JPRS-JST-92-003
20 FEBRUARY 1992

FOREIGN BROADCAST INFORMATION SERVICE

JPRS Report

Science & Technology

Japan

STATUS, DEVELOPMENT DIRECTION OF ADVANCED MULTIDISCIPLINARY RESEARCH AREAS

JPRS-JST-92-003
20 FEBRUARY 1992

SCIENCE & TECHNOLOGY
JAPAN

STATUS, DEVELOPMENT DIRECTION OF ADVANCED MULTIDISCIPLINARY RESEARCH AREAS

CONTENTS

Status, Development Direction of Advanced Multidisciplinary Research Areas

92FE0113A Tokyo SCIENCE AND TECHNOLOGY AGENCY REPORT in Japanese Mar 91 pp 1-178

[Interim report by the Hitachi General Planning Research Institute: "Survey of Status and Development Directions of Advanced Multidisciplinary Research Areas in Japan"]

[Text] Overview

Advanced S&T in recent times has evolved towards multidisciplinary research areas that straddle several specialized areas. From now on it is essential for Japan to efficiently and effectively drive research in such multidisciplinary research areas so that it can promote the creative basic research that is its duty as a scientifically and technologically advanced nation.

For this reason it was decided that the "Survey of Status and Development Directions of Advanced Multidisciplinary Research Areas in Japan" would be carried out over the two-year period from 1990 through 1991. The objective is to gain knowledge about the current state and development directions of multidisciplinary research areas, and also about effective research promotion policies, by getting a grasp on the activities of study societies and the directions of ongoing research by individual researchers.

In FY 1990 we got a grasp on the current state of advanced multidisciplinary research areas in Japan by interviewing knowledgeable people, conducting questionnaire surveys of individual researchers and offices of academic societies, and investigating documentation. That resulted in the extraction of what are thought to be important areas of multidisciplinary research from now on: 1) intelligent materials, 2) frontier instrumentation and control technology, 3) gene manipulation technology, 4) neuroscience and neurotechnology, 5) organomolecular S&T, 6) chronobiology, 7) global environmental S&T, 8) recycling S&T, and 9) computing science and technology. We then compiled the information about the current state of affairs in each area and topics thereof. And, based on the results of the questionnaire surveys, we investigated the research environments of researchers working in multidisciplinary areas, the bottlenecks they encounter in accomplishing their research, and directions towards improvements.

In FY 1991, we plan to focus mainly on case studies of two or three research areas of the nine listed above. We will investigate the backgrounds from which multidisciplinary research areas arise; the developmental processes involved; and new directions of future development, including the state of affairs in foreign countries. We will then organize the data into the items that are thought to be important as policies for promoting basic research.

I. Summary of Survey Project

1. Objectives of Survey

The advanced S&T of recent times is evolving towards multidisciplinary research areas. As the background behind this we can take the up the activation of research exchange at the level of individual researchers: existing academic societies and the various kinds of study societies that go beyond the boundaries of academic systems, workshops that are held, etc.

From now on, in order to promote the creative basic research that is its duty as a scientifically and technologically advanced nation, it is essential that Japan accelerates this kind of researcher exchange, and efficiently and effectively searches for research seeds, which will come forth as a result of that exchange, and cultivates those seeds.

Therefore, by getting a grasp on ongoing activities such as study societies and on the directions of ongoing research by individual researchers, we will gain knowledge about the current state and development directions of multidisciplinary research areas, and also about effective research promotion policies.

2. Survey Items

(1) First Year (FY 1990)

(a) Listing study societies, etc.

We shall make lists of study societies, workshops, etc., (including informal meetings and meetings planned for the future) as well as academic societies that have been newly established or sponsored over the past few years, and lists of those representatives and key persons. These lists will be based on, for example, surveys of documentation on groups registered with the Japan Science Council. For those groups not registered with the Japan Science Council, we will conduct questionnaire and interview surveys of national research labs, learned researchers, academic societies, etc.

(b) Survey of general state of study societies, etc.

We shall conduct questionnaire surveys (and interview surveys when necessary) of researchers involved in the study societies that were listed, and the researchers of industry, government, and universities, about the current state of multidisciplinary research areas and future development.

(c) Classification of study societies, etc.

Based on the results of surveys of the general state of affairs, we shall classify and organize the data on multidisciplinary research areas that are currently developing; together with systematizing the data, we shall compile directories of researchers in those areas.

(2) Second Year (FY 1991)

(a) Analysis of the formation process of multidisciplinary research areas; survey of future development directions

We shall extract the representative areas of multidisciplinary research from those areas that we surveyed during the first year. We shall interview the main members of those areas, we shall conduct interviews about the backgrounds and processes from which new multidisciplinary research areas arise, future development directions, etc.

(b) Survey of characteristics of development in multidisciplinary research areas in foreign countries

By surveying learned and experienced people with questionnaires and interviews, and surveying documentation, we shall get a grasp on the directions of development in multidisciplinary research areas in foreign countries, and then organize that data.

