early dementia

Also under development are methods for diagnosing mild cognitive impairment (MCI: a condition characterized by mild recent memory loss without dementia or significant impairment of other cognitive functions), which is regarded as very early dementia but not clinically diagnosed as dementia. According to a report on Alzheimer's disease published in 1999 by the U.S. National Institute of Health, an epidemiological survey of a community cohort revealed that 40% of people who had been given the diagnosis of MCI in accordance with certain diagnostic criteria, developed Alzheimer's disease within 3 years of the diagnosis. In Japan, efforts are underway to make draft diagnostic criteria for MCI highly adaptable to Japanese people.

2.6 Strategies for promoting research on Alzheimer's disease in Japan

In March 1997, the Bioscience Section of the Scientific Council, Ministry of Education, Culture, Sports, Science and Technology submitted a report titled "Promotion of Brain Research at Universities, etc." and then, in May 1997, the Brain Science Committee, Life Science Section, Council for Science and Technology submitted a report titled "Long-term Prospects of Brain Research." In the latter report, three areas of brain research were set up including "Understanding the Brain," "Protecting the Brain" and "Creating the Brain." In addition, a strategic timetable was developed in the latter report, targeting the suppression of various diseases including Alzheimer's disease, which was planned to be overcome within 15 years (as of 1997). Moreover, also in the Second Science and Technology Basic Plan, elucidation of the mechanism of brain aging and suppression of nervous system diseases were adopted as challenges to be addressed.

Based on the above-mentioned policies, research in the field of brain science in Japan as a whole has been greatly encouraged and studies on dementia have also been promoted. In 1997, the "Brain Science Institute (BSI)" was established under the Institute of Physical and Chemical Research as the engine that will drive brain science research. At the BSI, the Laboratory for Alzheimer's disease and the Laboratory for Proteolytic Neuroscience of the Aging in Psychiatric Research Group take charge of studies on Alzheimer's disease and are investigating the mechanisms of the occurrence of neurofibrillary degeneration, nerve cell death, degradation of Aβ, etc.

Publicly funded studies aiming to address challenges to be dealt with for the suppression of Alzheimer's disease, which were invited from the public, have also been performed. Under the Scientific Research Subsidy System, various challenges to be addressed have been chosen as themes of fundamental studies (in the fields of

pathology, pharmacology, pharmaceutical sciences, medicine, neuroscience, etc.), which are to be promoted with public monetary support. In addition, studies on dementia (including those on Alzheimer's disease) have been conducted as studies in the fields with high priority or in special fields almost in succession since 1989. Furthermore, as part of the Millennium Project, "Studies in Special Fields C" has been set since 2000, and "Studies in Frontier Brain Science" including studies on Alzheimer's disease have been started to deal with one of the themes in the Studies in Special Fields C.

Under the Funds for the Coordination of Advancement of Technology System and under the Core Research for Evolutional Science and Technology (CREST) system set up by the Japan Science and Technology Corporation, brain-related themes have been selected for study to be publicly funded every year from 1997 and from 1995 to 2000, respectively. Under these systems, studies on Alzheimer's disease have been performed from 1996 to 2001.

In addition, also under the Scientific Research Subsidiary System established by the Ministry of Health, Labor and Welfare, studies on Alzheimer's disease have been conducted.

According to the Human Frontier Science Program (HFSP), monetary support has been provided to studies on brain functions within the international framework for the promotion of such studies. Within the framework, basic research on dementia including Alzheimer's dementia has also been performed.

2.7 Conclusion — Challenges to be addressed through research on Alzheimer's disease —

Now that several genes associated with the onset of Alzheimer's disease have been identified, postgenome research on the disease will assume more significance from this day forward. While elucidation of the pathways leading to abnormal protein accumulation is one of the important challenges to be addressed in future studies, as discussed in section 2.4, it is also significant to analyze conformational structures of proteins or complexes of proteins as functional units involved in such pathways. In addition, studies on SNPs (single nucleotide polymorphisms: a kind of genetic polymorphism) associated with sporadic (non-familial) Alzheimer's disease will become more important from now on. In order to promote such postgenome research, it is crucial to have collaboration among specialists in various fields including medicine, pharmaceutical sciences and science.

Since Alzheimer's disease will constitute a bigger concern with the increasing graying of Japanese society, studies on the disease need to be conducted more widely and deeply. In addition, since studies on Alzheimer's disease are not pure academic research but a sort of purpose-oriented research, it is desired that researchers who are not clinicians as well as experts in government, academia and industry should participate in such studies. Some people point out that Japan has no established system to introduce researchers in such fields as science, pharmaceutical sciences and agriculture into research on diseases.

Alzheimer's disease occurs "only in the highly developed human brains" and it is essential, in every study conducted by experts in the government, academia and industry, to use biological samples (tissue samples, DNA samples) taken from patients with the disease. Therefore, it is important to construct systems for appropriate collection and accessible supply of samples for research taken from Alzheimer's disease patients. Until now, even universities with attached hospitals have faced difficulty in obtaining samples for research from affected patients, and most institutes for research on Alzheimer's disease have purchased from overseas brain banks. In order to further facilitate studies on Alzheimer's disease from now on, it is required that brain banks be established in Japan to collect biological samples (samples of brain tissue, cerebrospinal fluid, blood, etc.) from a large number of patients with Alzheimer's disease and supply those samples to researchers with due consideration for the significance of informed consent, protection of private information as well as ethical implications of such sample collection and distribution.

Acknowledgement

This report summarizes the contents of the lecture delivered by Professor Takeshi Iwatsubo, Graduate School of Pharmaceutical Sciences, Faculty of Pharmaceutical Sciences, University of Tokyo under the theme "Recent trends in Research on Alzheimer's dementia" at the National Institute of Science and Technology Policy on December 11, 2001, while incorporating the data from our study.

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3

Trends in Research and Development of Functional Foods

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3.1 Introduction

Concerning the research and development of functional foods, it is clearly stated in the Comprehensive Strategy to Promote Science and Technology, planned in 2001 by the Council for Science and Technology Policy of the Cabinet Office, that "It is necessary to conduct scientific research on human health and food functions from the viewpoint of disease prevention to develop functional foods and new diagnostic techniques," and the research on functional foods has been referred to as one of the research fields on which more and more emphasis should be placed within the next 5 years or so.

In addition, in 1991, a system for the approval of "foods for specified health uses (FOSHU)" (foods that are intended to contribute toward attaining specific health purposes and for which license or approval for the claims to be listed on their labels that they help or are suited to maintain or improve health has been obtained from the Minister of Health, Labour and Welfare) was established under the Nutrition Improvement Law. Moreover, as of December 2001, the number of food items that have gained approval, etc., for FOSHU labeling climbed to 289, and the sales of FOSHU foods in fiscal 2001 was estimated to exceed 400 billion yen. In this way, FOSHU foods have rapidly penetrated into the life of the Japanese.

On the other hand, many challenges should be tackled in the research and development of functional foods including risk-associated, indiscriminate consumption by general consumers of so-called "health foods" due to the release of new information exaggerating the functionality of foods by the media, as well as limited scientific evidence showing the functionality of foods against the backdrop of the fact that very few research papers about food functionality have been published in major scientific journals on a worldwide basis.

This article outlines the present state of research and development of functional foods, and discusses subjects such as: i) how evaluation of food functionality should be conducted; ii) measures to be taken by the Japanese government to promote research and development of functional foods; and iii) how information on functional foods, which has been sorted out based on scientific evidence, should be provided to the Japanese people.

3.2 Definition, etc., of functional foods

3.2.1 General definition of functional foods

It has been known that foods have not only the i) primary function (function to supply nutrients) and ii) secondary function (function to gratify the five senses) but also the iii) tertiary function (function to beneficially affect human health, physical ability and mental state), for instance, a function to exert beneficial effects in terms of the maintenance of health or recovery to health by regulating physiological systems including the gastrointestinal system, circulatory system, endocrine system, immune system and nervous system. Against the backdrop of the fact that scientific evidences showing such tertiary functions of foods have been obtained, foods designed and processed so that they can exercise such body-regulating functions are generally called functional foods.

However, there have been no regulations in which the definition of "functional food" is clearly provided in Japan. Definitions relating to functional foods include the one in Article 8, Item 5 of the Enforcement Regulations of the Nutrition

Improvement Law, in which "foods that are to be taken by the people in daily diet for specific health-keeping purposes and for which license for claims to be listed on their labels that they may help to achieve such purposes has been obtained from the Minister of Health, Labour and Welfare" are defined as "foods for specified health uses (FOSHU)," and target processed foods in consideration of the need to assure the truthfulness of claims on labels relating to functional ingredients.

3.2.2 Difference in the definition between Japan and other countries

While there have been no clear definition of functional foods in other countries as well, the following scientific definitions given in Table 1 have been formulated by authoritative researchers, etc.

As can be seen from Table 1, no essential difference exists between the definition of functional food in the United States and that in EU, while the United States has legally defined "nutraceuticals" as a regulatory category separate from the functional food category. Nutraceuticals are defined as "foods derived from such naturally-occurring, physiologically active substances as those contained in dietary supplements, herb products, etc., and provide medical or health benefits, including prevention and treatment of diseases." Nutraceuticals are deemed to fall under the category of functional food in Japan and EU countries, but, in the United States, they are regarded as a separate category not covered by the functional food category, which characterizes the regulatory system for food products in the United States.

3.2.3 regulatory systems for foods with health claims

The regulatory system for foods with health claims was established in Japan in April 2001 as an extension of the labeling system for FOSHU foods (established in 1991) in order to cope with the growing complicated and diversified functions expected from foods against the backdrop of growing consumer awareness of nutrition and interest in promoting health. Under the system, a category for foods with nutrient function claims has been newly set up separately from that for traditional functional foods (Table 2). Foods with nutrient function claims are foods that correspond to such dietary supplements as those having penetrated deeply into the marketplace in the United States, etc., and for which the government has created specifications and labeling standards so that they can meet the recommended amounts of nutritional intake and can support health-related policies in Japan.

The range of foods falling under the FOSHU foods has been enlarged since April 2001 to cover FOSHU products in the forms of tablets or capsules.

3.3 Research and development of various functional food components

To date, many functional components of foods having beneficial effects on the gastrointestinal system, circulatory system, endocrine system, immune system, nervous system, etc., have been found based on scientific evidences obtained in epidemiologic studies, in vitro studies, studies

Table 1: Definitions of functional foods in the United States and the European Union (EU)

Country (name of the relevant researcher or research institution)	Definition
US (US Institute of Medicine)	Any processed food or ingredient for processed food that may provide a health benefit beyond the traditional nutrients it contains.
EU (Bellisle et al.)	Food products containing ingredients (including nutrients) that may exert a beneficial effect on one or more physiological functions of the body.

Source: Materials prepared by Dr. Morio Saito at the National Institute of Health and Nutrition, an independent administrative institution (IAI).

Table 2: Categories of Supplement Foods

Category	Definition	Sample Claim
Foods for specified health uses *(need to be licensed individually)*	Foods that are intended to contribute to a specific health purpose and for which license or approval for claims to be listed on their labels that they help or are suited to maintain or improve health has been obtained from the Minister of Health, Labour and Welfare.	・ This product may help maintain normal blood pressure. ・ This food product may help improve bowel movement.
Foods with nutrient function claims *(need to meet certain standards)*	Foods intended to contribute to the supplementation or supply of nutrients, which tend to be insufficiently taken by the elderly, people with unhealthy dietary habits, etc. When daily intake of the relevant nutrient from the food product meets a specific standard, the product can bear a specific claim about the functions of the nutrient	・ Vitamin D is a nutrient that promotes calcium absorption in the bowel and helps with bone formation. ・ Calcium is a nutrient necessary for the formation of bones and teeth. (Warning, etc.) ・ This product is not intended as a treatment for disease or to promote health by the intake of large amounts. product has not been individually evaluated by the Ministry of Health, Labour and Welfare.

Source: Authors' compilation by making reference to the materials prepared by the Ministry of Health, Labour and Welfare

using animal models, and clinical studies involving human subjects. The following sections detail the representative food-derived functional ingredients.

3.3.1 Lactic acid bacteria

Lactic acid bacteria, a group of bacteria that powerfully degrades carbohydrates into lactic acid, is mainly used in the processing of cheese, lactic acid bacteria drinks, etc. The physical form of their cultures may be added to such fermented food products to be taken by humans, and their cultures themselves are often ingested as a drug for controlling intestinal functions.

Known functions of lactic acid bacteria include: (1) promotion of intestinal peristaltic movement; (2) regulation of the intestinal bacterial flora; (3) inhibition of the proliferation of noxious bacteria; and (4) boosting of the immune functions.

In recent years, a novel term "probiotics" (a concept that intake of live microorganisms in adequate amounts may provide benefits to hosts by improving the intestinal bacterial flora) has become familiar to us.

In European countries, probiotics has become a field that is ripe for scientific studies on its clinical effects on various diseases, its action mechanism, etc. For example, the group led by E. Isolauri of the University of Turku, Finland has shown that the intake of Lactobacillus rhamnosus is associated with decreased incidence of atopic dermatitis in children.

In addition, in Japan, under the initiative of the Japan Bifidus Foundation, etc., universities and food manufacturers have started to actively conduct research and development of probiotic products and it is expected that future evolution of such research will lead to the elucidation of the molecular mechanism underlying the regulation of immune responses by probiotic cultures.

3.3.2 Oligosaccharide

The prefix "oligo" comes from the Greek word meaning "few." While carbohydrates such as starch and cellulose are called polysaccharides, complexes of 2-10 molecules of such monosaccharides as glucose and fructose are called oligosaccharide. The representative examples of oligosaccharides are fructo-oligosaccharide, soybean oligosaccharide, galacto-oligosaccharide and xylo-oligosaccharide.

Oligosaccharide is known to have, for example, the following functional features: (1) to have lower calorific value because it is not absorbed at the wall of the small intestine and reaches the large intestine; (2) to promote the activities of Lactobacillus bifidus by inhibiting the proliferation of noxious bacteria in the large intestine; and (3) to have a weaker sweet taste and is less prone to cause dental caries. Many FOSHU foods containing oligosaccharides have been put on the market with such nutrient function claims as "beneficial for the intestines" and "improves gastrointestinal health."

Since the development of manufacturing techniques (techniques for synthesis or extraction) is a significant challenge to be dealt

with in order to commercialize functional oligosaccharides, sugar alcohols, the Japanese government has given higher priority to research and development activities aiming to develop such techniques when allocating research funds.

3.3.3 Polyphenols

Polyphenols are pigments contained in many foods and may function as antioxidants. Some polyphenols are known to exert physiological effects by inhibiting the overproduction of reactive oxygen species that may cause arteriosclerosis and aging. In France, the incidence rate of death due to coronary artery disease is lower than those in other European countries despite frequent intake of diets high in animal and dairy fats, which is called the "French paradox." As the clue to this paradox, Renaud reported the correlation between higher wine consumption and the lower incidence of death due to coronary artery disease in an English medical journal "The Lancet" in 1992. Furthermore, in 1993, Frankel et al. published a report in "The Lancet" that polyphenols, antioxidants contained in red wine, exhibit inhibitory effects in vitro on the oxidation of LDL-cholesterol, which is a crucial step to the development of arteriosclerosis, and polyphenols gained the spotlight overnight. The representative examples of known polyphenols include catechins contained in green tea, red wine, etc., tannins, rutins found in onions, etc., as well as isoflavones contained in soybeans.

The catechin, a representative polyphenol, is an ingredient in green tea giving the astringent taste and is known to have physiological effects including, for example, (1) antioxidant effects, (2) antibacterial action, (3) anticariogenic effect, (4) deodorant effect, (5) reactive oxygen scavenging effect, (6) inhibitory effect on serum cholesterol increase, (7) inhibitory effect on blood glucose increase, (8) inhibitory effect on blood pressure increase, (9) antitumor action, (10) antiallergic action, (11) antithrombotic effect, and (12) ultraviolet-absorbing effect.

3.3.4 Lipids

Since triacylglycerol represents about 95% of dietary lipids, the functionality of lipids has been studied with regard to triacylglycerol as having a typical fatty acid composition. There are two types of fatty acids making up lipids, including saturated fatty acids, which have all the hydrogen the carbon atoms can hold, as well as unsaturated

Table 3: Types of food items, etc., within each category of FOSHU health claims

Category of health claims	Types of foods	Relevant food components
Food suited for those who want to improve gastrointestinal health	Fermented milk, lactic acid and bacteria drinks, carbonated beverages, soft drinks, powdered soft drinks, table sugar, cookies, instant noodles, fried instant noodles, cereal, etc.	Lactic acid bacteria, fructo-oligosaccharides, xylo-oligosaccharide, soybean oligosaccharide, actosucrose, galacto-oligosaccharides, isomalto-oligosaccharides, psyllium seed husk, indigestible dextrin, etc.
Food suited for those who take insufficient amounts of calcium	Soft drinks, tofu (soybean curd)	CMC (Citric Acid, Malic Acid and Calcium), CPP (Casein Phospho Peptide)
Food suited for those who care about cholesterol levels	Soft drinks, biscuits, sausage, cooking oils, etc.	Soy protein, chitosan, depolymerized sodium alginate, diacylglycerol
Food suited for those who have higher blood pressure	Soft drinks, lactic acid and bacteria drinks, powdered soup	Glycoside from Eucommia leaves, gasein dodeca peptide, lactotripeptide, katsuobushi (dried bonito) oligopeptide
Food suited for those who care about anemia	Soft drinks	Heme iron
Food suited for those who worry about dental caries	Chocolate, gum, candy	Maltitol, palatinose, erythritol, green tea polyphenols
Food suited for those who care about blood glucose	Soft drinks, powdered soft drinks	Indigestible dextrin

Source: Authors' compilation by making reference to the materials prepared at the National Institution of Health and Nutrition

fatty acids, which contain one or more double bonds between carbon atoms. Among unsaturated fatty acids, the ones in which the first double bond occurs three carbons from the methyl (CH_3) end of the molecule, are called n-3 (omega-3) series. Omega-3 fatty acids have long been thought to have a LDL-cholesterol-lowering effect, and various functions of those fatty acids, particularly docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA), are already on their way to becoming elucidated.

Among the effects of DHA, not only the LDL-cholesterol-lowering effect but also beneficial effects on the susceptibility to allergy, vision-improving effect, anti-cancer effect, etc., have recently received attention.

Moreover, the intake of diacylglycerol, which is processed from plant oil, has been proven to be associated with a lower rate of postprandial increase in blood triglycerides, and cooking oils containing diacylglycerol have gained licenses for FOSHU labeling and have rapidly penetrated into the Japanese marketplace in recent years, attracting people's attention.

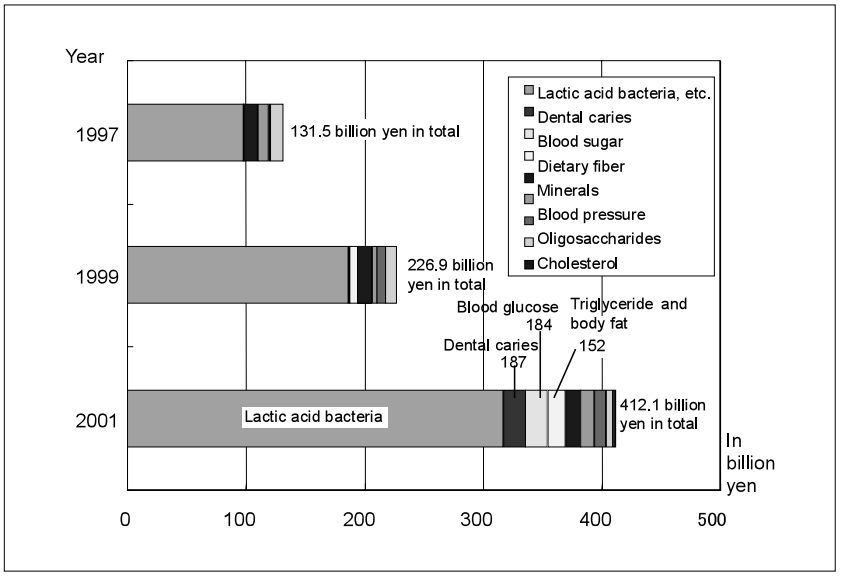
3.4 Trends in research and development of foods with health claims

As mentioned at the outset of this article, the total number of food product items that have gained approval, etc., for FOSHU labeling, for which a regulatory system was established in 1991, climbed to 289 as of December 2001. In addition, the number of product items that gained approval for FOSHU labeling reached an all-time high in 2001. The current categories of health claims, types of food items falling under each category, as well as the relevant functional food components are summarized in Table 3.

The "types of foods" and the "relevant food components" within the category of "food suited for those who want to improve gastrointestinal health" cover a fairly broad spectrum, and a survey conducted by the Japan Health Food and Nutrition Food Association showed that product items falling under this category represent as high as 57.8% of product items that have gained approval for FOSHU labeling.

Moreover, according to a questionnaire survey targeting food manufacturers conducted by the Japan Health Food and Nutrition Food Association, the sales of FOSHU products in fiscal 2001 was 412.1 billion yen (based on manufacturers' suggested retail prices), having increased by 182% from 226.9 billion yen in fiscal 1999. Among the FOSHU foods, marked increase in the sales of FOSHU products intended for those who care about "dental caries," "blood glucose" and "serum triglyceride and body fat" is worthy of special remark. Based on these data and in light of trends in application for FOSHU approval by food

Figure 1: Sales of FOSHU products by functional component or targeted health-related condition



Source: Materials prepared at the Japan Health Food and Nutrition Food Association (a legally incorporated foundation)

manufacturers, the Japan Health Food and Nutrition Food Association expects that the ratio of FOSHU food products (including foods in the above-mentioned three groups) other than those using lactic acid bacteria to all FOSHU products will increase.

In the process for putting FOSHU products on the market, in vitro studies, studies using experimental animals and clinical studies involving human subjects are conducted by food manufacturers to evaluate the efficacy and safety of the relevant food components, and evaluations of candidate FOSHU foods are officially performed based on scientific data obtained in such studies before the approval for FOSHU labeling. However, problems exist in the process, including the fact that studies for efficacy and safety assessment are conducted in as few as about several tens of subjects, as well as the fact that ingestion periods in such studies are relatively short (about 1 month in ordinary cases; about 3 months at the longest).

3.5 Trends in policies on functional foods in countries other than Japan

3.5.1 Trends in the United States

In the United States, under the Nutrition Labeling and Education Act (NLEA), the Food and Drug Administration (FDA) has authorized 12 health claims (reduction-of-disease-risk claims) for nutrients or other substances in conventional foods or dietary supplements that have been shown to be related to a disease or health-related condition based on sufficient scientific evidence (Table 4). Food manufacturers may make these FDA-authorized health claims on the labels of the processed food products, etc., they manufacture and market without individual petition to FDA.

On the other hand, among functional foods, a characteristic trend observed in the United States is toward high market penetration of dietary supplements marketed in the forms of tablets, capsules, liquid or powder. Under the Dietary Supplement Health and Education Act (DSHEA), dietary supplement products may bear structure/function claims on their labels, which describe the effect a particular food or nutrient has on the structure or function of the body. When a food manufacturer intends to put a dietary supplement product on the market, the manufacturer must notify the FDA about the ingredients of the relevant product, and details of the structure/function claims to be made.

Nevertheless, it has been pointed out that functional foods and dietary supplements still have safety problems, and the US government, as its national nutritional policy, would rather control and regulate them to promote proper intake by consumers than try to get them into widespread use. In 1993, the Office of Special Nutritionals was established in the FDA and constructed a database on the adverse events associated with the intake of dietary supplements (The Special Nutritionals Adverse Event Monitoring System) to provide convincing information that enables consumers, etc., to take dietary supplements safely through candid disclosure of such information to consumers, etc., on the Internet. In this database, data on 2,621 cases of health hazards and an associated 3,451 items of dietary supplements have been stored during the period from 1993 to October 20, 1998 (the database has not been updated since October 20, 1998). Based on the information entered into the database, the most commonly reported symptoms include vomiting,

Table 4: Health claims authorized by FDA

	Type of health claim by food components
1	Calcium and Osteoporosis
2	Dietary Lipids (Fat) and Cancer.
3	Dietary Saturated Fat and Cholesterol and Risk of Coronary Heart Disease
4	Dietary Sugar Alcohol and Dental Caries
5	Fiber-containing Grain Products, Fruits and Vegetables and Cancer
6	Folic Acid and Neural Tube Defects
7	Fruits and Vegetables and Cancer
8	Fruits, Vegetables and Grain Products that contain Fiber, particularly Soluble fiber, and Risk of Coronary Heart Disease
9	Sodium and Hypertension
10	Soluble Fiber from Certain Foods and Risk of Coronary Heart Disease
11	Soy Protein and Risk of Coronary Heart Disease
12	Stanols / Sterols and Risk of Coronary Heart Disease

Source: Authors' compilation by making reference to the material titled "Food Labeling and Nutrition" published on FDA's home page

diarrhea, headache, etc., while it should be noted that 184 cases of "death" have also been reported.

3.5.2 Trends in countries other than Japan and the United States

When turning our eyes away from the United States toward EU countries, there have been no directives concerning health claims, and discussions are under way on the concept of and labeling for dietary supplements in EU member countries.

In the Codex Alimentarius Commission (in the FAO/WHO food standards program), adoption of health claims was decided in the 24th Workshop on Food Labeling held in May 1996 and discussions have been continued about health claims since the 25th Working Party was held in April 1997, but agreement has been reached only at Steps 1-3 (the stage for final approval is Step 8).

Among the achievements in research and development activities in EU countries, world attention has focused, for example, on xylitol, which has an anticariogenic effect and on which studies advanced considerably in the 1970s, as well as a margarine product named "Benecol" developed in 1995, which contains "plant stanol esters" and helps maintain normal serum cholesterol levels. Both of them were developed in Finland. In Finland, the National Technology Agency of Finland (TEKES) takes charge of the financial support for the research and development of functional foods. In the TEKES's research and development program entitled "Innovation in foods" to be implemented from 2001 to 2004, high priority was assigned to research and development activities in the field of food and health, and research funds invested into this field totaled up to 50 million Euros (approx. 6 billion yen). In this program, special emphasis is placed on the efficient commercialization of the results of research and development activities under the program as well as on the promotion of collaboration between people in the field of food science and people in other fields (including medicine and biotechnology).

3.6 Circumstances surrounding the promotion of research and development of functional foods in Japan

Concerning the circumstances surrounding the promotion of research and development of functional foods by the Japanese government, as shown in Table 5, research project funds provided by the Ministry of Agriculture, Forestry and Fisheries make up a sizable proportion of all funds allocated by the government.

During three years from 1997 to 1999, the Ministry of Education, Culture, Sports, Science and Technology funded the Funds for the Coordination of Advancement of Technology to i) research for the evaluation and elucidation of the antioxidative properties of foods, ii) research for the evaluation and elucidation of the inhibitory effects of foods on the aging-related change in brain functions, and iii) research for the elucidation of the physical properties of foods related to mastication (chewing) as "research aiming at the comprehensive analysis of food functions with the graying of Japan in view as well as at the application of the results of the analysis," in which many researchers from the Ministry of Agriculture, Forestry and Fisheries, Ministry of Education, Science, Sports and Culture, Ministry of Health, Labour and Welfare, the Environment Agency, and private companies participated.

In the past, the Ministry of Agriculture, Forestry and Fisheries provided research funds mainly for research on the isolation and identification of functional components in foods as well as research on the development of methods for evaluating the functional components in foods. Recently, research institutions under the Ministry have launched new challenges such as research on the interaction between functional components and one aiming at the utilization of combinations of functional components for better dietary habits. In addition, the Ministry has given financial support to private companies, etc., for, as example, their research on the methods for synthesizing functional components, particularly carbohydrates, as well as research aiming at the development of methods for manufacturing

Table 5.: Amounts of budget for main research programs on functional foods in fiscal 2002
(Unit: million yen, figures in parentheses are amounts in fiscal 2001.)

(Ministry of Agriculture, Forestry and Fisheries)

Research at public research institutions	Comprehensive research on the functionality and safety of foods for the establishment of healthy eating habits (planned term: 2000-2005)..... 355 (255) The purpose of this program is to promote comprehensive research on the functionality and safety of foods for the purpose of establishing healthy eating habits that may contribute to the prevention, etc., of lifestyle-related diseases, with the aim of realizing a vigorous society where many people live to an advanced age in good health. (Details of the research) • Elucidation of the mechanism of the action of functional components as well as interaction between such components • Evaluation of the effects of functional components in vivo • Proposal for the establishment of healthy, Japanese-style eating habits by utilizing two or more functional components
Publicly funded research at private companies, etc.	Program for the development of techniques for the multipurpose utilization of carbohydrates produced by the application of carbohydrate engineering (term: 1998-2002) ..... 36 (53) The purpose of this program is to develop, for example, techniques for the efficient production of useful carbohydrates created by applying the results of research by independent administrative institutions as well as to promote the development of manufacturing methods for novel foods utilizing such carbohydrates for many purposes.
	Program for the development of techniques for the improvement of the functionality of foods (planned term: 1999-2003) ..... 56 (74) The purpose of this program is to design and improve functional components of foods by using leading-edge technologies such as biotechnology as well as to promote the development of new ingredients for foods with improved functionality, reaction at the time of eating, taste, etc.
	Program for the development of new techniques for the isolation and extraction of components of foods to be utilized in the food industry (planned term: 2000-2004) ..... 49 (73) The purpose of this project is to promote the development of, for example, supercritical fluid extraction techniques, and isolation or extraction techniques utilizing membranes with the aim of efficiently isolating, extracting and concentrating food components for general-purpose use by applying the results of research conducted at independent administrative institutions.
	Program for the development of techniques for the evaluation and manufacturing of health-oriented foods by the application of life sciences (newly adopted program)(term: 2002-2005) ..... 58 (0) The purpose of this program is to scientifically evaluate the effects of foods by utilizing biomarkers (simple biological markers), etc., found at independent administrative institutions as well as to promote the development of methods for manufacturing foods that may help maintain good health.
Others	Program for research and development aiming at the creation of new programs by the Institute for the Promotion of Research on Bio-Oriented Technology Research Advancement Institution (BRAIN) (planned term: 2000-) • Development of functional crops with health benefits (rice and vegetables with, for example, preventive effects on lifestyle-related diseases, cedar pollen allergy and infectious diseases) .....(188) • Development of foods with health claims utilizing the functional components of citrus fruits .....(56) • Development of foods utilizing the antiallergic effects of tea.....(54) (The budget for this program is provided as that for contracted research activities by the government-academia-industry consortiums.)

Budgets for programs listed in the box in the "Others" row are not funds that were directly earmarked in the national budget for those programs in fiscal 2001, and the amount of budgets for those programs in fiscal 2002 have not been determined yet.

(Ministry of Health, Labour and Welfare)

Programs for research in human genome, regenerative medicine, etc.	• Research for the assurance of the safety of foods produced by the application of biotechnology and development of multifunctional foods ..... (100) (Only a very small amount of funds was provided for the development of multifunctional foods.)
Programs for comprehensive research on foods and chemical substances (This program corresponds to the one that had been called "Programs for comprehensive research for Safety in Daily Living" until 2001.)	• Research on the safety and effects of FOSHU ingredients ..... (14) • Research on the safety and effects of the ingredients for FOSHU foods ..... (16) • Research on the safety and effects of FOSHU ingredients ..... (10)
Programs for comprehensive research in human sciences including drug discovery Programs for research for the evaluation of medical techniques	• Research on the inhibitory effects of transesterificated lipids containing EPA and DHA on body fat deposition ..... (2) • Research for the evaluation and analysis of new functional food ingredients from the standpoint of food science..... (7) • Research for the establishment of methods for certification tests of hypocariogenic, noncariogenic and anticariogenic foods as well as for the application and popularization of such methods ..... (4)

*Since programs funded by the Ministry of Health, Labour and Welfare are those for which themes of research in various fields including food science were invited from the public, budgets for the programs listed above could not be calculated for 2002.

Source: Authors' own compilation

functional foods.

On the other hand, the Ministry of Health, Labour and Welfare (MHLW) adopts just a few research programs on functional foods every year, as programs to which the MHLW Scientific Research Funds are to be provided by the Ministry, although in small amounts, as part of research funding projects for which themes for research are invited from the public, including the Comprehensive Research Project on the Safety of Foods and Chemical Substances and the Comprehensive Research Project on Human Science such as Drug Discovery. The programs mainly include those for research for the evaluation of safety and efficacy of FOSHU foods, and the researchers at the National Institute of Health and Nutrition, National Institute of Infectious Diseases, etc., are in charge of research for the evaluation of interaction between FOSHU foods and drugs, as well as risks associated with the intake of FOSHU foods by disease-affected people.

3.7 Conclusion
— Challenges to be addressed in future research and development of functional foods —

A broad view of the efforts that are underway in Japan to promote research and development of functional foods revealed the following challenges to be addressed in future research and development activities:

(1) Promotion of research for the accumulation of substantial scientific evidences

While in vitro studies, studies using experimental animals, clinical studies involving human subjects, etc., have been conducted in the process of research and development of functional foods, including FOSHU foods as a main subcategory of foods with health claims, problems still exist in the process, including, for example, the functionality of foods is evaluated in studies involving human subjects with limited sample size and with relatively short ingestion periods.

In order to further promote research and development of functional foods, continuous efforts to reinforce research techniques, including the development of biological markers that can be utilized in the exploration of functional components and in the evaluation of such components, are of importance. From now on, it may be necessary to evaluate the efficacy of functional foods on a massive scale and with a long-term perspective by grasping the actual conditions of the consumption of functional foods by consumers and by epidemiologically analyzing the efficacy of such foods in terms of maintenance and improvement of health.

(2) Risk factors for diseases and ways in which research on functional foods should be conducted

Studies on food functionality have often been conducted by isolating a single component from the relevant food to examine the presence or absence of beneficial effects of the component, and recent studies have yielded splendid products including the identification of novel functional food components.

The basic methodology of current research on functional foods is that, by targeting a single disease risk factor (e.g., cholesterol levels), a functional food should be designed so that it can reduce the risk of the relevant disease. However, in light of the fact that diseases are actually induced by two or more independent risk factors, it may also be necessary, in the future, to consider new methods for designing functional foods targeting two or more risk factors.

(3) Establishment of systems for research enabling the application of the results of research and development of functional foods to actual diet

In order to pursue research on functional foods with a macroscopic purpose to improve the health of the Japanese, it may be essential to establish not only systems for research by people belonging to food manufacturers or agricultural departments at universities, but also systems for research for the utilization and evaluation of functional foods by, for example, investigating whether optimum amounts of functional components are received by the people from daily diet, investigating appropriate methods for preparing functional foods, and assessing the

applicability of functional foods to preventive medicine.

In Japan, comprehensive researches on the metabolism and recommendable amounts of intake of nutrients, kinds and composition of foods, methods for preparing foods, etc., have been conducted exclusively by authoritative research groups at departments oriented toward domestic science (nutritional science and food science) at universities. However, in 1999, 941 and 266 out of about 43,000 postgraduates at the domestic-science-oriented departments decided to take a master's course and doctoral course, respectively, at a graduate school in the course of domestic science, indicating the fact that the number of postgraduates who decide to proceed to a graduate school in the course of domestic science tends to be much smaller than those in other academic courses. In addition, people as human resources who are conversant with analytical methods in organic chemistry have not sufficiently developed in Japan. Currently, there is immense pressure from medical institutions for domestic-science-oriented universities to develop supervising dieticians as human resources having expertise that enables them to play active parts as medical staff, so, being the case, it may be difficult for such universities to put energies only into fostering researchers who are conversant with analytical methods in organic chemistry. Therefore, for the time being, it is desired that the interchange of researchers who are playing leading roles in the field of chemical analysis of functional food components be promoted and that measures be taken to aid such researchers in securing minimum access to facilities, equipment and funds that are required in laboratories for the study in domestic science. In addition, we should recognize the significance of the functions served by "faculties of nutritional science within medical departments of universities," which rarely exist now in the universities in Japan.

(4) Supply of information on functional foods to consumers

As indicated by the circumstances surrounding dietary supplements in the United States, excessively great reliance on functional foods and intake of such foods in incorrect ways may pose health hazards to consumers. In consideration of such risks associated with the intake of functional foods, the FDA has taken measures, in addition to the measures mentioned in Section 3.5, to protect consumers from such risks in collaboration with scientists, including the supply of information on its home page on the scientific findings from research on functional foods and amounts of intake that are deemed acceptable to secure consumers' safety*. In addition, the FDA, on its home page, has advised that pregnant women as well as patients with such conditions as diabetes mellitus, hypertension and heart disease should consult with a doctor before they start taking such foods, and has called attention to the interaction between functional foods and drugs.

* http://www.cfsan.fda.gov/~dms/ds-savvy.html
(Tips For The Savvy Supplement User:)

In Japan, on the other hand, information on functional foods based on scientific evidence is infrequently provided by the government agencies concerned at present. In recent years, there have been increasing opportunities for consumers in Japan to obtain information on dietary supplement products developed and manufactured in foreign countries, and it has become increasingly easy for Japanese consumers to buy such products by mail order, etc. Under these circumstances and in light of the fact that a lot of complaints (10,688 complaints in fiscal 2000) about so-called "health foods" have actually come into the National Consumer Affairs Center of Japan from consumers who suffered from health hazards associated with the intake of such foods, the government agencies concerned, from now on, should provide not only information concerning the labeling system within the jurisdiction of the competent authorities of the government but also detailed information on risks associated with the intake of functional foods based on scientific evidences. Moreover, it is also important to promote research on functional foods to obtain scientific evidences about the effects of excessive intake and interaction with drugs.

Acknowledgements

Together with data from our study, this article summarizes the contents of the lecture delivered by Mr. Morio Saito, director of the Department of Food Science Research for Health at the National Institute of Health and Nutrition, under the theme "Trends in Research and Development of Functional Foods and Foods for Specified Health Uses" at the National Institute of Science and Technology Policy on February 15, 2002.

We are deeply grateful to Dr. Saito who, on the occasion of the making of this article, willingly provided us with guidance and the related materials. In addition, our profound thanks go to Mr. Kazuo Takimura at the General Affairs Department of the Japan Health Foods and Nutrition Food Association (a legally incorporated foundation) as well as to Professor Yukie Ikegami at the Faculty of Food Science, Department of Home Economics, Otsuma Women's University for providing us with valuable information.

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4

Trends in Research and Development on Next-Generation Devices (from IEEE IEDM)

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4.1 Introduction

The IEEE IEDM (International Electron Devices Meeting) was held in Washington DC, the United States, from December 2 through December 5, 2001. This meeting is known as one of the most authoritative meetings that serve as opportunities for presenting achievements of research into leading-edge technologies.