(c) Analysis of survey results

From the results of the systemization of multidisciplinary research areas and the results of interviews about the future directions of development in the main areas, we shall infer the future directions of development in advanced research.

We shall also analyze the formation process and main factors involved in the major areas, and organize the items thought to be important as policies for promoting basic research.

Figure I-1 is a summary in the form of a flowchart of the survey items mentioned above.

3. Expected Outcomes

(1) To compile basic materials on the advanced multidisciplinary research areas that Japan should promote now and in the future.

(2) To draw up policies for promoting basic research that will be effective in the evolution of multidisciplinary research areas.

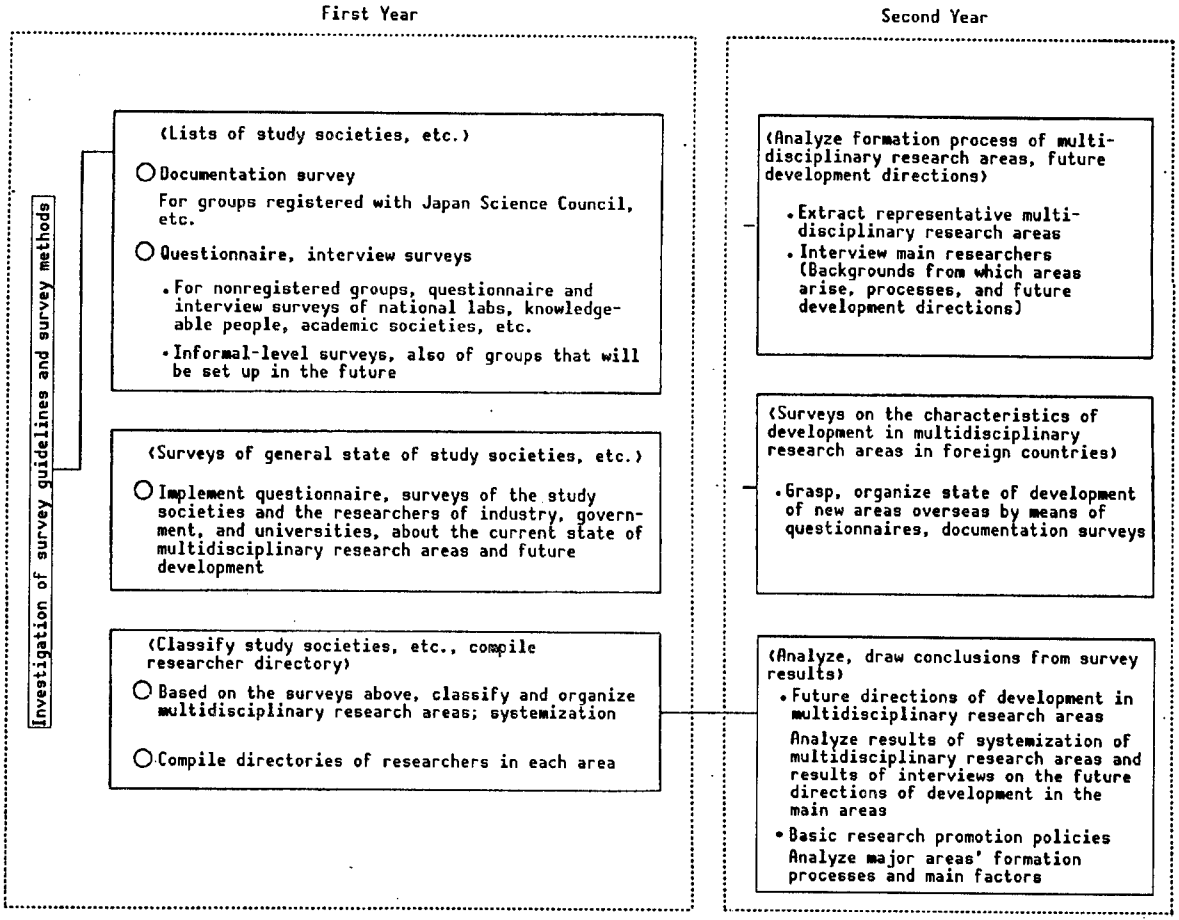


Figure I-1. Survey of Current State of Multidisciplinary Research Areas in Japan and Development Directions

4. Survey Plan

(1) Survey Schedule

Figure I-2 shows the survey schedule.

(2) Content of Survey

(a) First year (FY 1990)

The objective in the first year is to extract the areas of advanced multidisciplinary research thought to be important in the future. Figure I-3 shows the concrete survey items and methods.

(b) Second year (FY 1991) (Planned)

The objective in the second year will be surveys about development directions of representative multidisciplinary research areas, and policies for promoting those. Figure I-4 shows the survey items and methods.