Each year, the latest achievements are presented at the meeting, including presentations on silicon MOS devices, which have increasingly been downsized, single-electron transistors (SETs), and carbon nanotube devices (also referred to as CNTs: carbon nano-tube transistors).

The number of attendants drastically decreased in 2001 due to the September 11 terrorist attacks and the IT slump (according to the organizer, the number dropped from approx. 2,000 in 2000 to 900 in 2001). However, there was a hot atmosphere in the venue since much greater achievements than had been previously expected were made in many fields including a presentation by IBM on a carbon nano-tube transistor, which indicated the device's higher feasibility and scalability than that of Si elements, and Fujitsu's presentation on an SOI MOS transistor that achieved the high level of RF property, which had been estimated to be achievable in around 2016 on the roadmap.

Concerning the participating nations, this year's meeting was characteristic in that European and Asian countries gained power in addition to the existing US-Japan bipolar structure. From Europe, even those nations having relatively small economic scales (e.g., Greece and Iceland) participated in the meeting by responding to research into leading-edge devices, which require huge investments, through multinational alliances. It can be said that efforts are being made by the EU as a whole to grapple with research into leading-edge devices.

In Asia, it is notable that South Korea and Taiwan, which are specialized in memory devices and liquid crystal devices, are expanding their spheres of research to basic areas, such as quantum devices, in addition to application products.

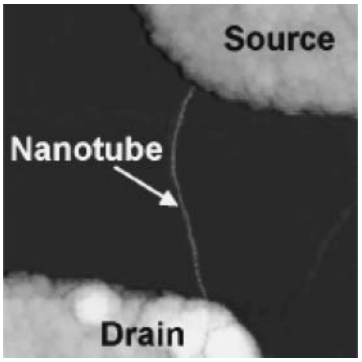
As courses of direction in research and development, it was noticeable that unlike that of Japan, particular focus was placed on the development of high dielectric-strength transistors (in Japan, development of GaN-based devices is focused on short-wave luminescent elements such as blue LED and laser), Si-Ge transistors and MEMS (micro electro mechanical systems).

Concerning MEMS, bio-MEMS and microfluidics discussion sessions were given separate timeframes from other sessions. Thus, it can be said that the IEEE Electron Device Society is particularly interested in these interdisciplinary areas.

Semiconductor device technologies are one of the technologies for which Japan has maintained a very high level in terms of international competitiveness. However, given that European and Asian nations are rapidly gaining power and pressing hard on Japan also in those fields close to basic research, it is necessary for Japan to establish focus areas of research and devise strategies from a comprehensive point of view as a country.

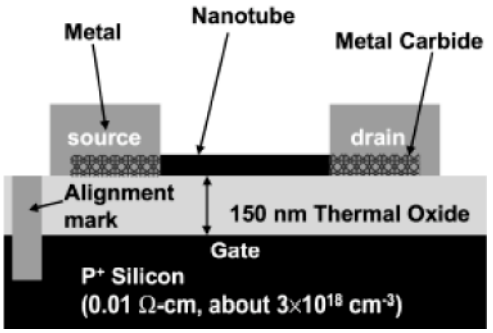
Japan has ceded its top position in production volume to South Korea in the fields of DRAMs and liquid crystal devices, where Japan used to have overwhelming power. Taiwan, which has emerged as a foundry for US companies, is building up

Figure 1: Carbon nanotube transistor



(Interval between the source and drain electrodes is 1 μm.)

Figure 2: Structure of the carbon nanotube transistor



leading-edge technologies and know-how on process technologies Thus, it is becoming extremely difficult for Japan to maintain its top position.

With regard to approaches toward research and development investments, borderless, large-scale investments are increasing, such as basic research by European countries that have formed alliance within the EU circles, sharing of design and process technologies between US manufacturers and Taiwanese foundries, and a joint venture in liquid crystals between Philips of the Netherlands and LG of South Korea.

With regard also to cooperation between academic, business and governmental sectors, the approaches taken in the US and Europe appear to be advancing more than Japan in terms of distribution of participating institutions.

This report will explain the research achievements in leading-edge devices presented at the IEEE IEDM, and examine the current problems and future challenges through comparison of research activities between the United States, Europe and Asian countries while identifying the position of Japan amid the global trend in research and development of advanced devices.

Table 1: Comparison between CNFET (presented at this meeting) and Si-MOS

	p-CNFET	100nm MOSFET	25nm MOSFET
Transconductance (μS/μm)	122	1000 (nFET) 460 (pFET)	1200 (nFET) 640 (pFET)
External resistance (Ω-cm per side)	< 70	~ 66 (nFET) ~ 143 (pFET)	~ 40 (nFET) ~ 86 (pFET)
Gate insulator(nm)	150	2.0	0.8

4.2 Presentation that attracted much attention

This section introduces those research achievements that attracted much attention at the meeting (the following figures are all excerpts from the collection of documents prepared for the IEEE IEDM).

1) Carbon Nanotube Transistor (CNFET)

This transistor was presented by the IBM Watson Lab. The presentation was made as part of the Nanoelectronic Devices session, which also contained a presentation for SET (single electron transistor). Nevertheless, although only half of the venue's seats was filled in the first part of the session, there were even standees just before the CNFET presentation started. Thus, the presentation was one of the hottest ones at this year's IEDM.

The main feature of the presentation demonstrated that the new device showed a high level of performance comparable to Si-MOS through improvements on the electrode structures of a series of the carbon nanotube transistors presented in 2001, and that the new device can be upgraded through down-scaling (i.e., miniaturization) as with Si-MOS.

As shown in Table 1, the carbon nanotube transistor's transconductance — factor that represents the performance of a transistor — is smaller than that of the Si-MOS. The reason is because the gate length is 1 μm greater than and the gate oxide film is 150 nm longer the Si-MOS

transistor. It is estimated that with the gate length at 100 nm, performance of 1,257 μS/μm can be achieved, and at 25 nm, 5,028 μS/μm can be achieved.

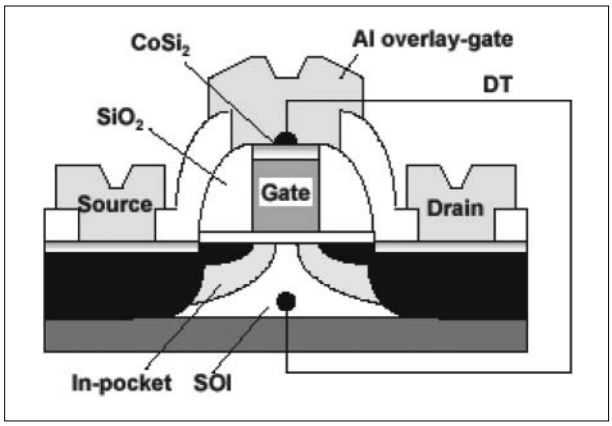
It was also impressive that the presenter mentioned Dr. Iijima of Japan as the discoverer and inventor of the carbon nanotube, thus correctly acknowledging the origin of their research.

2) SOI Transistor

Fujitsu Laboratories of Japan presented a Si-MOS whose fmax (maximum oscillation frequency) reaches 185 GHz (double the present value). In addition, this device's noise level is as low as that of AlGaAs/GaAs HEMT (i.e., 0.8 dB at 10 GHz).

The device is also characteristic in that it has the SOI (silicon on insulator) structure, as indicated in Figure 3, and the DT (dynamic threshold) structure where the gate electrode is connected to the body.

Figure 3: Structure of DTMOS



Thanks to this achievement, the high level of RF property, which had been estimated to be reachable around 2016 on the research and development roadmap of ITRS, was realized in 2001.

It is enormously significant that Si-MOS transistors, which can be densely integrated at low power consumption and are highly cost effective, may be used also in the RF area, which was previously achieved only with expensive compound semiconductors or high power-consumption Si bipolar transistors.

3) High Dielectric-strength GaN HEMT

The presentation was on a joint research project between UCSB (University of California Santa Barbara) and Yale University. The device is designed to gain a high dielectric strength by forming a SiO_2 layer immediately beneath the gate in the AlGaN/GaN-based HEMT structure and having electrons trapped by a charge generated from the SiO_2, thus to suppress the leak when the circuit is turned off.

The device demonstrates higher performance than preceding SiC-based devices, in terms of both dielectric strength and on-resistance.

It has a dielectric strength of 1,300V and an on-resistance of 1.7 $m\Omega/cm^2$.

Of dielectric-strength transistors, GaN-based transistors are the most advantageous in terms of

Figure 4: Comparison of roadmaps with ITRS

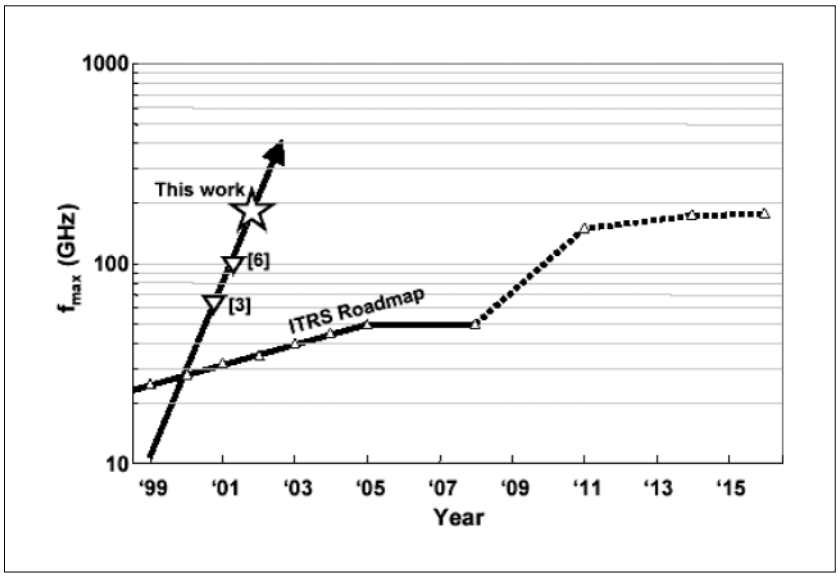


Figure 5: Structure of the high dielectric-strength HEMT

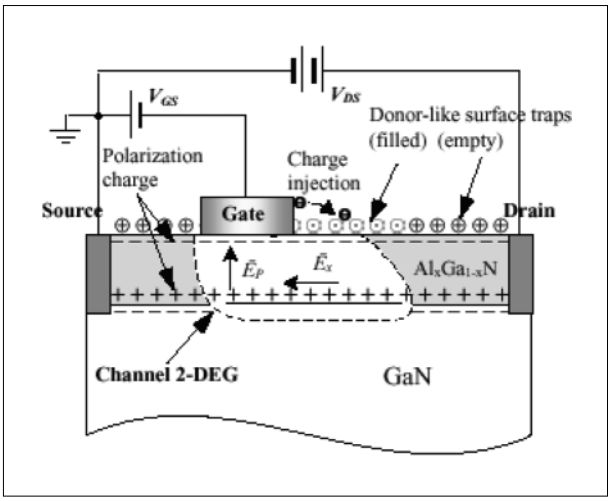


Figure 6: Pattern diagram of the operating principle

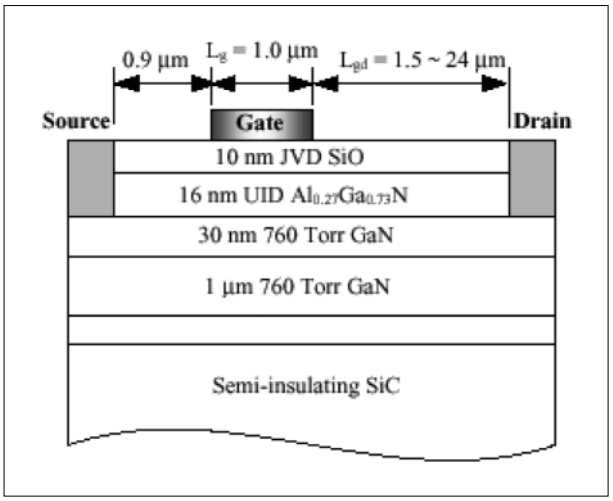
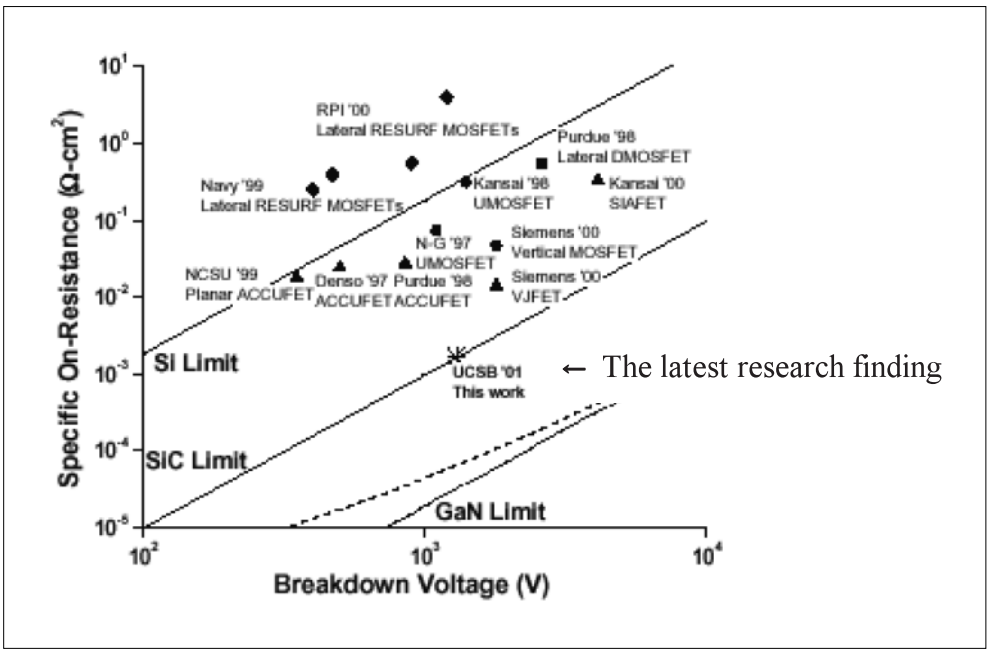


Figure 7: Comparison between GaN-, Si- and SiC-based devices



the physical properties of the material. In Japan, however, GaN research is mostly in the form of luminescent devices such as laser diodes and LEDs, rather than as a material of transistors.

4.3 Trends in research and development by country

This section will analyze the presentations at this year's IEDM from a sci-tech, political point of view. Table 2 shows a list of countries to which the research papers or reports presented at IEDM belong. The total number of the papers and lectures in the parentheses includes the number of keynote lecturers, but excludes panel discussion participants.

In the ranking in terms of the number of papers on research into leading-edge devices, the United States, Japan, South Korea, Taiwan and Germany represent the top 5 countries, respectively. Thus, the rankings are closely linked with the positions of those countries in the current world market for semiconductor devices. Additionally, this table indicates considerably high levels of technologies in 3 European countries: Belgium, where IMEC serves as the base for jointly developing semiconductors used in Europe; France, where institutions including state-run communication carrier Alcatel have gained top-class achievements in the development of communication devices; and the Netherlands, where Philips and other organizations have conducted a wide array of research projects ranging from basic technologies, including simulation and process technologies, to

Table 2: Number of Research Papers by Country

Ranking	Name of country	No. of papers
1	USA	97
2	Japan	56
3	Korea	19
4	Taiwan	13
5	Germany	11
6	Belgium	7
7	France	5
8	Netherlands	5
9	China (Hong Kong)	3
10	Spain	2
11	Singapore	2
12	Switzerland	2
13	Finland	1
14	Canada	1
15	Ireland	1
16	Greece	1
17	Argentina	1

Total number of papers and lectures: 216, inc. overlaps through joint research projects

high-frequency devices.

It is also notable that China (Hong Kong) provided three presentations. They consisted of one project conducted by China individually, and two research projects that were jointly conducted with Singapore and the United States. The next section analyzes these joint research forms in detail. These data are an important factor in analyzing the forms of research in those previously low-profile countries doing research on advanced devices, such as Spain, Ireland, Greece, and Argentina.

4.4 Forms of research and development

This section analyzes specific forms of research and development. Table 3 represents a table of institutions to which the presenters belong, categorized into Japan, the United States, Europe, Asia and other areas, and classified into business, academic and governmental institutions.

This table indicates that the number of presented research projects by academic and governmental organizations in Japan is very small for leading-edge devices. Furthermore, by analyzing the table together with Table 2, you can identify the status quo of joint research projects by country and by region (the number of overlaps represents the number of collaborations) and that there are fewer collaborations between business, academic and governmental institutions in Japan compared to other countries.

Research on leading-edge devices has reached the nano level, and quantum effects can no longer be disregarded. Thus, even engineers are increasingly required to have higher levels of physical and quantum-mechanical backgrounds in this area. It will be also essential to form collaborations with universities in order to fortify these physical foundations. In Japan, however, it appears that business-academic collaborations like those found in the US, Europe and other Asian countries are barely functioning as far as the present state is concerned. If IT and nano technologies are positioned as the next-generation pillar of Japan as an established technology-oriented nation, acute measures are urgently required.

Multinational joint research projects by region are analyzed as follows. Of the 216 presentations, research papers prepared across two or more nations accounted for 19. Of the 19 projects, multinational collaborations involving Japan represented only 2 (research projects by local affiliates are counted as research projects of the respective nations). Table 4 shows these data in a table.

In addition to the strength of joint research within the European region, those coalitions such as the US-EU alliance are also notable. The United States and EU announced an alliance in the field of nano technology in January. This can be considered an example of such a coalition.

Table 3: Numbers of business, academic and governmental Institutions by region

Region	Business	Academic	Governmental
USA	63	45	4
Japan	49	7	0
Europe	24	11	16
Asia	27	14	6
Others	1	2	0

Total number of papers and lectures: 216, inc. overlaps through joint research projects

Table 4: Number of multinational collaborations

Region	No. of collaborations
Europe - Europe	6
USA - Europe	4
USA - Asia	4
Asia - Asia	1
USA - Japan	1
USA - Europe - Asia	1
USA - Europe - Japan	1
USA - Europe - Others	1

In many cases, research on leading-edge devices requires a huge amount of capital investment such as research into semiconductor devices. In a sense, Japan has the potential to independently make huge capital investments or research investments, and therefore it is not appropriate to negatively regard all factors. However, it will also be necessary to promote coalitions with other nations from the viewpoint of improving investment efficiency and efficient management of intellectual properties.

Japan needs to consider the best form of research for efficiently forming multinational coalitions and efficiently demonstrating its leadership.

As a trend identified through more in-depth analysis of the data, it is indicated that Japan has fewer joint-research projects not only among business, academic and governmental institutions, but also among private companies as a group, and among universities as a group. This is another cause of concern.

In the United States, joint research projects between top-class universities are commonly conducted, such as those between MIT and Stanford University, and those between Yale University and the University of California Santa Barbara. On the contrary, in Japan, joint research projects such as collaborations between Tokyo University and Kyoto University are rare. In fact, there are only a small number of business-academic and inter-university coalitions in Japan. This is one of the problems to be tackled since it may also concern human resource demography including personnel affairs between universities.

4.5 Details of research areas

As a result of detailed analysis of research areas, it was learned that of the 7 presentations in the "DRAM Technologies" session, Japan represented 2, the United States 2, South Korea 2, and Germany 1. However, in the more theoretical "Scaling Trends of Advanced Devices" session, the US represented all the 5 presentations. And, in the "Device Simulation" session, the US represented 2, Japan 1 and Germany 1. Thus, the relative position of Japan was lowered.

Concerning the "Bio MEMS and Microfluidics" session, a separately organized event that attracted much attention, of the 5 presentations, the US represented 2, Germany 1, Singapore 1, and Greece 1. Japan provided no presentation in this session.

Although Japan is taking the lead in some of the basic areas such as with SET (single electron transistor), it can be said that our country is weak in the fields of theory building, such as device theories and simulations, and in the fields of interdisciplinary research such as bio-MEMS and microfluidics. This is yet another major problem.

4.6 Conclusion

The IEDM held in December demonstrated achievements of research into leading-edge devices that are suitable for the opening of the 21st century. In particular, it is greatly significant that with feasible support, the event showed the world of electronics that are not on an extension of the present times, such as carbon nanotube transistors, which will open up the nano-electronics world.

The Japanese research findings presented at the IEDM also deserve appraisal since they included top class achievements in the development of the Si-Ge-based high-speed transistor, which had been considered to be lagging behind, and that the realization schedule for SOI devices on the research roadmap was quickened by more than 10 years. Since Japan was acknowledged as the origin of the carbon nanotube, whose presentation gained the highest level of attention at the meeting, and acquired high acclaims also for its research efforts in those fields very close to basic research, such as research on single electron transistors, it can be said that those presentations fully demonstrated Japan's true abilities.

However, it is also an obvious fact that to some extent Japan has become alienated from the global trends in both form and method of research. Although all the international trends are not necessarily correct, Japan must establish a structure to further accelerate business, academic and governmental coalitions despite the fact that Japan is already encouraging those collaborations in accordance with promotional policies and the likes.

Following the IEDM, we had a discussion with

professors and students at Yale University. There was an interesting opinion in the discussion. The opinion was concerning Japan's and the United States' setting of research goals. It was pointed out that in Japan, most goals are set in the "buildup" style where the development of a new device comes first and then a future society using the device is predicted, while in the Unites States, goals are mostly set in the "break down" style in which the form of an ideal computer, for example, is determined first, then a device(s) required for the computer is/are designed.

Concerning the latest IEDM, it also suggested that unlike Japanese approaches toward research and development, aggressive approaches were taken in the development of the GaN transistor or the development of LEDs for short-distance data transfer in the States because these approaches were based on that kind of goals.

The idea by NNI (National Nanotechnology Initiative) in the US of developing a cube sugar size computer capable of storing the entire collection of books held by the National Library is also based on the same goals. It is not a figurative expression that a computer will have such an enormous capacity as a result of progress by various devices. The technology required to achieve that capability is not on an extension of the existing technologies, and discontinuous dots are inevitably required in drawing the line reaching the goal. This is an innovative breakthrough that can be clarified only by setting a high level of goals.

There are many criticisms concerning the goal of a basic plan that aims at establishing a research base for science and technology on which Japan can produce 30 Nobel Laureates in 50 years. However, the intension is not to count the Laureates every year and make an evaluation based on the number. With an extension of the conventional structure, our Nobel Laureates will not reach 30 in 50 years. The goal has been set on the grounds that it can be achieved only when the environment surrounding science and technology in Japan, including research bases, research forms, personnel training, and even intellectual creation and amalgamation, is established in a near ideal form.

Arguments are expected from the viewpoint of what the research bases, research forms, personnel training and intellectual creation for achieving this goal should be, and how the discontinuous dots lying on the process toward the goal should be connected for a breakthrough.

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5

R&D Trends in Speech Recognition / Synthesis and Natural Language Processing
— Challenges toward the Establishment of User-Friendly Human Interfaces —

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5.1 Introduction

Speech recognition and synthesis, and natural language processing have long been research subjects, as they are input/output technologies that allow people to operate devices in a natural manner. On early computers, the human interface method was text command input by the user and text message output by the computer. What followed was the graphical user interface that enabled icon-oriented displays and selection using a mouse pointer. More recently, advances in computer graphics as well as in image, audio and other multimedia processing have led to the creation of more diverse interfaces. In addition, in an effort to improve their ease of use, studies on screen designs and various kinds of input devices are ongoing.

Despite such activities, human interfaces furnished on information appliances still require certain levels of skill for users, not reaching a level of natural human communications. Ideal forms of human interfaces may be interacting with an information system through voice or natural language (sentences used in our daily communication) in some cases to pick up information from a foreign language with the aid of a machine translation system.

Interfaces using speech and natural language have long been studied and have evolved to the point where they have found application in limited areas. Voice input for word processors (dictation), and translation systems for roughly reading foreign-language information on the Web are already available. However, the current state leaves much room for improvement, because a recognition rate of daily conversation remains low and translation quality for complex sentences is insufficient.

Meanwhile, broadening users of the Internet, various kinds of information devices such as personal computers, mobile phones and personal digital assistances have diffused, increasing the demand for an interface that allows "anyone," inclusive of not only sophisticated users but also novices and the elderly, to use such devices "any time" "with ease." With this in view, the Council for Science and Technology Policy of the Cabinet Office is aiming at developing "human interface technology to give machines advanced communication skills to understand and interact with humans" in ten years as exploratory researches that will lead to next-generation breakthroughs.

This paper first describes the history and the current status of speech and natural language research, and discusses differences of approaches adopted by Japan and the U.S. to promote research projects. Then, it intends to suggest challenges to be addressed for facilitating research on next-generation human interfaces.

5.2 The development and the current state of human interface technologies

5.2.1 Speech recognition

(1) History of development

The history of speech recognition study, through which researchers have been trying to create a system capable of recognizing words spoken by humans, started back in 1952, when Davis and others at the Bell Laboratories made attempts toward recognition of spoken numerals by using the zero-crossing rate*1. Subsequently, in 1959, the research for the "phonetic typewriter," a device that can recognize monosyllables, was conducted at Kyoto University. A breakthrough that led to commercialization came in the 1970s, when the DP matching method*2, in which the variation in utterance duration is normalized through dynamic programming, was proposed concurrently in Japan and Russia, followed by another proposal by Japan concerning a two-level DP-matching algorithm in order to recognize continuous digit words. By commercialization of this technique, a minicomputer-based continuous-word recognizer was introduced onto the market in 1978 to help those operators who have to input data with their hands busy for sorting packages.

During the 1970s a statistical method, the Hidden Markov Model (HMM) was studied in the U.S. It became a standard technique for spoken word recognition in the 1980s. From the late 1980s through the early 1990s, the Defense Advanced Research Projects Agency (DARPA) conducted dictation projects. In this project, the n-Gram method, a technique in which the statistical probability among n words was proposed. It brought the realization of large vocabulary continuous speech recognition. On the basis of this achievement and the improved performance of PCs, dictation software for large vocabulary continuous speech recognition was first marketed in 1997 in the U.S. At the same time, the Japanese large vocabulary continuous speech recognition software appeared in the Japanese market.

In the first half of the 1990s, through DARPA projects focused on spoken dialogue question and answering (Q&A) systems, investigation of dialogue processing technology to handle Q&A started. The outcome was commercialized in 1998, as the automatic spoken dialogue processing system for telephone-based reservation/inquiry services (call center services).

On the other hand, Japanese researchers directed their commercialization efforts to voice recognition technology applicable to car navigation systems. To allow drivers to input their destinations and commands using their voice, an algorithm that can reduce processing loads without degradation in recognition capability was devised, and first built into products in 1995.

(2) The current state and challenges

The latest speech recognition technologies have reached the point where they are able to transcribe speech almost correctly as long as the speaker vocalizes words clearly. Moreover, their application to car navigation systems demonstrates that these recognition technologies are robust to certain noises.

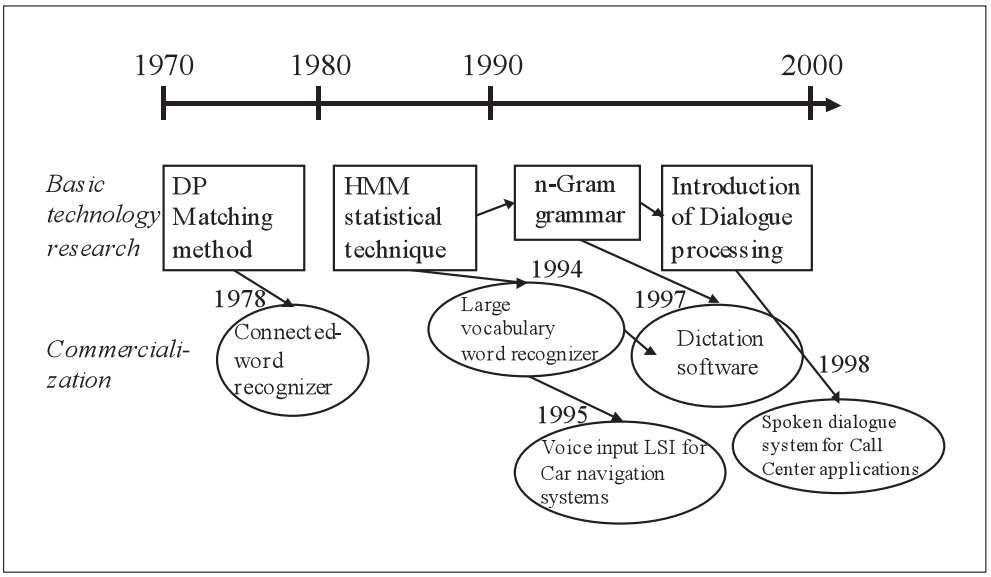
However, in areas such as hesitant "spontaneous speech" and "conversational speech" between friends, recognition performance remains poor. Also, the current technologies are not able to extract the speaker's intention or to make an adequate estimation of the speaker's situation.

5.2.2 Speech synthesis

(1) History of development

Research on speech synthesis has its roots in the 1950s as same as research on speech recognition, when researchers started seeking to output spoken messages from machines. K. Stevens at the Massachusetts Institute of Technology (MIT), G. Fant at the Royal Institute of Technology, Sweden (KTH), and others proposed the vocal-tract analog speech synthesizer — a device that can reproduce the acoustic characteristics of the vocal tract through an electric equivalent circuit. In the 1970s, NTT Electrical Communication Laboratories proposed speech synthesizer by using the linear prediction coding (LPC) to significantly reduce signal process calculations. In 1978, Texas Instruments (TI) succeeded a commercialization of a game device, Speak&Spell which can produce a certain number of spoken messages by using LPC method.

Figure 1: History of speech recognition research and commercialization



A technology to synthesize speech from arbitrary text was first developed by Klatt at MIT through the description of prosodic and phonological rules based on his knowledge and expertise. The achievement caught the attention of the Digital Equipment Corporation (DEC), and led to commercial introduction of a product named DECTalk in 1983. In the years that followed, as enhanced computer processing ability permitted acoustic waveforms to be edited and processed, waveform manipulation methods were pursued, resulting in improvements in clearness of synthesized speech.

During the 1990s, in order to produce natural, fluent speech synthesis having smooth concatenation of speech segments, considerable research energy was extended to make new model for prosodic and phonological rules derived from actual data. In the latter half of the 1990s, the HMM method, a basic technique for speech recognition, was used for segmentation of speech into phonemes so that the phoneme data for synthesis could be gotten automatically from real speech. As a result, a significant part of the preparation of data for synthesis process was automated, making it easier to create a speech synthesis system that can generate synthesized speech of a specific person's voice by collecting the person's basic voice data.

(2) The current state and challenges

Today's speech synthesis systems enabled by PC-based software can produce voices very close to humans' in terms of intonation and articulation, reaching a level where users are likely to have little odd impressions about them. The next challenge would be the synthesis of speech in a variety of styles such as recitation and conversation, and the addition of emotions.

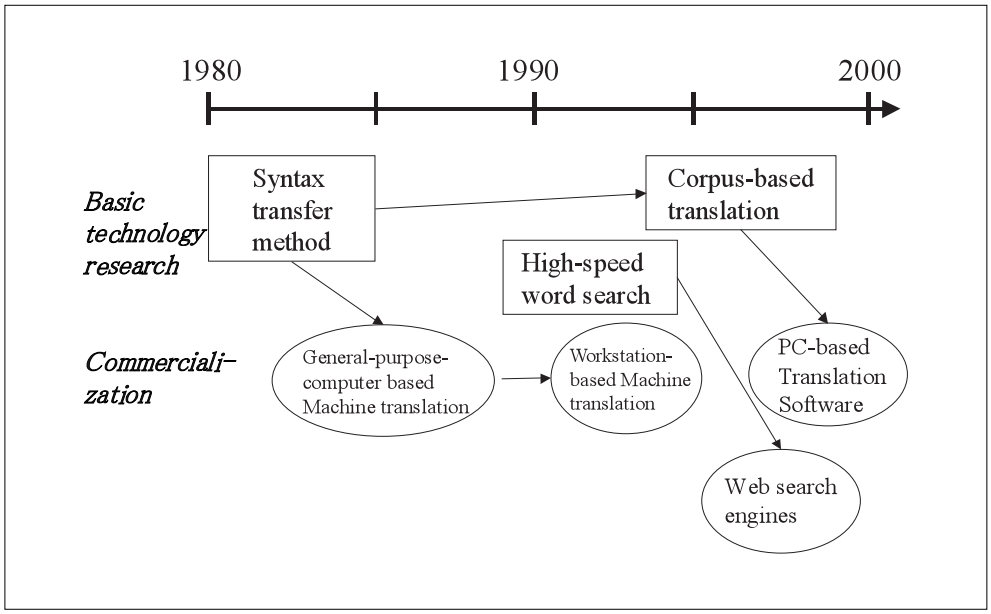
5.2.3 Natural language processing

(1) History of development

Natural language processing refers to a technology that allows computers to understand and generate natural language which people use for daily communication, and it plays the essential role in natural communication between humans and computers. The beginning of research on natural language processing goes back to the early attempts in the 1950s, which intended for translation by computers (machine translation). While U.S. researchers started with Russian-English translation, the Japanese counterparts began tackling their own subjects at Kyushu University and the Electrotechnical Laboratory.

In the U.S., the ALPAC report (written by the Automated Language Processing Advisory Committee (ALPAC) organized by the National Science Foundation) was released in 1966, which concluded that basic research was recommendable instead because machine translation was too complex to solve by using computing power and it's quality was too low to improve. Consequently, researchers shifted toward the area of basic linguistics, virtually bringing machine translation research in the country to a

Figure 2: History of natural language recognition research and commercialization



halt.

In the latter half of the 1970s, machine translation study drew strong attention in Europe and Canada, where needs were stronger. Through their research activities, the transfer method for translation of linguistically similar language pairs, which uses word-to-word correspondence between the two languages, was developed. The technology was commercialized, for example, to translate English weather forecasts into French in Canada in 1976.

In Japan, the syntax transfer method, in which the syntax of sentences was analyzed and target language sentences were reconstructed by using transferred syntax, was the mainstream because of the large linguistic distance between Japanese and English. During the first half of the 1980s, English-Japanese/Japanese-English translation systems for the abstracts of scientific papers were studied under a national project led by Kyoto University. In 1986, Japanese computer manufacturers introduced onto the market its first model of an English-Japanese/Japanese-English translation systems running on general-purpose computers. Whereas its translation quality was not enough for unedited use, the system served as a useful aid for translators to increase the efficiency.

To boost the capacity to generate grammars and lexicons, which had been limited in the conventional hand-made method, what advanced in the 1990s was the technology to construct them from enormous volumes of Japanese-English bilingual translated data. The new technology, called corpus-based translation*3, contributed to enhancing translation quality. With the advancement in computer performance, workstation-based translation software became commercially available in the early 1990s, followed by PC-based products in the late 1990s.

As an application of natural language processing, keyword search technology was developed in the 1990s to enable automatic document sorting and retrieval. This technology uses morphological analysis and word segmentation, which was established through machine translation studies. In addition, Web search engines, indispensable tools to search desired Web sites, depend on a combination of morphological analysis technology and high-speed word search technology by using parallel computing.

(2) The current state and challenges

According to a report by the Asia-Pacific Association for Machine Translation (AAMT), the performance delivered by current English-Japanese translation systems is high enough to help improve reading comprehension skills of people whose English ability is equal to or below TOEIC 700 (intermediate). For another leap in machine translation capability, semantic analysis among words and context analysis between sentences, which is an unsuccessful research area, should be encouraged.

With the growth of information available on the

Web, users are demanding better means to retrieve desired information among the vast and various resources. To this end, retrieval and summarization technologies that use something beyond keywords, such as meanings or concepts, should be sought after.

5.3 Challenges in the Promotion of next-generation human interface technology

As described in the previous chapters, both speech recognition and natural language processing are attempts to enable computers to perform some human capabilities. Long-lasting basic research has led to breakthroughs that served as the foundation for application and commercialization of these new technologies. However, their current levels still fall short of satisfaction of all users. This chapter discusses research direction, research environment, and research management issues to be addressed to develop next-generation human interfaces that functions more like humans.

5.3.1 Research challenges

The performance of speech recognition and natural language processing, which has made a significant leap forward through the use of statistical techniques in the 1990s, seems to face a big barrier recently. Current systems cannot provide phonemic recognition rates as humans have and cannot handle prosodic information. They also fail to provide semantics and contextual processing as well as to interpret the speaker's intentions and situations based on dialogues.

What is desirable is to create a new model to move beyond the status quo by actively assimilating knowledge of acoustics and linguistics into the conventional statistical approaches. Some pioneering efforts on the basic component technologies are found among the representative Japanese speech recognition research projects listed in Table 2, whose outcomes are awaited with anticipation.

In the long run, more attention should be paid to the aspect that recognition and language comprehension are deeply related to the cognitive and learning functions performed by the human brain. While digital information processing technologies have made remarkable advances in the 20th century, cognitive and learning mechanisms remain to be elucidated. Researchers will realize the need to look deeper understanding of the human brain mechanism, and this issue will stand as a major challenge in the 21st century.

5.3.2 Construction of databases for common use

To build the foundation of speech recognition and natural language research, data collection is crucial. However, the task requires considerable staff hours, it is difficult for a single research institute to make various kinds of speech databases. More specifically, in addition to the collection of huge volumes of data, manually checking analysis results which are attached for each data component is such enormous work that it cannot be handled by one laboratory alone.

A public-aided membership consortium that aims to construct linguistic databases to be shared among members was established in the U.S. in 1992 as the Linguistic Data Consortium (LDC), and in Europe in 1995 as the European Language Resource Association (ELRA), and both are continuing their activities to date. Many experts are working for these organizations to collect, maintain and distribute the databases. Their databases are offered inexpensively for academic research purposes, while their commercial use is offered at higher prices.

Japan has also seen its own attempts to create common databases, none of which have lasted long or led to sustainable activities thus far. Databases constructed through a project most likely become unavailable as soon as the project ends, due to a lack of financial support to maintain and upgrade the databases afterwards.

In 1999, following the U.S. and European precedents, the Language Resource Consortium (GSK; acronym for the Japanese phrase Gengo Shigen Kyoyukiko), an organization to collect, maintain and expand databases for common use, was formed in Japan, even though it has yet to start any substantial activity due to the lack of funds. Raising funds for building the foundation of research is not easy, as the foundation itself would not yield any immediate practical outcome.

A common database not only serves as a research foundation, but also allows fair performance evaluation of the systems by using the same database. From this perspective, construction of common databases is hoped for as a means to facilitate fair competition among research institutions.

5.3.3 Difference between Japanese and U.S. research projects

The gap between Japan and the U.S. is said to be widening in terms of the speed of commercialization from R&D results. This can be seen in some cases of the commercialization of speech recognition technologies.