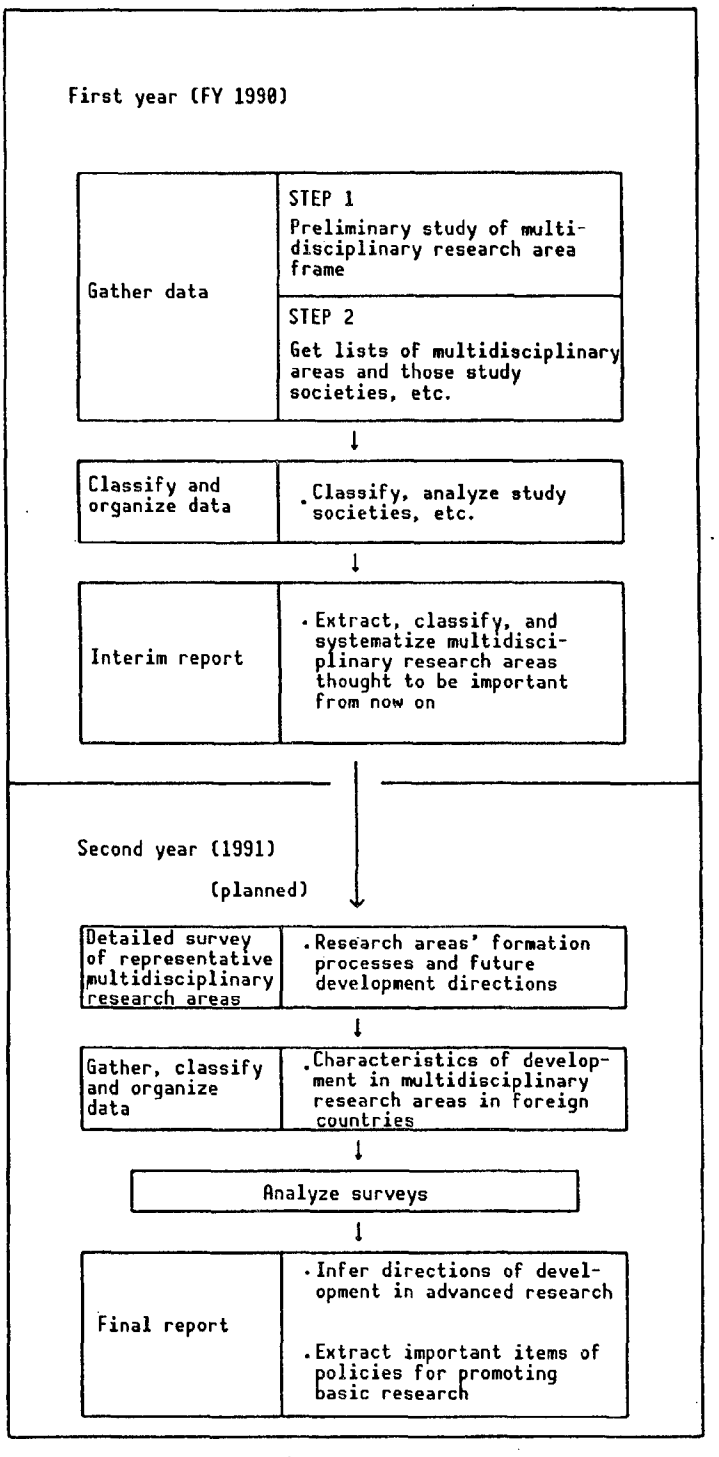


Figure I-2. Survey Schedule

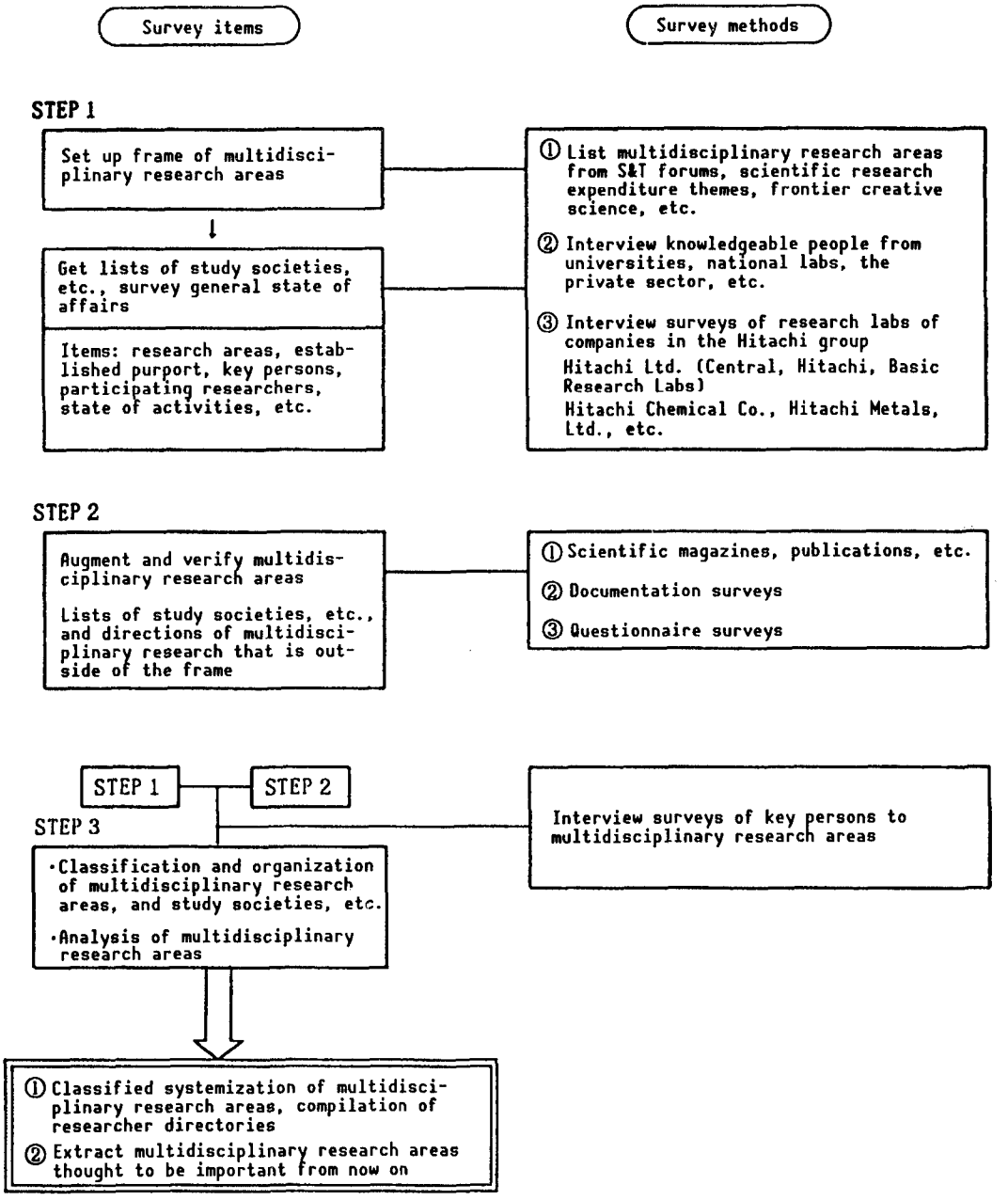


Figure I-3. First-Year Survey Items and Methods

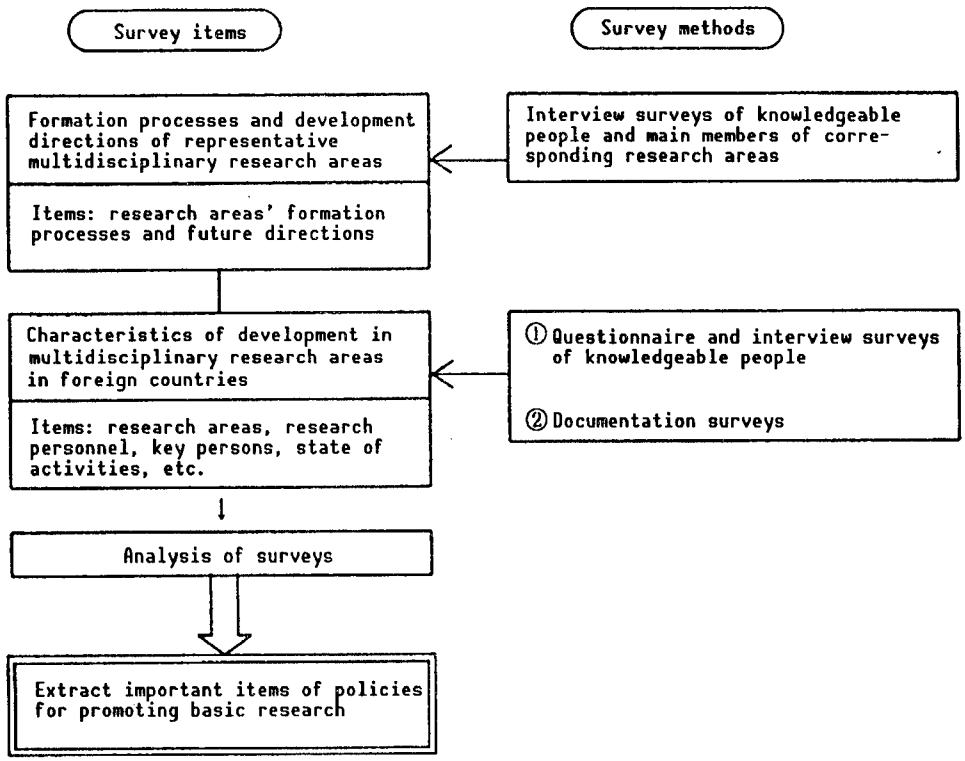


Figure I-4. Second-Year Survey Items and Methods (Planned)

5. Implementation System

Figure I-5 shows the system for implementing the surveys.

Figure I-5. Survey Implementation System

6. Survey Promotion Committee

(1) Functions

To promote the survey and to provide advice about the content of the survey.