In the U.S, DARPA played an important role in R&D of speech recognition. As shown in Table 1, the organization concretized projects goal with clear application concepts. In these projects, DARPA funded two or more research institutions to achieve the same goal, so that they studied to reach the goal in competition with others. In more detail, a database for evaluations was created at the point of project start and shared among participants. The institutions involved, most of them universities, contended for higher performance through making prototype systems with integration of many component technologies to demonstrate possible applications. After the project, the resulting intellectual property rights (IPRs) were transferred to the respective institutions, which were then allowed to transfer the technologies to private enterprises such as venture firms, solely through their own decisions when necessary. An example can be seen in the DARPA-funded research project on spoken dialog technology for air travel information, conducted from 1990 through 1994. In 1995, researchers at the institutions in charge — MIT, Carnegie Mellon University (CMU), and SRI International— established two venture firms in Boston and Silicon Valley. They built phone-based automatic reservation/inquiry systems by using speech recognition technology, which was utilized to support 24-hour call center services with minimal staff. Today, in the U.S., voice automation systems for call centers are expanding their scope of application beyond flight reservations, to a variety of reservation/information services. The majority of the market is controlled by the two venture companies, which have now grown to considerable scale.

In Japan, the major national projects on speech recognition as shown in Table 2 are in progress. Except for the "Spoken Language Translation Research Project" by ATR and the recent project for "The Realization of Advanced Spoken Language Information Processing from Prosodic Features," all of them aim to improve the recognition performance for either read text or spoken dialogue, as in the case with U.S. DARPA projects. While the "Research on Human-Machine Dialogue System through Spoken Language" project members created prototypes for evaluation, the other projects have carried out only component technologies so that each university can focus on its part. This method contributed to the development of constituent technologies, but did not clearly indicate the overall performance level of each resulting system due to the absence of an evaluation scheme for the integrated outcome. On the other hand, industry has been making their

Table 1: U.S. DARPA projects and commercialization of their results

Period	Project	Project objective	Result in commercialization
Latter half of 1980s First half of 1990s	Dictation projects Resource Management Task (small-scale dictation) (1987-1990) Dictation of WSJ newspaper (1991-1996)	Dictation of reading aloud newspaper	Release of the PC-based "Dictation" software (from IBM, etc.)
Latter half of 1990s	Q&A dialogue projects Air travel information system: ATIS (1990-1994) Web information retrieval: TIDES (1998-2000) Communicator (1999-2003)	Flight reservation and weather forecast inquiry in spoken dialogue.	Spoken dialogue systems for call centers (by two U.S. venture firms)
Early 2000s	Talking-agent project: Human Centered System (2002-2007)	Construction of a talking digital secretary agent.	

Table 2: Major voice recognition projects in Japan

Term	Project Name	Description	Funding
FY1986-1989	Advanced Man-Machine Interface through Spoken Language	Research on speech recognition of recitation.	Grant-in-Aid for Scientific Research on Priority Areas by MEXT
FY1993-1995	Research on Understanding and Generating Dialogue by Integrated Processing of Speech, Language and Concept	Research on dialog comprehension through integrated processing of speech and language.	Grant-in-Aid for Scientific Research on Priority Areas by MEXT
FY1993-1999	Spoken Language Translation Research Project	Automatic translation of conversation for hotel reservations between English and Japanese speakers.	ATR (former ATR Interpreting Telecommunication Research Laboratories)
FY1996-2000	Research on Man-Machine Dialogue System Through Spoken Language	Creation of a spoken dialogue system to retrieve academic literature from the Internet.	Research for the Future Program by the Japan Society for the Promotion of Science
FY1997-1999	IPA Japanese Dictation free software project	Development of continuous speech recognition software for Japanese.	Project of the Information-technology Promotion Agency (IPA)
FY1999-2003	Spontaneous Speech: Corpus and Processing Technology	Establishment of the technology for spontaneous speech recognition, understanding and summarization	Science and Technology Agency Priority Program, Organized Research Combination System
FY1999-2003	Integrated Understanding of Multidimensional Acoustic Signals	Research on sound spatiality, speech analysis/synthesis, speech recognition, spoken dialogue, and recognition of sound information.	COE formation program by MEXT
FY2000-2002	Development of the Anthropomorphic Dialogue Agent	Development of the basic software for the technology to generate human-like dialogues by machines.	Project of the Information-technology Promotion Agency (IPA)
FY2000-2003	The Realization of Advanced Spoken Language Information Processing from Prosodic Features	Integration of prosodic studies, ranging from basics to application.	Grant-in-Aid for Scientific Research on Priority Areas (B) by MEXT

own effort to push ahead with application and commercialization on the basis of academic findings. Under the situation where industry and academia are not eager to collaborate with each other, technology transfers from a university to a venture firm, as seen in the U.S., have not occurred in Japan. In other words, current and past national projects of Japan place emphasis on the advance of basic research rather than the promotion of business-academia collaboration.

In the panel discussion on "Present State and Future of Large-Scale Projects on Speech and Language"[1] conducted by the Spoken Language Processing SIG of IPSJ, cited were problems associated with national projects, such as the difficulty to take risky and adventuresome approaches for cerate totally new innovation and absence of a support to maintain the outcomes after the project ends. This suggests what should be coped in the future Japanese project funding program, namely, fostering "a culture where serious competitiveness without fear of failure" is valued in place of the current "success-oriented culture," and utilizing the results of a project to the next project.

Another point indicated by the university professors interviewed was that, in the information research field, research staff including postdoctoral fellows, working at universities are too scarce to deal with large-scale systems and thus they tend to choose more specific component technologies as their research subjects.

In the U.S., academic organizations always make effort to get funds from external sources, as their basic funds are limited. Since a national project can provide them with the critical amount of research grants, competition to acquire them is so fierce that even a basic research project has a distinct objective. In the case of DARPA-funded speech recognition projects, fair competition is said to have accelerated research activities. A swift

and smooth technology transfer from research to commercial is also contributing to the country's overall strength in technology development.

5.4 Conclusion

Amid the spread of information devices, the next-generation human interface technology is expected to solve the digital divide and to improve machines' friendliness to users even including beginners. In an age when every kind of information is available through networks accessible via mobile devices just around the corner, ubiquitous access to information is becoming a reality. The ultimate goal should be to enable people to easily obtain desired information through natural communication with information devices.

Revitalization of basic research is one of desired way in order to attack many obstacles on the path to such goal. Now that improvement in performance has hit the ceiling in some respect, a new attempt to break through is needed.

With the growing global trend in basic researches depend more on universities' effort than business enterprises' effort, an expectation for universities basic research outcomes is increasing. To allow them to carry out research projects on the basis of risky but innovative ideas, the culture should be changed where fair competition and evaluation are ensured, and those failed are more tolerated and encouraged to make another endeavor.

Furthermore, with an eye to focusing energy on prompt commercialization of created breakthrough technologies, measures should be taken to foster activities less mature than the U.S., such as industry-academia collaboration and technology transfer.

Glossary

*1 Zero-crossing rate
This is the number of zero crossings of the waveform within a certain frame period, and indicates an approximate amount of energy of the waveform. This method was able to get characteristics of speech sound with relative ease on hardware.

*2 DP matching method
The duration of each phoneme in speech varies in each utterance. The method uses dynamic programming to normalize the variation and find the most likely pattern.

*3 Corpus-based translation
The use of corpus here refers to a large-scale database consisting of example sentences and their translations. The corpus-based machine translation uses grammars extracted from the corpus and a part of example translations in the corpus. The resulting translation quality is higher than that of conventional machine translation based on empirical methods.

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6

Trends in Technologies to Combat Contaminated Soil Environments

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6.1 Introduction

In the 1960s, pollution problems such as the Itai-itai Disease, Minamata Disease and Yokkaichi Asthma emerged to become major social issues. To cope with this, preparations were advanced such as 1967's Basic Law for Environmental Pollution Control, Air Pollution Control Law and Water Pollution Control Law, and countermeasure technologies have also progressed in tandem with these.

Nevertheless, in the case of soil contamination, the seriousness of contamination had not become apparent, and for this and other reasons, legislation had not yet been enforced. Meanwhile in recent years, there have been many cases where soil contamination became evident in soil surveys attendant to land redevelopment and sale, and independent surveys that businesses conduct as part of environmental management relating to ISO14001 (certification), and along with increasing concern, measures to combat this have become a pressing issue.

Looking at recent trends, the Council for Regulatory Reform's "Interim Report on Regulatory Reform in Six Priority Areas" (July, 2001), highlights the necessity for legislation concerning soil and ground water contamination, and the Council for Science and Technology Policy (CSTP), Cabinet Office's "Promotion Strategies for Prioritized Areas" (September, 2001), notes the necessity for technological development concerning soil and ground water contamination. Furthermore, the Central Environment Council released a report in January 2002 entitled, "On the Desired State of Systems concerned with Measures to Preserve Soil Environments." According to the report, a mechanism is being planned whereby governors of Tokyo, Hokkaido, and all the prefectures can oblige land owners to conduct soil contamination surveys in instances where factories and businesses handling hazardous substances terminate their business or change (land) usage to residential areas, etc., or where the possibility of serious soil contamination is recognized. Furthermore, funding, the cornerstone of this mechanism, and how expenses should be borne when persons responsible for contamination can not be specified and so forth, are set to be discussed in future.

Against this kind of backdrop, this paper analyzes the latest technological trends concerning measures to combat soil and ground water contamination, and takes up the themes that should be resolved, with a focus on technical aspects.

6.2 The current state of soil contamination and laws and regulations

6.2.1 Soil contamination within Japan

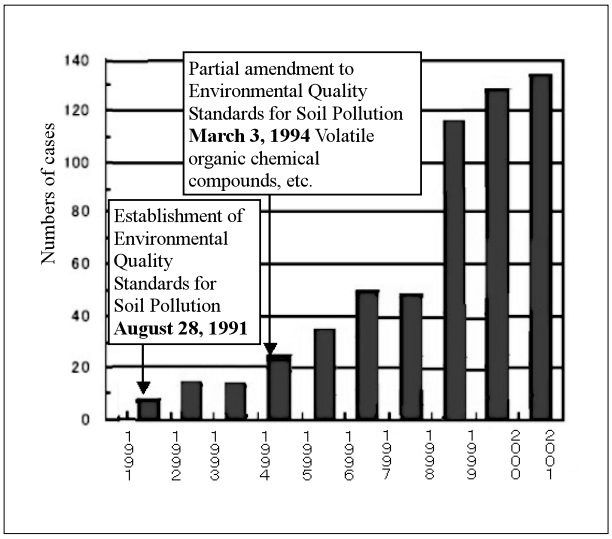
The "Overview of Soil Contamination Surveys and Countermeasure Examples, and Survey Results on Countermeasure Effectiveness in the Year 2000" (February, 2002, Ministry of the Environment), reports on the numbers of proven cases of soil contamination until the end of March, 2001, ascertained by Tokyo, Hokkaido and all the prefectures. Figure 1 shows the numbers of proven cases of soil contamination by year that exceeded Environmental Quality Standards (EQS) for Soil Pollution values [*1], and we can see that in recent years in particular, the number of proven cases of soil contamination has risen dramatically.

The cumulative number of cases since the establishment of the Environmental Quality Standards for Soil Pollution (1991), is 574.

Factors cited for this are that the number of soil surveys has increased due to (1) companies' efforts towards gaining ISO14001 (certification) and (2) soil surveys, etc., based on the ordinances and outlines of local autonomous bodies. It is conceivable that the growth trend in cases of excessive soil contamination will continue in the future as well.

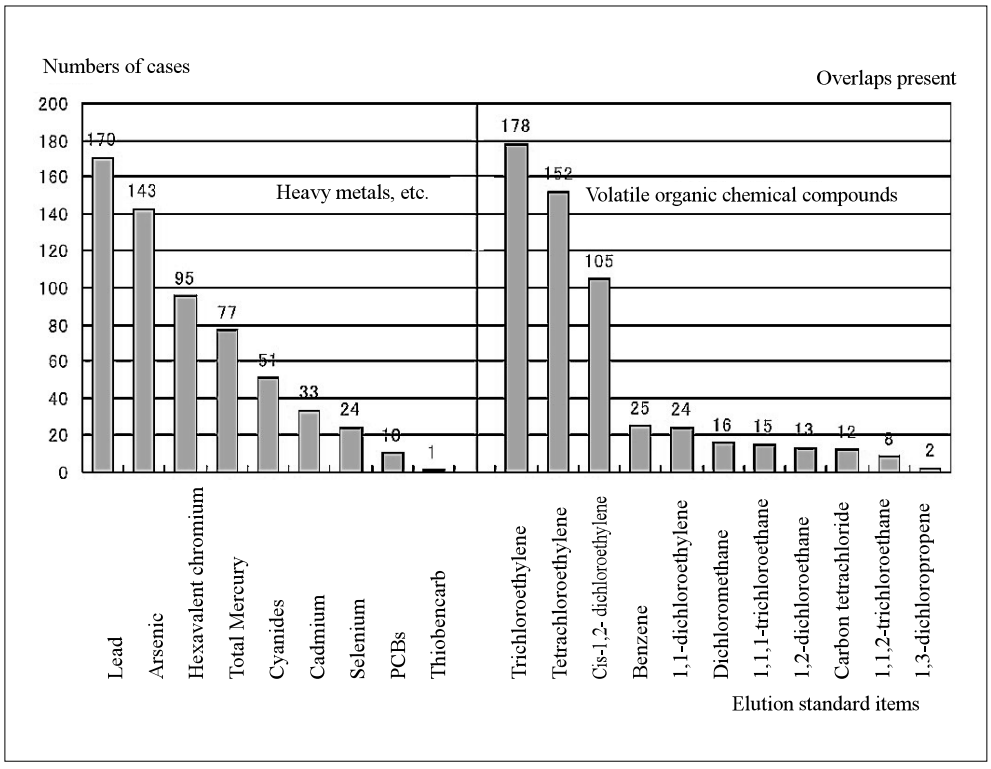
Figure 2 shows the cases exceeding the Environmental Quality Standards for Soil Pollution *1 of Figure 1 by substance targeted for regulation. Among heavy metals, etc., lead and arsenic account for approximately 60%, and there are many proven cases of contamination in metal products manufacturing industries and chemical industries. And among volatile organic chemical compounds, chloroethylenes that were being used in semiconductor manufacturing processes, etc., account for about 80%, and there are numerous proven cases of contamination from electrical machinery and devices manufacturing industries and the cleaning industry. These are harmful substances that are causing concerns about health-related problems, and there is also a strong need for combative measures.

Figure 1: Numbers of proven cases of soil contamination by year



Source: Composed from Ministry of Environment data, "Overview of Soil Contamination Surveys and Countermeasure Examples, and Survey Results on Countermeasure Effectiveness in the Year 2000" Feb., 2002

Figure 2: Numbers of excessive cases by substances targeted for regulation (cumulative)



Source: Ministry of the Environment "Overview of Soil Contamination Surveys and Countermeasure Examples, and Survey Results on Countermeasure Effectiveness in the Year 2000" (Feb., 2002)

6.2.2 Current state of soil contamination regulations in developed countries

In European and American countries such as the United States and Holland, countermeasures concerning conservation of soil environments were adopted from an early stage, and reports of soil contamination from businesses and land owners are compulsory under law; surveys by administrative organs are also being conducted. Table 1 shows an outline of systems to combat soil contamination enacted in Europe and America.

6.2.3 Current situation in Asian countries

Environmental problems in developing countries present a variety of aspects. For example, in Asian countries that are undergoing rapid industrialization and urbanization, it is necessary to deal with the environmental issues of industrial pollution, urban pollution and global-scale environmental deterioration while advancing development. In Thailand for instance, principally arsenic-based groundwater and soil contamination from the manufacture and use of agrochemicals is a serious problem. Similar problems are also being reported in China and other Asian countries. Furthermore, in West India and Bangladesh, an estimated 17 million people are drinking groundwater contaminated with arsenic eluted from geologic strata, and the situation is acute [1].

Looking at systems of environment-related laws in place in Asian countries, in the same way as Japan almost all laws apart from those concerning soil have been established. But even if a system is in place, its effectiveness is an issue. Reasons indicated for this are (1) even if a law is

Table 1: Overview of soil contamination countermeasure systems in Europe and America

Name of country	System concerning soil contamination countermeasures and overview
Holland	**1983: Provisional Soil Purification Law** **1987: Soil Conservation Law (revised in 1994 in a form including the Provisional Soil Purification Law)** **1997: BEVER Project (goal to repair contamination) commences** Began with the commencement of soil purification resulting from disclosure of the Lekkerkerk incident (ground water contamination) in 1980. Currently it establishes two levels of standards concerning soil contamination: target value and intervention value.
Germany	**1998: German Federal Soil Protection Act** A framework for formulating unified standards of regulation concerning soil contamination countermeasures established in each province of Germany. Objective is to permanently conserve or recover soil functions. Establishes fundamental obligations towards land users such as the (1) obligation to prevent the ecological functions of soil from being damaged; (2) obligation to act in such a manner that harmful soil changes do not occur; (3) obligation to unseal sealed ground when it can be requested so as to recover soil functionality; (4) obligation of purification; (5) obligation to perform contamination surveys, and so on.
Denmark	**1999: Contaminated Land Law** Began with the disposal of uncovered waste materials in the 1970s. Revises the Waste Materials Disposal Law and the Environmental Protection Law. Stipulates the introduction of a registration system for contaminated sites; setting of the order of priority for carrying out purification measures; obligation of administrative agencies to carry out surveys and purification measures.
England	**1990: Environmental Protection Law** **1999: Environment Law** Using the concept of comprehensive contamination regulations, promotes control of the total amount by unified management of contaminants discharged into the air, water and soil from industrial facilities, the number one source of contamination. Establishes liability to purify contamination; a system for registering contaminated land and specific facilities; administrative procedures to protect the lives of private citizens; and provisions of requesting court injunctions, etc.
United States	**1980: The Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA, commonly known as Superfund)** **1999: Superfund Redevelopment Initiative** Soil and groundwater contamination problems became conspicuous in the latter half of the 1970s. Support is being given to formulate national guidelines and boost funding, etc. Contaminated areas that exceed a certain level of risk are registered on the National Priority List (809 locations as of February, 2002).

Source: Author's own compilation

formulated, the establishment of its enforcement ordinance is lagging behind or has not been established, (2) compared to developed countries, the budget, human talent and technology to implement environmental measures are inadequate.

6.3 Current state of measures to combat soil contamination

6.3.1 Features of soil contamination

Compared to water and air, soil has a complex composition, and reacts in various ways to hazardous substances.

Heavy metals, one type of general pollutant, resist dissolving in water and are easily adsorbed by soil. Therefore, heavy metals and so on that have penetrated into the ground exist in the soil close to the surface, and often do not diffuse to deeper levels. But when they surpass the absorbing capabilities of soil, hexavalent chromium, cyanide and so forth, which are highly mobile and highly soluble in water, spread to deep subterranean levels along with rain water percolation, and there is a possibility that the range of contamination will expand by the flow of groundwater.

Among volatile organic chemical compounds on the other hand, organic chlorine compounds are indecomposable in the natural world, and are degradation resistent substances that remain for long periods in the environment. Furthermore, since they have extremely strong permeability, they penetrate deep underground while contaminating the soil, mixing in and diffusing in groundwater to cause groundwater contamination. Furthermore, since they are also volatile, some of them vaporize and resolve from the groundwater, and there is a possibility that they will once again contaminate the upper layers of geologic strata. Therefore, even if the contamination source is confined to a small area, the contamination often diffuses and reaches a wide area along with groundwater flow.