(2) Organization

The committee consists of the 13 members shown in Table I-1.

Table I-1. Survey Promotion Committee

	Name	Affiliation, Position
Chairman	M. Koshiba	Tokai University, Physics Department, professor
Member	A. Asai	Hitachi Ltd., Basic Research Lab, chairman
Member	T. Usui	Research Corporation of Japan ERATO, manager
Member	T. Endo	RIKEN, Chemical Engineering Lab, head researcher
Member	S. Ogawa	RIKEN, Cellular Control Chemistry, head researcher
Member	T. Kasami	Toshiba, ULSI Lab, director
Member	F. Kodama	NISTEP, general head of research officers
Member	Y. Sakurai	Tokyo Women's Medical College, professor
Member	H. Sasagibe	RIKEN, Biopolymer Physics Lab, head researcher
Member	T. Tsurujima	Electrotechnical Lab, Electronic Devices Section, manager
Member	O. Fukunaga	Tokyo Institute of Technology, Engineering Department, professor
Member	T. Murata	Nippon Steel, New Materials Enterprise Headquarters' Development Section, manager
Member	Y. Watanabe	Osaka Bioscience Lab, head of 3rd Research Section

II. Survey Results

Chapter 1. Survey Methods

The survey methods are summarized in Figures I-3 and I-4. Here we will describe how we implemented interviews of knowledgeable people, questionnaire surveys of general researchers and academic society offices, and the documentation survey.

1.1 Interview Survey

We interviewed knowledgeable people about their summaries of recent formal and informal study societies, workshops, etc.; the current state of

multidisciplinary research areas and development directions; and, in promoting research in the applicable areas, how effective systems that promote that research should be. The knowledgeable people, interviewed were the researchers of Table 1.1-1.

Separate from this, we interviewed researchers within Hitachi Ltd., with the objective of surveying the current state of multidisciplinary research areas. Table 1.1-2 shows the names of the Hitachi researchers who were interviewed.

Table 1.1-1 Register of People Interviewed

	Name	Affiliation	Position	Field of Specialization
1.	H. Tanihata	RIKEN	Senior researcher	Linear accelerators
2.	H. Sasabe	"	"	Biopolymer physics
3.	H. Katsumata	"	"	Magnetism
4.	I. Yamaguchi	"	"	Optical engineering
5.	K. Takeuchi	"	"	Separation engineering
6.	M. Aono	"	"	Surface engineering
7.	T. Endo	"	"	Chemical engineering
8.	H. Toyota	"	"	Semiconductor engineering
9.	T. Iizuka	"	"	Biophysics
10.	M. Takami	"	"	Inorganic chemistry, physics
11.	T. Kira	"	"	Reaction physics, chemistry
12.	H. Kuzuhara	"	"	Biorganic chemistry
13.	T. Shibata	"	"	Microbiology
14.	F. Hanaoka	"	"	Radiobiology
15.	Y. Yamaguchi	"	"	Microbiological control
16.	S. Ogawa	"	"	Cellular control chemistry
17.	Y. Aoyagi	"	"	Laser science
18.	T. Ishii	RIKEN Life Sciences Tsukuba Research Center	"	Molecular genetics
19.	A. Sakakura	"	"	Eucaryotes
20.	K. Shinozaki	"	"	Genetic analysis
21.	Y. Sakaki	Tokyo Univ., Advanced S&T Research Center	Professor	Electronic engineering
22.	Y. Ishida	Tokyo Univ., Production Technology Research Center	Professor	Metals
23.	A. Sawaoka	Tokyo Inst. of Technology Ceramics Center	Center director	Ceramics
24.	N. Ogata	Sophia Univ. Physics Department	Professor	Biopolymers
25.	S. Aizawa	Creative Science Takatani Polymer Structure Project	Group	Biophysics
26.	M. Kikuche	Sony (K.K.)	Consultant	Semiconductors
27.	H. Kuroda	Tokyo Univ., Physical Sciences Department	Professor	SOR chemistry

[continued]

[Continuation of Table 1.1-1]

Name	Affiliation	Position	Field of specialization
28. M. Koshiba	Tokai Univ., Physical Sciences Department	Professor	Elementary particle physics
29. T. Sata	RIKEN	Director	Machinery
30. Y. Nagai	Tokyo Univ., Medical Department	Professor	Basic medicine
31. H. Yanagida	Tokyo Univ., Advanced S&T Research Center	Center director	Sensors
32. T. Yamagawa	Tokyo Prefecture Clinical Medicine Research Institute	Director	Sugar chains, polymer films
33. G. Chiba	Japan Research Corp.	Director	Group
34. Y. Goto	"	Managing director	Ceramics
35. Y. Sakurai	Tokyo Women's Medical College	Professor	Medical engineering
36. I. Kobori	Meiji Univ., Politics and Economics Department	Professor	Economic geography
37. M. Ishiguro	Suntory (K.K.) Biomedical Research Institute	Head of 2d Research Lab	Computer chemistry (creating drugs)
38. Y. Shiraki	Tokyo Univ., Advanced S&T Research Center	Assistant professor	Photonic materials

Table 1.1-2 Register of Hitachi Researchers Who Were Interviewed

Name	Affiliation	Position	Field of Specialization
1. Y. Inagami	Central Research Lab	Researcher	Computer architectures
2. M. Okunaka	Basic Research Lab	Sr. researcher	Organic nonlinear optical materials
3. H. Okamoto	"	Researcher	Electrode surface rhythm reactions
4. Y. Tamioka	"	Researcher	Configuration control of functional proteins
5. S. Ishibashi	"	Sr. researcher	Bioelectronic materials
6. T. Yuasa	"	Sr. researcher	Crop breeding
7. S. Usui	"	Researcher	Automation of DNA base sequence determination process
8. K. Sakamoto	"	Researcher	In vivo molecular mechanisms, elucidation and applications

1.2 Questionnaire Surveys

(1) Questionnaire Survey of General Researchers

We conducted a questionnaire survey of general researchers with the objective to broadly survey their summaries of the current state of study societies and research themes in multidisciplinary research areas, and measures for promoting research in the corresponding areas. For the subjects of the questionnaire survey, we randomly extracted equal numbers of industry, government, and university researchers from the register of academic society members, as shown in Table 1.2-1, for a total of 1,524 names.

Reflecting the tenor of this investigation, we limited the aggregate subjects to researchers who are carrying out either "pure scientific research" or "basic research with applications in mind," and excluded those researchers who are carrying out "product development research." We also limited the aggregate subjects to researchers who are "currently carrying out" or "plan to carry out in the future" research in multidisciplinary areas, and excluded those researchers who "are not and will not carry out" such research. That resulted in 387 aggregate subjects from the 664 people who responded (58% of those who responded; the number of aggregate questionnaires was 25% of the number of questionnaires sent out).

Although Chapter 3 discusses the details of the methods used to implement the questionnaire survey of general researchers, Section 2.5.2 of Chapter 2 is also based on the information obtained from the questionnaire survey.

(2) Questionnaire Survey of Academic Society Offices

In addition to the questionnaire survey of general researchers, we conducted a questionnaire survey of the offices of the 32 academic societies shown in Table 1.2-1, the purpose of which was to investigate the state of "study societies, departmental meetings, etc., that have been newly set up within the past few years." A discussion of those results is in Chapter 2, Section 2.1.1.

1.3 Survey of Documentation, etc.

In order to survey the research trends in multidisciplinary research areas, we conducted individual documentation surveys for each multidisciplinary research area. References documents are shown at the end of Sections 2.3.1 to 2.3.9 of Chapter 2.

Likewise, with the objective of surveying research trends in multidisciplinary research areas, we attended the following symposia:

1. 1990 51st Symposium of the Applied Physics Society (Morioka, September 1990)
2. Creative S&T Promotion Enterprises' 1990 Research Report Presentations (Tokyo, November to December 1990)
3. Third Sasaki Memorial Symposium, "Mesoscopic Electronic Properties" (Tokyo, December 1990)
4. First Symposium on Intelligent Materials (Tokyo, March 1991)

Table 1.2-1. Subjects of Questionnaire Surveys

	Name of academic society	Number surveyed	Number surveyed by area	Remarks			
				No. of members	Wt.	JICST-based classification of area	
1	Japan Mathematics Society	24	Mathematics 24	4,700	1	Mathematics	
2	Japan Physics Society	81	Physics 186	15,658	1	(All areas of physics)	Physics
3	Applied Physics Society	105		21,000	1		
						Measurement and instrumentation	
4	Japan Chemistry Society	189	Chemistry 243	37,736	1	Chemical engineering	
						(All areas of chemistry)	Basic chemistry
5	Japan Polymer Society	54		10,520	1	Polymer chemistry	
6	Japan Biophysics "	15	Biological sciences 243	2,600	1.2	Theoretical biology, biophysics	Biology sciences
7	Japan Biochemistry "	63		12,002	1	Biochemistry, molecular biology	
8	Japan Genetics "	15		1,200	2.5	Genetics, evolution theory	
9	Japan Immunology "	21		3,700	1	Immunology	
10	Japan Ecology Society	15		2,238	1.3	Ecology, environmental biology	
11	Japan Cell Biology "	15		1,403	2	Cytology	
12	Japan Microbiology Ecology Society	15		511	6	Microbiology, virology	
13	Japan Virology "	15		2,771	1.1		
14	Japan Botany Society	15		2,300	1.3	Botany	
15	Japan Zoology Society	15		2,502	1.2	Zoology	
16	Japan Radiobiology "	15		458	6.5	Radiobiology	
17	Japan M.E. Society	24		4,806	1	Bioengineering	
18	Japan Astronomy "	15	Astronomy, geology 45	2,400	1.2	Astronomy, geology	
19	Japan Geology Society	15		1,850	1.6		
20	Terrestrial Electromagnetism, Earth, Planets Soc.	15		628	5		
21	Japan Agricultural Chemistry Society	66	Agricultural sciences: 102	12,900	1	Agricultural, forestry and fishery sciences	
22	Japan Forestry Society	15		2,500	1.2		
23	Japan Fisheries "	21		4,077	1		
24	Systems Control and Information Society	15	Engineering 681	2,466	1.2	Systems and control engineering	
25	Information Processing Society	159		31,456	1	Information engineering	
26	Japan Solar Energy "	15		700	4	Energy engineering	
27	Japan Nuclear Power "	33		6,560	1	Nuclear engineering	
28	Electronic Information & Communications Soc.	141		36,879	0.75	Electrical engineering	
29	Electricity Society	90		23,792	0.75		
30	Japan Machinery "	159		42,159	0.75	Mechanical engineering	
31	Japan Environmental "	15		463	6.5	Environmental engineering	
32	Japan Metals Society	54		10,763	1	Metals engineering	
	Total	1,524	1,524				