6.3.2 Soil contamination treatment technology

In the "Guidelines and Standards for Research and Countermeasures Concerning Soil and Groundwater Pollution" (Environment Agency, 1999), measures to combat soil contamination are classified into the following types of contamination: "heavy metals" *2 and "volatile organic chemical compounds"*3. In addition, pollution countermeasures are classified as "emergency measures" and "permanent measures." Emergency measures are measures for cases where permanent measures can not be implemented, and consist of measures to prevent ingestion by humans and measures to prevent diffusion of contamination. The latter are measures to ensure that target substances that elute due to rain water do not spread to the surrounding soil and groundwater in the future. Table 2 shows an overview of emergency measures among the measures to combat soil contamination

As for permanent measures, the following are treatment technologies for which a considerable number of cases have been executed so far:

1) With heavy metals, etc., use is often made of landfill disposal, transporting them to a final place of disposal; and solidifying and making them insoluble using cement, etc., at the site.
2) With volatile organic chemical compounds,

Table 2: Emergency measures for soil and groundwater contamination

Technique	Overview
Measures to prevent ingestion by humans	Installation of keep out fences and bulletin boards
	Instruction to prevent drinking of groundwater, switching of water source
Measures to prevent spread of contamination	Installation of collecting channels, settling basins, etc.
	Covering of contaminated soil by paving, tree planting
	Covering with sheets, etc.; installation of windproof nets; installation of barrier wells
Monitoring	Observation of soil and water quality, air, etc.

Source: Author's own compilation

in many cases contaminants are adhered to active carbon using the soil vapor extraction method and the groundwater pumping-up method, and this active carbon is finally treated in meltdown furnaces.

In recent years it has become even more difficult to secure a final place of disposal, and there is a growing need for treatment technology that enables low cost, in on-site treatment (soil treatment at the contamination site).

6.4 Trends in the development of new technologies to treat soil contamination

Table 3 shows permanent measures for soil contamination that are currently at the stage of practical application, including technologies that have a record of little usage. As it stands, all the technologies require further improvements in terms of cost and labor saving. In particular, the following technologies are cited as those for which R&D is being vigorously undertaken: technology for treatment at the contamination site; technology for treatment in a short time frame; technology to reuse contaminated soil rather than just contain it; and technology that uses the decomposing power of organisms.
Below, we show technologies from among the countermeasure technologies show in Table 3 that are attracting particular attention of late.

6.4.1 Physical and chemical treatments

(1) In-site oxidation decomposition method

A technique that decomposes volatile organic chemical compounds and renders them harmless by directly injecting an oxidizer (potassium permanganate, etc.) into a contaminated groundwater system. Since it utilizes a chemical reaction in site, the purification treatment can be completed at low cost and in a short time frame compared to the ground water pumping-up method and soil vapor extraction method, etc. What is more, since the injected oxidizer reacts and resolves the contaminants in a short time frame, injection of a solvent for recovery is not required.

(2) Permeable reactive barrier

A method that purifies contaminated groundwater by installing a permeable reactive barrier in the contaminated groundwater downstream area (site boundary, etc.) that contains iron powder, which has the ability to purify contaminants. When groundwater contaminated with volatile chlorine compounds passes through the permeable reactive barrier, it causes a reduction reaction with the iron powder in the permeable reactive barrier, and ethylene and even ethane are resolved and rendered harmless. Since power for maintenance is not required after installing the permeable reactive barrier, it is anticipated that a significant reduction in maintenance and management work and expenses is possible compared to the groundwater pumping-up method, the representative purification method.

6.4.2 Biological treatment

(1) Bioremediation

A soil and groundwater contamination repair technology that utilizes the substance-decomposing capabilities of microorganisms, it is classified into two according to the method by which microorganisms are utilized :

1) Method that gives nitrogen and other nutrient salts to microorganisms inhabiting contaminated areas, propagates micro-organisms at the site, and increases purification activity (biostimulation)
2) Method that introduces cultivated microorganisms into contaminated areas, and purifies contamination (bioaugmentation).

International interest is also high, and recently, the Fifth International Environmental Biotechnology Symposium was held in Kyoto in July, 2000, and in June, 2001, the 8th Bioremediation International Symposium was held in San Diego. Since subterranean soil and groundwater that requires environmental repair are generally anaerobic conditions, research on the utilization of anaerobic microorganisms is also being carried out. Microorganisms are being discovered that can decompose even substances resistant to degradation like highly chlorinated PCBs, by dehalogenation reaction under anaerobic

Table 3: Permanent countermeasure technologies for soil and groundwater contamination

◎: Treatment technologies with many cases of employment

Technique	Technology classification	Name of technology	Target substance		Overview, etc.
			VOC	Heavy Metals	
In site treatments	Physical and chemical treatments	Electrokinetic separation method		○	Removes heavy metals using electrodes inserted in the ground
		Soil vapor extraction method	◎		Treatment that pressure fits air, etc., into the ground and adheres contaminants to active carbon, etc.
		Groundwater pumping-up method	◎	○	Treatment that adheres contaminants from pumped-up groundwater to active carbon, etc.
		In site oxidation resolution method	○		Technology that directly injects an oxidizer into a groundwater system, resolves VOCs and renders them harmless
		Permeable reactive barriers	○		Technology that installs a permeable reactive barrier containing iron powder in a contaminated groundwater downstream area and purifies it
		High-pressure Jet-propelled Agitation, Displacement, Solidification	○	○	Injects cement at high pressure into the ground, and replaces contaminated soil with a concrete hardening body
		Containment	○	○	Containment with sheet pile and an impermeable layer (clay layer).
	Thermal treatment	Thermal desorption and volatilization		○	Treatment that thermally resolves contaminants and adheres them to active carbon, etc.
		Glass solidifying		○	High-temperature melting by an electrothermal source. Requires exhaust gas treatment.
	Biological treatment	Bioremediation	○		Utilizes the resolving power of injected microorganisms and resolves and renders trichloroethylene, etc., harmless (uses non-genetically modified microorganisms)
Excavation treatments (Ex site)	Physical and chemical treatments	Soil classification and washing		○	Classifies by soil viscosity and dissolves target substances in washing liquid.
		Chemical treatment	○		Treatment that resolves target substances by oxidation, reduction and catalytic reactions, etc., and adheres them to active carbon.
		Solidification and solubility retardation		◎	Makes insoluble by cement solidification, use of solubility retardants, etc.
		Containment	○	○	Containment with impermeable sheet, continuous underground wall, sheet pile, etc.
		UV irradiation		○	Dechlorination of PCBs by UV rays.
	Thermal treatment	Thermal decomposition (incineration)	○	○	Heats contaminated soil in an incineration furnace, etc., and removes volatile metals.
		Pyrolysis (Molten solid processing)	○	○	Heats contaminated soil in a melt furnace, treats volatile substances with exhaust gas and solidifies heavy metals, etc., in slag
	Biological treatment	Slurry treatment		○	Adds water to soil to form slurry, and after oxidation-decomposition, completely decomposes PCBs by microorganisms (non-genetically modified).
	Other	Land fill disposal	○	◎	Landfill disposal at final place of disposal

(Note) VOC: volatile organic compound; PCB: polychlorinated biphenyl

Source: Author's own compilation

conditions.

Furthermore, in the "Development of Remedial Technologies for Soil Contamination" project (conducted by NEDO: New Energy and Industrial Technology Development Organization) carried out from 1995 to 2000, empirical tests were conducted to confirm the effectiveness of bioremediation and to investigate effects on the environment. From 2001 NEDO began developing technology to use microorganisms to purify soil contaminated by heavy oil, etc.

(2) Phytoremediation

Phytoremediation is a contamination repair and purification technology that utilizes the ability of plants to store and decompose environmental contaminants. In addition to the feature that it can be applied to purifying low concentration, broad-ranging contamination, its scope of application is confirmed to be extremely broad, from organic chemical compounds to radioactive substances.

In technological development the US leads the way, and the discovery of a type of fern that efficiently absorbs arsenic[2] and technology that enhances plants' resistance and amount of accumulation in respect to heavy metals by genetic manipulation[3] have been reported. Venture companies that deal with Phytoremediation are also appearing, but cases of practical application are few.

(3) Cost of biological treatment

Since the circumstances of pollution cases (scale and concentration of contamination, target substances, etc.) are diverse, it is difficult to quantitatively compare and discuss phyto-remediation and conventional technologies such as physical and chemical techniques. For this reason, we compared treatment costs and other limited items. The results are shown in Table 4.

For the cost of phytoremediation treatment, we look at overseas cases of trial calculation reports. According to a trial calculation carried out by D.J. Glass of the per-ton cost of treating contaminated soil, the phytoremediation treatment cost is $25-100, whereas chemical treatment and incineration treatment is $100-500, the cost of treatment being about five times higher[4]. And looking at a case conducted by F. Chris comparing phyto-remediation and bioremediation, the per-square yard cost of treating of soil contaminated with pesticides is about $80 in the case of phyto-remediation and $8.4-197 for bioremediation [5].

However, to carry out a detailed comparison of these costs, it is necessary to study costs such as expenses required for the land during the period necessary for soil purification.

Table 4 : Performance comparison of soil contamination treatment technologies

○ Fexcellent, △ Faverage, × inferior

Item for comparison	Phytoremediation	Bioremediation	Chemical treatment	Heat treatment
Target substances for treatment	• Heavy metals • VOC	• VOC	• Heavy metals • VOC	• Heavy metals • VOC
Cost (initial cost)	○	○	△～× differs for each technology	△～× differs for each technology
Need for external energy	○	△	×	×
Speediness (Purification in short time frame)	×	△	×	×
Effect of soil temperature and humidity, etc., on treatment capability	×	×	○	○
Application to areas contaminated at low concentration over a wide area	○	○	×	×

(Note) VOC: volatile organic compound

Source: Author's own compilation

6.5 Conclusion

In this paper we have examined the current state of overseas soil contamination regulations and the current state and developmental trends, etc. in soil contamination countermeasure technologies in regard to soil contamination, which has numerous technically difficult aspects compared to air and water contamination and whose legislation had been lagging behind.

Looking at the current state of technologies to combat domestic soil environment contamination, there is a problem of having insufficient places of final disposal, and investing efforts into technological development for treating contaminated soil on site and at low cost is considered to be vital.

Furthermore, with the introduction of laws and regulations, it is conceivable that the numbers of cases requiring purification of contaminated soil will increase, and it will become even more important to be able to treat at low cost and in a short time frame.

In addition, measures are also being sought to combat environmental contamination that is being caused by endocrine disrupting chemicals (so-called environmental hormones) that exist in trace amounts over wide areas. The treatment of contamination extending over wide areas, typified by environmental hormones, is a difficult field to deal with using conventional technology such as physical and chemical treatments.

Considered in this way, the promotion of research towards establishing biological treatment technologies taken up in Section 6.4.2, is desired. Also, in terms of dealing with the treatment of soil contaminated with heavy metals, etc., the development of technologies of the type that combine bioremediation and phytoremediation, will probably be necessary also.

The above mentioned types of issues are themes that neighboring Asian countries are also facing. The development of technologies to combat soil environment contamination, including bio-remediation mentioned above, is something that from the perspective of international contribution, this country also must surely position politically and promote.

Glossary

*1 Among investigation cases, cases that were proven not to meet Environmental Quality Standards for Soil Pollution. Environmental Quality Standards for Soil Pollution concerning dioxins, and cases of farmland soil contamination based on the Agricultural Land Soil Pollution Prevention Law, are excluded from this target.

*2 15 items: cadmium, cyanides, organic phosphorus, lead, hexavalent chromium, arsenic, mercury, alkyl mercury, PCBs, thiuram, simazine, thiobencarb, selenium, fluorine and boron.

*3 11 items: Dichloromethane, Carbon tetrachloride, 1,2-dichloroethane, 1,1-dichloroethylene, Cis-1,2-dichloroethylene, 1,1,1-L trichloroethane, 1,1,2-trichloroethane, Trichloroethylene, Tetrachloroethylene, Benzene, 1,3-dichloropropene.

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7

The Trend of the R&D Policy in the U S
— Transition of priority areas in the R&D budget allocation of the federal government —

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7.1 Introduction

On January 10, 2002, President Bush signed all the appropriation bills for fiscal 2002, and, subsequently, the government budget for fiscal 2002 was approved. The government budget for fiscal 2002 was fixed after 3 months elapsed from the commencement of fiscal 2002 on October 1, 2001. On February 4, 2002, the President announced the Budget Message (the budget compilation policy to be delivered by the President to Congress) for fiscal 2003.

In this report, we analyze the characteristics of the R&D budget in the government budget for fiscal 2002 (from October 2001 to September 2002) and the Budget Message for fiscal 2003, and then review the trend of the R&D policy of the U S government.

Table 1: The compilation process of the discretionary budget in the US.

Time	Description
In early February	The President delivers the Budget Message to Congress.
From mid-February to the end of September	Deliberations in Congress
	Congress submits the appropriation bill to the President.
	The President signs the bill.*
	The budget is approved.
October 1	New fiscal year starts.

* When the President does not sign the appropriation bill, the bill can be approved if more than 2/3 of Congress vote in favor of it.

7.2 Budget compilation system in the U S

The government budget in the U S is composed of; (1) the discretionary budget requiring legislation in accordance with the appropriation act, and (2) the obligative budget that can be renewed automatically once it has been approved in accordance with the authorization act. The governmental R&D budget is included in the discretionary budget and will be finalized in the budget compilation process shown in Table 1.

7.3 Transition of the governmental R&D budgets

The transition of the governmental R&D budgets for the past 20 years is shown in Figure 1.

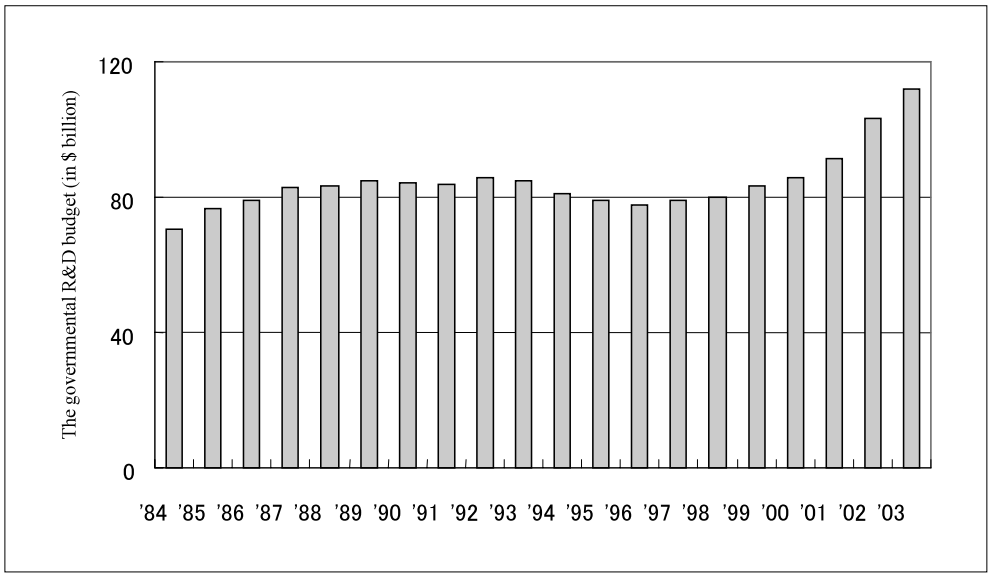
The governmental budgets increased significantly in fiscal 2002 and 2003. The reason is because of the drastic increase in the R&D budget for countermeasures against terrorism, due to the influence of the simultaneous multiple terrorist attacks against the US on September 11, 2001, and the increase of R&D investments as a stimulant for the recession.

7.4 The governmental R&D budget for fiscal 2002

7.4.1 Outlines of the governmental R&D budget for fiscal 2002

As for the governmental R&D budget for fiscal 2002, the breakdown by institute is shown in Figure 2, and their increasing rates from the previous year by institute are shown in Figure 3,

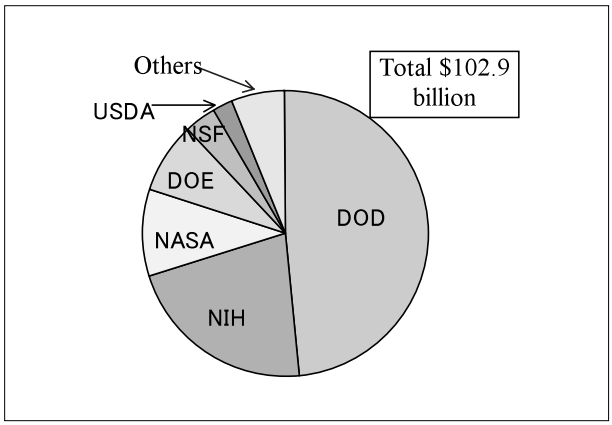
Figure 1: Transition of the governmental R&D budgets



* The figure for fiscal 2003 is the R&D budget in the Budget Message

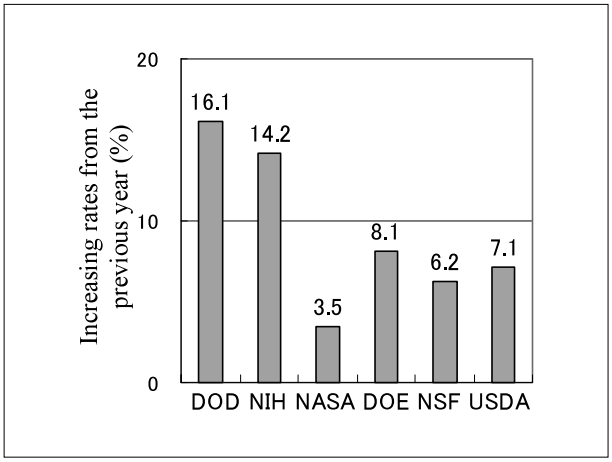
Source: Document released by OMB (Office of Management and Budget)

Figure 2: R&D budget for fiscal 2002 by institute



Source: Data provided by AAAS
(R&D Budget and Policy Program)

Figure 3: Increasing rates from the previous year of R&D budgets by institute for fiscal 2002



Source: Data provided by AAAS
(R&D Budget and Policy Program)

respectively.

7.4.2 Characters of the R&D budget for 2002 by institute

(1) DOD

The R&D budget of the DOD (Department of Defense) for fiscal 2002 increased by 16.1% from the previous year. This is the biggest rate of increase for the past 20 years. As a background to this, there are the drastic increase of the R&D budget related to the development of the missile defense system, which is one of the most important issues of the Bush Administration, and the drastic increase of the R&D budget for countermeasures against terrorism due to the influence of the simultaneous multiple terrorist attacks against the U S.

(2) NIH

The R&D budget of the NIH (National Institutes of Health) for fiscal 2002 increased by 14.2% from the previous year. The reason is because the budget increased as a part of the NIH's budget doubling campaign (a 5-year campaign started from fiscal 1999) and the R&D budget for countermeasures against terrorism increased significantly due to the influence of the simultaneous multiple terrorist attacks against the US.

(3) NASA

The R&D budget of NASA (National Aeronautics and Space Administration) for fiscal 2002 increased by 3.5% from the previous year. The

reason is because the R&D budget required for improving the security of NASA's facilities was newly appropriated due to the influence of the simultaneous multiple terrorist attacks against the US. The R&D budget of ISS (International Space Station) for fiscal 2002 decreased from the previous year. While, the research costs for biology and physics increased.