Chapter 2. State of Advanced Multidisciplinary Research Areas and Topics

2.1 Study Societies, Research Themes in Multidisciplinary Areas

2.1.1 Study Societies, Workshops, etc., in Multidisciplinary Areas

Table 2.1.1-1 shows the examples of study societies, workshops, and so forth that were obtained from the interviews of knowledgeable people.

We also added to this table the study societies, workshops, and so forth that were obtained from the questionnaire survey of academic society offices. The subjects of this questionnaire survey were the 32 offices of the academic societies listed in Table 1.2-1. In response to the question that depended on the entry "study societies, departmental meetings, etc., newly set up within the last few years," there were no responses on four questionnaires, and on 14 questionnaires the responses were "no such study societies, departmental meetings, etc." So, from the remaining 14 responses, we entered into the table those that do not overlap with the study societies, departmental meetings, etc., obtained from the interview survey. However, for those academic societies that have numerous study societies, departmental meetings, etc., we just show the numbers of those meetings.

Incidentally, during the interviews, the following kinds of opinions were heard quite often in response to the questions about study societies and research themes:

- there is a research theme, but our research activities are not yet organized;
- our announcements of research papers and other such activities are in a form that is incorporated into an existing academic society.

That is, among the areas of advanced multidisciplinary research, cases are seen where activities are organized, as shown in Table 2.1.1-1. On the other hand, though, there is also the type of research where, rather than becoming organized, the research theme must first "get on its feet." Then, too, negative opinions about organized activities were also seen, as in:

- an academic society is not the place to broaden a concept;
- if a person is absorbed in his research, even if he is tackling it alone, that already is a new area.

When we take these kinds of opinions into consideration, at the very least we can say that it was not enough to just survey study societies, workshops, and so forth in order to search out the trends in advanced research.

Table 2.1.1-1 Examples of Study Societies in Multidisciplinary Areas

Name of study society, workshop, etc.	Key persons (affiliation)	Content
(Related to living organisms) Symposium on Eucaryotic DNA	Y. Koike (Cancer Research Society Cancer Research Institute) T. Matsukage (Aichi Prefecture Cancer Research Institute) M. Yoshida (Nagoya Univ. Dept. of Medicine)	Clarifying the mechanisms of DNA duplication, transcription recombination, and recovery
Chromosome structure workshop	M. Yanagida (Kyoto Univ.) T. Nishimoto (Kyushu Univ.) T. Shibata	FY 1990 Scientific Research Fund Priority-Area Research Research on structure and functions of chromosomes (chromatin dynamics, etc.)
Workshop on cellular cycle control	T. Uno (Tokyo Univ. Applied Microbiology Lab) K. Seno (National Genetics Lab)	Worldwide, number of researchers is increasing Important research that searches for basis of aging, cancer, and injury regeneration
DNA synthesis workshop	M. Inuzuka (Fukui Medical School) T. Okazaki (Nagoya Univ. Physical Sciences Dept.) H. Yoshikawa (Osaka Univ. Medical Department)	Although three-fourths are researchers of procaryotic cells, the world trend is, conversely, three-fourths are researchers of eucaryotic cells
Workshop on cell cycle and chromosome dynamics	M. Yanagida (Kyoto University)	Research on cell cycle and chromosome dynamics
Research workshop on genetic recombination	E. Ogawa (Osaka Univ.) H. Ikeda (Tokyo Univ. Medical Research Lab) E. Ohtsubo (Tokyo Univ. Applied Microbiology Lab) T. Shibata (RIKEN)	Will become basis for understanding about mutation and other such aspects of the evolution of living organisms

[continued]

[Continuation of Table 2.1.1-1]