(4) DOE

The R&D budget of the DOE (Department of Energy) for fiscal 2002 increased by 8.1% from the previous year. The reason is because activities for developing weapons against terrorism targeting nuclear facilities were strengthened after the simultaneous multiple terrorist attacks against the US. As a result of this, the DOE's R&D budget related to national defense increased significantly, while the R&D budget related to the energy field and the budget related to science stayed almost the same as in the previous fiscal year.

(5) NSF

The R&D budget of the NSF (National Science Foundation) for fiscal 2002 increased by 6.2% from the previous year. The reason is because the respective R&D budgets of the NSF for the cross-departments type Nanoscale Science, Engineering, and Technology Initiative and the US. Global Change Research Program increased significantly due to the influence of the simultaneous multiple terrorist attacks against the US. The fact that the competitive funds to be supplied to researchers from the USDA increased significantly upon strong request from Congress also influenced this increase of the R&D budget of the USDA.

(6) USDA

The R&D budget of the USDA (United States Department of Agriculture) for fiscal 2002 increased by 7.1% from the previous year. The reason is because research activities related to the security of food and researches against terrorism targeting the food supply system were strengthened. And the fact that the competitive funds to be supplied to researchers from the USDA increased significantly upon strong request of Congress also influenced the increase of the R&D budget of the USDA.

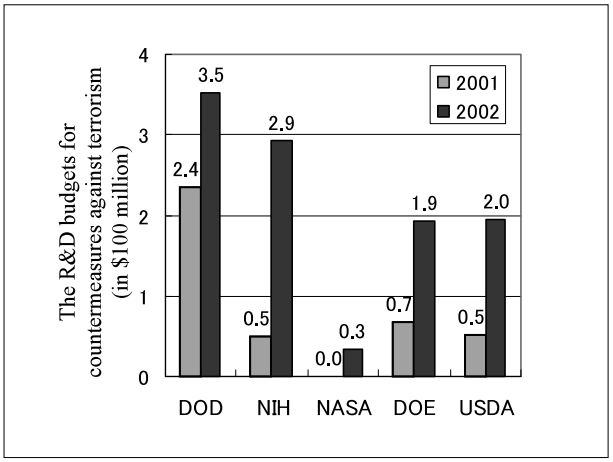
7.4.3 The R&D budget for countermeasures against terrorism

In this section, we analyze the R&D budget for countermeasures against terrorism, which strongly influenced the governmental R&D budget for fiscal 2002. While the R&D budget for countermeasures against terrorism for fiscal 2001 was $580 million, the same budget in the President's Budget Message for fiscal 2002 decreased to $560 million. However, after the simultaneous multiple terrorist attacks against the US., the President and Congress decided to disburse $400 million of the budget for countermeasures against terrorism immediately. Consequently, a part of this budget was appropriated in the R&D budget for countermeasures against terrorism for fiscal 2002, and, as a result, the R&D budget for countermeasures against terrorism for 2002 increased significantly in the end to $1.5 billion.

The R&D budgets for countermeasures against terrorism for fiscal 2001 and 2002 by institute are shown in Figure 4. In all institutes, the R&D budgets for countermeasures against terrorism for fiscal 2002 increased significantly from the budgets for fiscal 2001.

As for the R&D budgets for countermeasures against terrorism added to the budget for fiscal 2002, some of them are to be disbursed only for this year and the others will be disbursed

Figure 4: The R&D budgets for countermeasures against terrorism by institute



* The R&D budget of NASA for countermeasures against terrorism for fiscal 2001 was zero. The R&D budgets of the NSF for countermeasures against terrorism for both fiscal 2001 and 2002 were zero.

Source: AAAS Special Report on Counter - Terrorism R&D.

continuously in the future. Although it was unknown whether the budget for countermeasures against terrorism would be disbursed continuously or not at the time when the budget for fiscal 2002 was approved, we can analogize the future directions of the budget for countermeasures against terrorism from the President's Budget Message for fiscal 2003 as mentioned below.

7.4.4 Comparison with the President's Budget Message for fiscal 2002

The increasing rates of the governmental R&D budgets from the previous year, which the President submitted in the Budget Message before the simultaneous multiple terrorist attacks against the US, are shown in Figure 5.

In the Budget Message for fiscal 2002, the R&D budgets for both the DOD and the NIH increased by more than 10% from fiscal 2001, while the R&D budgets for other institutes were the same or decreased from fiscal 2001.

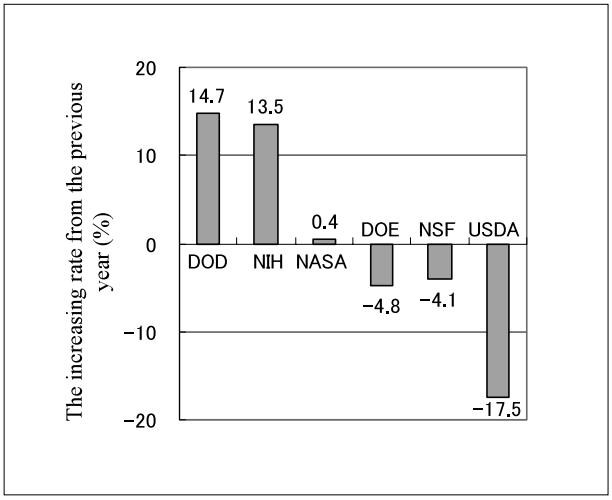
The budgets of the DOD and the NIH increased since President Bush publicly pledged to actively support these institutes during the presidential election.

On the other hand, the R&D budgets of institutes other than the DOD and the NIH decreased since the President, planning to strongly reduce taxes over 10 years, had no margin to increase the R&D budgets for these institutes. The stance of President Bush is in contrast to the stance of President Clinton, who actively increased the R&D budgets of the DOE, the NSF and the USDA.

7.4.5 Influences of the simultaneous multiple terrorist attacks against the US on the governmental R&D budget for fiscal 2002

How did the simultaneous multiple terrorist attacks against the US influence the R&D budget of the U.S. government? The R&D budgets for other than countermeasures against terrorism have also increased as well as the budget for countermeasures against terrorism increased significantly. As an example of the former, we can cite the fact that the R&D budget of the NSF, not having an R&D budget for countermeasures against terrorism, finally increased.

Figure 5: The increasing rates from the previous year of the R&D budgets by institute in the Budget Message for fiscal 2002



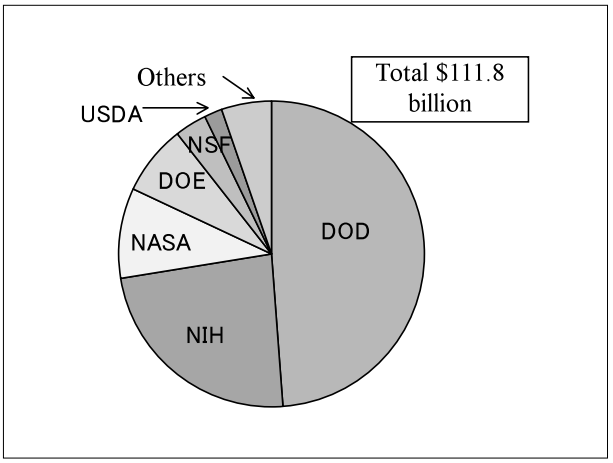
Source: AAAS Analysis of R&D in the FY 2002 Budget.

The national finance of the US, which had been in the black for 4 years since 1998, will fall into the red in fiscal 2002. This is a big change because an accumulated black ink balance of $5.6 trillion was expected for 10 years since 2002 in the Budget Message for fiscal 2002. However, both the President and Congress recognized that the nation will be in a state of emergency in fiscal 2002, suffering from the influences of the simultaneous multiple terrorist attacks against the U.S., and agreed to actively support R&D even if the national finance falls into the red.

7.5 The President's draft of the governmental R&D budget for fiscal 2003

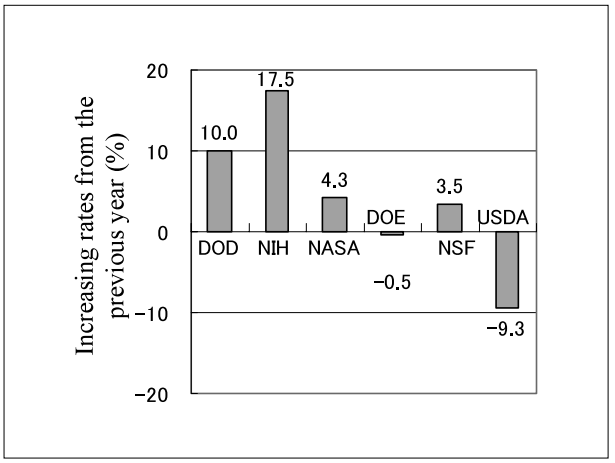
The R&D budgets by institute in the Budget Message for fiscal 2003 are shown in Figure 6, and the increasing rates of the budgets by institute from the previous year are shown in Figure 7, respectively. In the Budget Message for fiscal 2003, the R&D budget is $111.8 billion, which is an increase of 8.7% from the approved budget of the previous year. As a background to this, there is an intention on the part of the President to accept a red ink balance in fiscal 2003, continuously from the budget for fiscal 2002, and to actively support R&D.

Figure 6: R&D budget by institute in the Budget Message for 2003



Source: Data provided by AAAS
(R&D Budget and Policy Program)

Figure 7: Increasing rates from the previous year of the R&D budgets by institute in the Budget Message for 2003



Source: Data provided by AAAS
(R&D Budget and Policy Program)

7.5.1 Characteristics of the R&D budgets by institute in the Budget Message for 2003

(1) DOD

The R&D budget of the DOD increased by 10.0% from the previous year in the Budget Message for fiscal 2003. The reason is because the budget for developing weapon systems has been drastically increased. On the other hand, the budgets for general researches and technology development for other than weapons decreased from the previous year.

(2) NIH

The R&D budget of the NIH increased by 17.5% from the previous year in the Budget Message for fiscal 2003. As a background to this, there is the fact that fiscal 2003 will be the last year of the 5-year campaign for doubling the NIH's budget, and the entire budget of the NIH has increased drastically in order to maintain the commitment to the public. Among the institutes under the NIH, the budgets of the NIAID (National Institute of Allergy and Infectious Diseases) and the NCI (National Cancer Institute) have increased drastically in particular.

Since the NIAID leads in the development of countermeasures against bio terrorism in the NIH, the R&D budget for countermeasures against bio terrorism of the NIAID increased by 57.3% from the previous year. The NIAID is also an institute leading research activities on AIDS, which the Bush Administration attaches importance to, and the budget for researching on AIDS was also increased by 10%.

In the same way, for the research activities on cancer, which the Bush Administration also attaches importance to, the budget for researching on cancer of the NCI representing the NIH increased to $4.7 billion, which represents an increase of 12.2% from the previous year.

(3) NASA

The R&D budget of NASA increased by 4.3% from the previous year in the Budget Message for fiscal 2003. As a background to this, there is the fact that the R&D budget of the SAT (Science, Aeronautics and Technology) program and the funds for space science research activities have increased drastically. The funds for the BPR (Biological and Physical Research) have increased in particular. On the other hand, the budget of the manned space flight programs including the ISS (International Space Station) plan decreased from the previous year.

(4) DOE

The R&D budget of the DOE decreased by 0.5% from the previous year in the Budget Message for fiscal 2003. There is the influence of the fact that the R&D budget related to national defense, which increased in fiscal 2002 due to the influence of the simultaneous multiple terrorist attacks against the U.S., decreased in the Budget Message for fiscal 2003. It influences significantly that the budget for developing weapons, which had been added to

the budget for 2002 as a budget for countermeasures against terrorism, has not been appropriated to the budget for fiscal 2003. However, among the R&D activities related to the national defense of the DOE, the R&D budgets for the advanced science-computing program and research activities related to nuclear weapons have increased.

For the R&D budgets related to science, the budgets for physics research, fundamental energy research and computing, etc., have increased. However the entire budget related to science is almost equivalent to the previous year in general, since the budget for the project developing the spallation neutron source facility was decreased.

The R&D budgets related to energy have decreased slightly. In these R&D budgets, the priority is shifting from natural gas or petroleum to clean coal. And it is also characteristic that the priorities in the DOE are shifting from the PNGV (Partnership for a New Generation of Vehicles) developing vehicles with high petrol consumption efficiencies, to the FreedomCAR project, which is the joint development of vehicles using fuel cells between the government and the automobile industry in the U. S.

(5) NSF

The R&D budget of the NSF increased by 3.5% from the previous year in the Budget Message for fiscal 2003.There is the significant influence of the fact that the NSF obtained the earth science research program from the DOC (Department of Commerce), the hydrology research program from the DOI (Department of Interior) and the environment science technology R&D from the EPA (Environmental Protection Agency), respectively.

In addition, drastic increases of the budgets for mathematic research and IT research also contribute to the increase of the R&D budget of the NSF.

(6) USDA

The R&D budget of the USDA decreased by 9.3% from the previous year in the Budget Message for fiscal 2003. The reason is because the budgets of research activities related to food security, which had been added to the budget for fiscal 2002 as an influence of the simultaneous multiple terrorist attacks against the U. S., and countermeasures against terrorism targeting the food supply system are not appropriated in the Budget Message for fiscal 2003.

7.5.2 Foresights of deliberations related to the governmental R&D budget for fiscal 2003 in Congress

Since the importance of countermeasures against terrorism and territory defense has currently been raised as an influence of the simultaneous multiple terrorist attacks against the U. S., it is highly expected that the R&D budget of the DOD, which has increased from the previous year in the Budget Message for fiscal 2003, will be approved by Congress. Furthermore, since Congress will be going through elections races in November 2002, it is highly expected that Congress will approve increasing the budget of the NIH, for which national support can be easily obtained. Since the budgets of the DOD and the NIH account for about 3/4 of the governmental R&D budget, it is expected that the entire governmental R&D budget for fiscal 2003 will increase from the previous year.

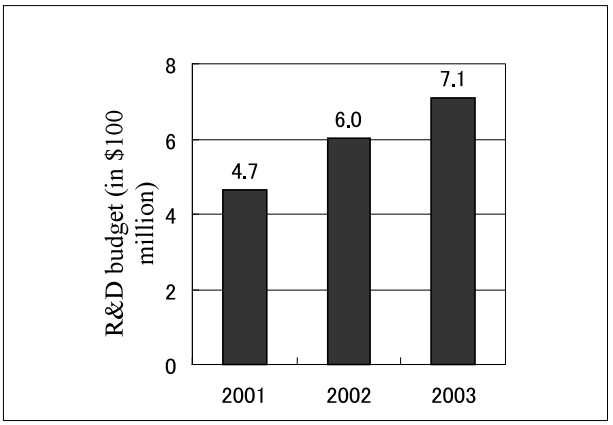
Many congressional members of the Democratic Party feel that the R&D budget in the Budget Message must be increased more and the R&D required for countermeasures against terrorism and boosting the economy must be properly executed. On the other hand, some the conservatives of the Republican Party have the opinion that the entire discretionary budget including the R&D budget must be squeezed in consideration of the large-scaled tax reduction and the economic recession.

Since Congress, with elections ahead, shows a marked trend toward increasing the budget, there is a high possibility that the governmental R&D budget for fiscal 2003 will exceed the Budget Message.

7.6 Interdepartment program

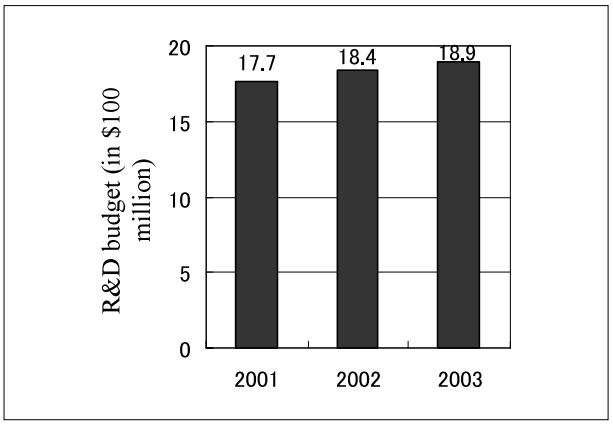
Transitions of the R&D budgets of the interdepartments type initiatives such as NNI (Nanoscale Science, Engineering, and Technology Initiative), NITR&D (Networking and Information

Figure 8: Transition of the budget of NNI



Source: Data provided by AAAS (R&D Budget and Policy Program)

Figure 9: Transition of the budget of NITR&D

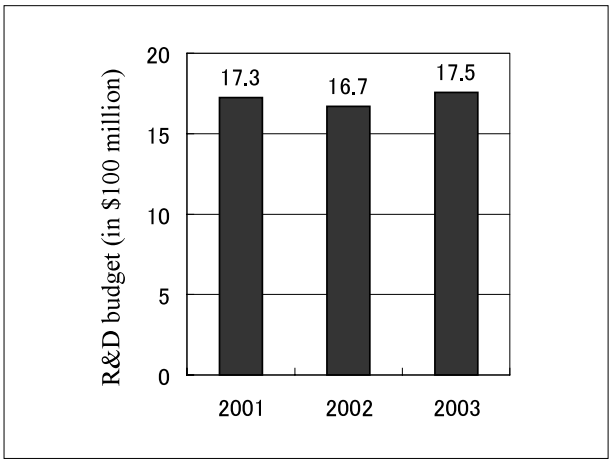


Source: Data provided by AAAS (R&D Budget and Policy Program)

Technology R&D initiative) and USGCRP (U. S. Global Change Research Program) are shown in Figure 8 to 10, respectively.

The R&D budget of NNI has increased constantly. The R&D budgets of NITR&D and USGCRP have showed a trend toward increasing. The reason why the R&D budget of USGCRP for fiscal 2002 decreased from the budget for fiscal 2001 is that the R&D budget of NASA, taking charge of a major part of the program, was decreased.

Figure 10: Transition of the budget of USGCRP



Source: Data provided by AAAS (R&D Budget and Policy Program)

7.7 Conclusion

The governmental R&D budget has showed a trend toward increasing. In particular, the R&D budgets of the DOD and the NIH, accounting for 3/4 of the entire budget, have increased significantly. It is expected that both the President and Congress will actively support R&D and accept a red ink balance in the national finance. The governmental R&D budget will in general continue to increase as importance is attached to R&D for countermeasures against terrorism and R&D for boosting the economy.

Acknowledgements

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8

Trends in French Science, Technology, and Innovation Policy — The MINATEC Industry-Academia-Government Nanotechnology Innovation Center Project —

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8.1 Introduction

In recent years, Europe has joined the United States and Japan as an active base for nanotechnology research and development. Among the Europeans, France determined its basic science and technology policy within an interministerial committee on science and technology created in July 1998 and chaired by then-Prime Minister Lionel Jospin. In October, The National Science Council was formed with representatives of industry, academia, and government. Since then, France has seen rapid development of fields of emphasis, budgeting, and large-scale reforms of its public research institutions.

In June 1999, the government determined the following fields as high priority.

1) Life sciences
2) Information and communications technology (ICT)
3) Humanities and social science
4) Energy and transportation
5) Earth/environmental sciences, space

Within these fields, nanotechnology receives great emphasis as a base technology for the life sciences and ICT.

The passage of the Law on Innovation and Research loosened regulations restricting the commercial activities of researchers at public research institutions. At the same time, the National Center for Scientific Research (CNRS) underwent reforms including stronger ties with universities, the National Science Fund (FNS) was established to provide funding, the Research and Technology Fund (FRT) was upgraded, and a committee was set up to oversee the high-priority areas.

The Center for Innovation in Micro and Nanotechnology-MINATEC (Pole d'Innovation en Micro et Nanotechnologies) is a joint industry-academia-government project connected with this trend of major reforms in science, technology, and innovation policy.

Centered around CNRS (National Center for Scientific Research), CEA-LETI (Atomic Energy Commission-Electronics and Information Technology Laboratory), INPG (Institut National Polytechnique de Grenoble), and department government agency AEPI (Agence d'Etude et de Promotion de l'Isere), the project is creating an international research and development base covering a broad array of micro and nanotechnologies for industry, academia, and government.

With a 150 million Euro budget for the five years 2001-2005 (note that that is the budget for construction of the Innovation Center, not the total research budget), seven facilities will be built on a 60,000 m^2 site within the Grenoble national research park in southeastern France (total area: 80,000 m^2).

This project features an inside strategy that integrates basic and applied research with business startups through industry-academia-government cooperation. This has included advanced nanotechnology such as carbon nanotube devices and single electron devices, as well as microtechnology such as MEMS, biochips, semiconductors, and optics.

Since 1998, France has strengthened cooperation

among industry, academia, and government, reformed its national research institutes, made a strategic shift away from nuclear power in its physics research, and added a vision of regional growth. MINATEC is thus also worthy of attention as a microcosm of France's new policies on science, technology, and innovation.

8.2 Background: Characteristics of Grenoble

A number of European and French national research institutes are located in the Grenoble area, which is also home to numerous joint projects between corporations and the research centers of scientific and technical universities.

Seventeen thousand researchers are employed at industry, academic, and government research organs in the area. (Four thousand of them are in the private sector and 13,000 in the public sector. Seven thousand work in applied research, while 10,000 work in basic research.)

Looking at the details of public sector research institutions, international research institutes such as ESRF (European Synchrotron Radiation Facility) and EMBL (European Molecular Biology Laboratory) employ 1,150 people, while French national research organs such as CEA (French

Table 1: Employees of public research institutions in Grenoble

International Centers		National Centers		University research	
ESRF	500	CEA	3,000	UJF	2,300
ILL	400	CNRS	1,400	INPG	1,230
GHFML	100	INSERM	2,970		
EMBL	55	F.T. R&D	350		
IRAM	90	CRSSA	300		
		INRIA	330		
Total	1,145		8,350		3,530

Source: Pole University - data for 2000

***Abbreviations:**

International Centers
- ESRF European Synchrotron Radiation Facility
- ILL Institut Laue-Langevin
- GHFML Grenoble High Magnetic Field Laboratory
- EMBL European Molecular Biology Laboratory
- IRAM Institute of Millimetric Radioastronomy

National Centers
- CEA Atomic Energy Commission
- CNRS National Center for Scientific Research
- INSERM French Institute of Health and Medical research
- F.T. R&D France Telecom Research and Development
- CRSSA Research Center of the Army Health Services
- INRIA National Institute for Research into Information Technology and Automation

University Research
- UJF Joseph Fourier University
- INPG Institut National Polytechnique de Grenoble

Table 2: Researchers in private corporations in Grenoble

Enterprises	Jobs	Nationality	Activity
ST Microelectronics	1,000	France, Italy	Semiconductor
Schneider Electric	450	France	Electric Equipment
Hewlett-Packard	400	USA	IT
Lafarge	350	France	Cement
Pechiney	300	France	Aluminum
Bull	230	France	IT
Sun Microsystems	200	USA	IT
Air Liquid	150	France	Chemicals
Xerox Research Center Europe	120	USA	IT
. . .	. . .		
	~ 4,000		

Note: Includes only corporations with at least 100 employees.

Source: Author's compilation on the basis of AEPI materials.

Atomic Energy Commission) and CNRS (National Center for Scientific Research) employ 8,350, and university research facilities employ 3,500.

College and university students in the area number 52,000, including those attending four universities that include INPG (Institut National Polytechnique de Grenoble), one of MINATEC's core institutions, and Joseph Fourier University, which focuses primarily on science and medicine, as well as business and teacher-training schools.

8.3 The perspective of regional scientific and technical policy

France is organized into 22 regions, which are further subdivided into 96 departments. Grenoble is located in the department of Isere in the region of Rhone-Alpes. Populations are as follows (see Table 3).

At 43,700km², the area of Rhone-Alpes is equivalent to that of Switzerland, Belgium, or the Netherlands, while the population equals that of Denmark or Ireland.

Within the Rhone-Alpes region, the department of Isere, with its concentration of research institutes, demonstrates extremely high growth in innovation. Table 4 shows the number of international patents received.

The number of international patents in Isere grew rapidly between 1998 and 1999. This can be seen as a result of the loosening of regulations preventing publicly-employed researchers at public institutions from starting businesses or working on the side, as mentioned Section 8.1.

While this result can be seen as peculiar to Grenoble with its concentration of public research institutes, the skillful joining of industry, academia, and government has been vital in making it a driving force of the local economy.

Table 3: Population

France	60.42 million
Rhône-Alpes	5.68 million
Isére	1.10 million

Source: AEPI materials

Table 4: International Patents

Patents Fields	1998	1999	Growth rate
France	13,251	13,592	2.6%
Rhône-Alpes	1,512	1,536	1.6%
Isére	235	314	33.6%

Source: AEPI materials

8.4 The system for accelerating industry-academia-government cooperation

National policy had already concentrated government and academic research institutions in the Grenoble area, but simply locating facilities near each other was not sufficient to promote industry-academia-government cooperation. Many of France's major corporations were operated by the government. Cultural traditions included little awareness of entrepreneurism, and a sudden change to a U.S.-style environment was not possible. While there were many major differences, the environment was rather similar to that of Japan.

To promote industry-academia-government cooperation under such conditions, it is considered important to provide motivation within the project system for voluntary cooperation. For example, systems were put in place to cause corporations to feel the necessity of cooperation with university and government research institutes, to instill an entrepreneurial spirit in students, and to provide early returns on investment so that investors could act with confidence.

We will examine each of these perspectives in turn.

— Investors

MINATEC undertakes not only futuristic nanotechnology research, but also research on microtechnology that is currently being commercialized. This enables investors to diversify risk across short-term and long-term research.

MINATEC also offers the advantages of investment that holds a high probability making a transition from microtechnology to nanotechnology and that offers an early return on investment in microtechnology.

— Corporations

Similarly, by positioning research agendas not only in futuristic nanotechnology but also in current microtechnology, those in areas that do not initially require the advanced physics background of semiconductor miniaturization, for example, can still obtain the necessary advanced physics background for nanoscience as generations are replaced. Engaging in joint research with national laboratories at the micro stage can enable a smooth transition to nanotechnology in the future. (This is because the transition to the nano level will not be linear, but will be a non-linear process based on technological breakthroughs.)

For universities, the concentration of outstanding science and engineering undergraduates and graduate students enables them to establish a pool of human resources.

— Universities

From the perspective of universities, a concentration of corporations simplifies the search for research partners. Because many European funding sources require corporate partners for applied research, this is quite necessary. While exploratory research does not necessarily require a partner, such funding often has one-year time limits or other restrictions.

Showing students the entrepreneurial process up close is considered to be a vital task for universities. As mentioned above, unlike the USA, France has had a history of nationalized industry, and the entrepreneurial mindset has yet to fully flower. Having students observe venture companies formed through spin-offs from large corporations and start-ups from national laboratories will help to foster such a mindset. This will stimulate spontaneous start-ups.

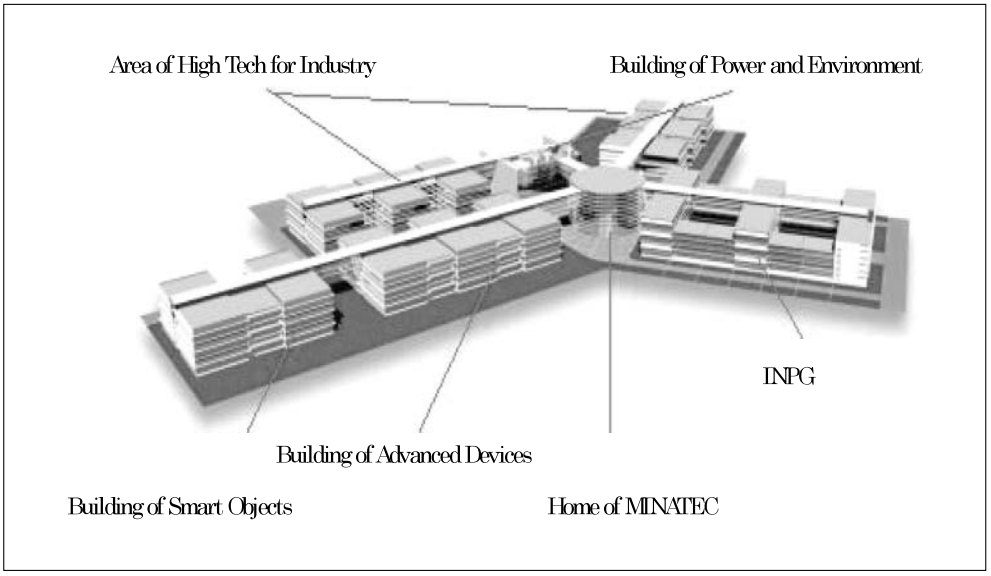
In addition to the creation of the above systems to motivate industry-academia-government cooperation, consideration was also given to construction of buildings.

Currently, national laboratories, universities, and research parks where corporations are concentrated are all located in separate buildings in different areas, although they can all be reached within 10 minutes by trams running between them. Even 10 minutes, however, is considered too distant to facilitate industry-academia-government cooperation, and a system is being constructed that will combine the buildings themselves into a single location.

As is shown in Figure 1, MINATEC itself will be surrounded by wings for national research institutes, for university engineering departments, and for corporate research, with personnel allowed to pass freely among them. Provisions are made so that meetings and seminars among industry, academia, and government can be held at any time.

Locating these research facilities near the center

Figure 1: MINATEC building layout



Source: Based on CEA-LETI materials

of the city not only facilitates free interaction among the research institutions and universities, it creates a very congenial living environment for researchers through integration with their lifestyles.

While in Japan new facilities are generally constructed outside of city centers, MINATEC is being built on the site of old CEA facilities that have been torn down.

To attract and retain outstanding researchers, it is considered vital to provide not only for the convenience of the researchers, but also for the comfort of their families.

Grenoble is a highly accessible city. Lyon, France's second city, is less than an hour away by train, while Paris can be reached in three hours on the TGV. International airports in Lyon and Geneva, Switzerland, are only an hour's drive away.

There is much to be learned from the structure of these systems for attracting researchers, corporations, and investors and leading them naturally and inevitably towards industry-academia-government cooperation.

The positioning of such cooperation not as an end in itself but as a means leading inevitably to the promotion of research and development is vital.

8.5 The role of international researchers

Along with the series of reforms to its science and technology policy (fields of emphasis, reform of national research institutions, loosened regulations for researchers, strengthened industry-academia-government cooperation) it implemented in 1998 and 1999, France has made active efforts to attract international researchers through steps such as an expanded plan to accept post-doctoral researchers.

The role of international researchers and exchange students at MINATEC is also a very important one. Currently there are approximately 6,000 researchers and students from foreign countries in the Grenoble area, and they are an important motivating force for furthering research.

While there are concerns about technology outflow, the benefits are believed to far outweigh any possible losses through such outflow. These benefits include not only the diversification and vitalization of research accompanying researchers from other cultures, but also, from a more utilitarian point of view, access to the management techniques and entrepreneurial expertise of countries such as the USA that are as advanced in business as they are in research and development.

Various steps are taken to retain international researchers. A language school teaching in six languages is located at Grenoble's national railway train station, so that those who have not already studied French may begin doing so. The families of researchers may also take advantage of primary school instruction in four languages and secondary school instruction in six at no charge.

8.6 Attracting foreign corporations

As shown in Table 2, 3 of the top 10 private sector corporate laboratories in Grenoble belong to American corporations. Hewlett-Packard, Sun Microsystems, and Xerox are all leading companies in the USA.

International developments in Grenoble are not limited to France and Europe. US corporations

Table 5: Foreign corporations in Grenoble

1	USA	68
2	Germany	25
3	Italy	21
4	UK	14
5	Switzerland	9
6	Sweden	6
7	Canada	5
7	Japan	5
7	Finland	5
10	Netherlands	4
10	Belgium	4
12	Denmark	3
13	Spain	2
13	Ireland	2
15	Norway	1
15	Austria	1
15	Israel	1
15	Turkey	1
15	Australia	1

Source: AEPI materials

have been actively making use of Grenoble's research resources.
This not only shows the importance the French government attaches to foreign direct investment (FDI) in research and development in France, it also demonstrates the active efforts made to recruit international researchers and an awareness of the importance of international resources.(see Table 5)

8.7 Alliances with foreign research institutions

In addition to utilizing international research resources by recruiting international researchers and attracting foreign corporations, MINATEC has also formed alliances with several research institutions outside of France.
Particularly noteworthy are links with IMEC in Belgium, SEMATEC in the USA, and CSEM (Swiss Center for Electronics and Micro Technology) in Switzerland.
Cooperation with IMEC and SEMATEC focuses on research into next-generation semiconductor and device technologies. ASML (Netherlands), which along with Nikon and Canon is the leader in lithography technology, the key to semiconductor micromachining, has a laboratory in Grenoble. No doubt they, as well as the Americans and Japanese, are engaged in advanced research. They bear continual watching.
CSEM is a leader in the MEMS and micromachining technologies that are garnering so much attention now. They have been contracted to build micromachines for NASA's Mars exploration satellite.They also cannot be overlooked.

8.8 Research at CNRS

Having given an overview of the MINATEC project and the foundations of research in Grenoble, in this section we will discuss research at CNRS, a major player in MINATEC.
CNRS operates MINATEC along with CEA-LETI, another core national research laboratory, but their research agendas differ somewhat. While CEA-LETI focuses more on relatively applied fields such as electronic devices, CNRS is involved with the more academic fields of nanoscience.
The CNRS research agenda includes:

* Carbon nanotubes
* Single-electron transistors
* Nanomagnetics
* Nano-optics
* Nanomanipulation
* Microrobotics
* Microfluidics

Currently the most attention is being given to carbon nanotubes. CNRS carries out research into interconnection through the self-organization of carbon nanotubes and other areas closely related to their basic physical properties. They are also engaged in advanced research in fields adjacent to nanomeasurement, such as the utilization of synchrotron radiation.

8.9 Research at CEA-LETI

As noted above, CEA-LETI research tends to be in applied fields such as:

* Silicon device technology
* Optical device technology
* Information and communications technology
* MEMS technology
* Biotechnology (DNA chip technology, nano-biodevice technology)
* Molecular device technology
* Carbon nanotube devices

In the same field of carbon nanotube technology, for example, they are working on turning them into actual devices. They have already demonstrated an emitter for field emitting displays (FEDs).
They are researching not only ICT-related nanotechnologies, but also a broad range of fields combining biotechnology with nanotechnology, from DNA chips to nanobiology.

8.10 Conclusion

Having thus introduced the MINATEC project, two things stand out above all else. They are its consistency with the reforms in science and technology and innovation policies, and the logical

and dynamic way in which the planned project is being run.

As far as research standards are concerned, Japan leads France in more areas than not. France longs for the participation of Japanese researchers, laboratories, and corporations in the carbon nanotube field it is paying so much attention to.

However, having once lagged alongside Japan in industry-academia-government cooperation to promote research and development, France is now rapidly developing high-tech ventures start-ups and distancing itself from Japan in that area.

That is because moving research and development forward depends not only on research standards, but also very much on project and research management.

France is steadily implementing policies to form a base for research by loosening the restrictions preventing national laboratory researchers from doing other work or starting companies, by utilizing international researchers, by seeking FDI, by forming alliances with research institutions in other countries, by forming partnerships, and by providing tax incentives for private-sector corporate research and development. Details of motivation and synergies are being studied and considered, and dynamic systems are being constructed. All of this is very meaningful.

What is important is that industry-academia-government cooperation is not an end in itself. It is a means of promoting research and development through a dynamic system that naturally leads to such cooperation.

(Original Japanese version: published in March 2002)

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).

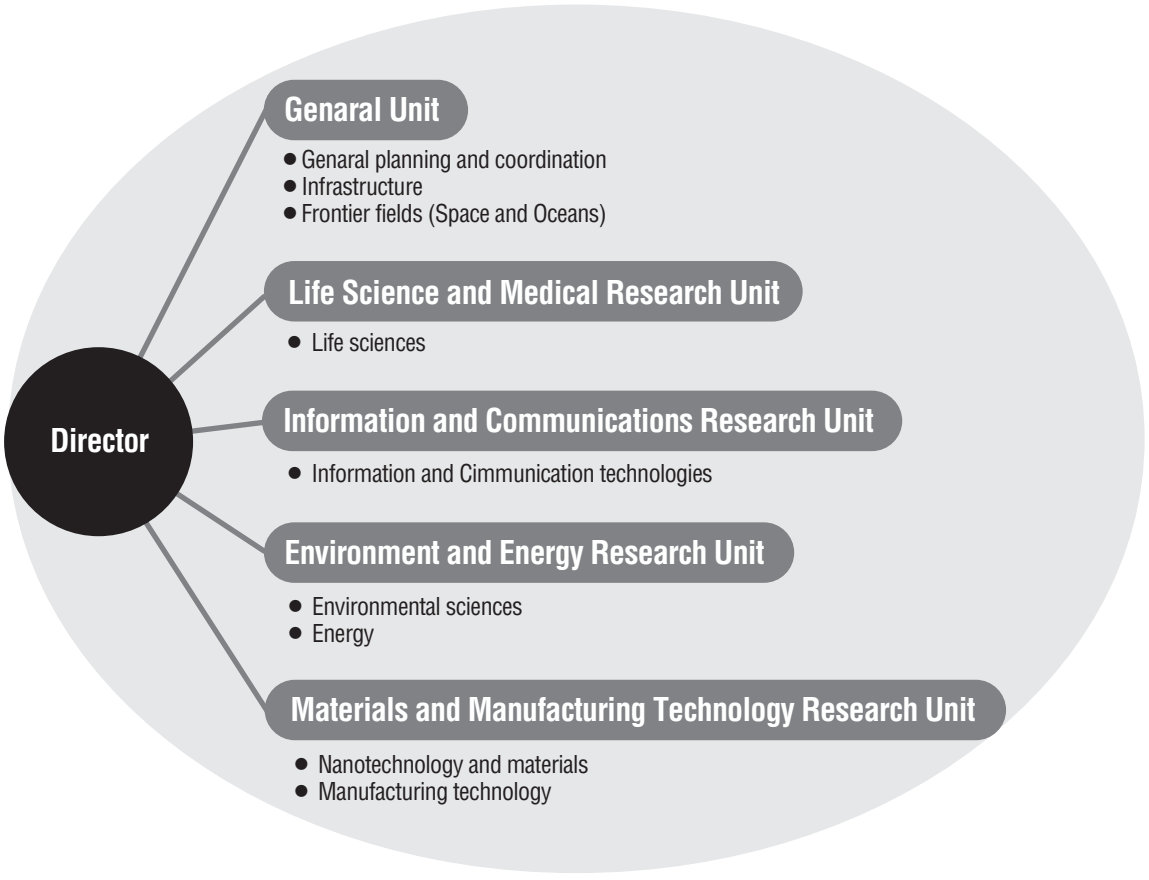
3. Technology foresight and S&T benchmarking survey

— 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

- Life Sciences
- Information & Communication Technologies
- Environmental Sciences
- Nanotechnology and Materials
- Energy
- Manufacturing Technology
- Infrastructure
- Frontier
- Science & Technology Policy

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