Name of study society, workshop, etc.	Key persons (affiliation)	Content
Symposium on Biomedicine	F. Takahisa (Tokyo Univ. Medical Dept.) Y. Imura (Kyoto Univ. Medical Dept.)	Joining molecular biology with medicine, including clinical medicine, will enable difficult research on genetic diseases
Society for the Study of Plant Proteins and Nucleic Society for the Study of Plant Physiology		By eludicating basic problems at plant physiology and molecular genetics level, it will tie into wider applications in the future (plant breeding, flowering plants, the environment, etc.)
Biofunction-Related Chemistry Dept. meetings (in Japan Chemistry Society) Society for the Study of Chitin, Chitosan		Outer integuments of crustaceans, insects, etc., made up of chitin and chitosan, which are second most produced organic substances on earth next to cellulose. Research is for purpose of using these as biomass (e.g., artificial skin)
Carbohydrate Coming Age Forum	T. Yamagata (Mitsubishi Chemical's Life Sciences Lab)	International Carbohydrate Symposium
Biotechnology Development Research Group (MITI)		Sugar chain engineering Relationship between biomaterials and sugar chain engineering; fusion of sugar chain engineering and protein engineering
Society for Study of Structures and Functions of Complex Sugars (Japan Industrial Technology Promotion Association)	A. Kohata (Tokyo Univ. Medical Science Lab)	
Sugar Chain Engineering Dept. Meeting (Council for Aeronautics, Electronics and Other Advanced Technologies, Biotechnology Dept. Meeting)	Z. Yoshida (professor emeritus at Kyoto Univ.)	

[Continuation of Table 2.1.1-1]

Name of study society, workshop, etc.	Key persons (affiliation)	Content
Night Study Meeting	S. Aizawa (Creative S&T Promotion Enterprise)	Electronics based on biology
Genecell Study Society	S. Aizawa " " "	Gathering of young researchers from different fields (university level)
Study societies within Japan Forestry Society; 9 total, e.g., Forestry and Water Workshop	R. Tsukamoto (Tokyo Univ. of Agriculture and Technology) et al.	
Fisheries and Environmental Preservation Committee (Japan Fisheries Society)	A. Kawai (Kinki Univ. Agricultural Science Dept.)	
No name (A society for study of radiobiology)	T. Sugawara (Kyoto Emeritus Club)	
(Chemistry-related) Polymer Friendship Society	H. Hinami (Secretariat)	Semiconductor devices, optical computers, bioelectronics
Academic Promotion 142 Committee	M. Takeda (Tokyo Univ. Physical Sciences Dept.)	1) Liquid-crystal sensors 2) Photoresponsive material sensors 3) Dynamically responsive sensors
Society for Study of Molecular-Configuration-Controlled Polymeric Materials Petroleum Industries Activation Center (MITI) Society for Study of Basic New Materials (MITI) Polymer Materials Center (MITI) Study Societies in Japan Industrial Technology Promotion Group (MITI)		1) Mechanisms of chemical reactions—Within living organisms, nearly 100% targeted chemical reactions will be possible at room temperature and pressure. Goal is elucidation and application of these. 2) Chemistry of molecular recognition—Separation of optical isomers (to study configuration control and molecular recognition when cells divide)

[Continuation of Table 2.1.1-1]

Name of study society, workshop, etc.	Key persons (affiliation)	Content
Study societies within the Polymer Society, 23 total e.g., Society for Study of Medical-Use Polymers	Y. Ikata (Kyoto Univ. Biomedical Engineering Research Center) et al.	
Colloid and Surface Chemistry Dept. Meeting (Japan Chemistry Society [JCS])	A. Kuroda (Tokyo Univ. Physical Sciences Dept., Chemistry Sec.)	
Information Chemistry Dept. Meeting (JCS)	W. Okaki (Osaka City Univ., Engineering Dept.)	
Society for Study of CO_2 Fixation (JCS)	K. Ito (Nagoya Institute of Technology, Applied Chemistry Dept.)	
Global Environment Study Society (JCS)		
Society for Study of Molecular Clusters (JCS)	K. Honma (Himeji Institute of Technology, Physical Sciences Dept.)	
(Physics-Related) Separation Technology Roundtable Discussion	A. Hirata (Tokyo Metropolitan Univ.)	There is no movement to consolidate all research themes
Micromechatronics (not official name)	Y. Ikuta (Kyushu Institute of Technology)	With micropumps and valves, etc., can expect applications in medical fields
Society for Study of New Lasers (February theme of Electricity Society) Society for Study of Laser Processing (March, September themes of Electricity Society)	Y. Fujii (Toko Univ. Biology Lab)	Free electron lasers Anticipation of shorter-wavelength lasers and smaller equipment

[Continuation of Table 2.1.1-1]

Name of study society, workshop, etc.	Key persons (affiliation)	Content
Nuclear-Order Processing (Ministry of Education)		Surface physics, chemistry, electronics, devices, materials, etc.
Epitaxial Growth Special Committee		Physics, computational physics, organic chemistry, devices, materials, etc.
Materials Association Forum		Surface analysis, materials, electronics, etc.
HIM (High Intelligence Material) backed by Watanabe Memorial Enterprise Association, close relationship with universities		Neurocomputers, devices, software, materials, etc.
International Conference on Radioactive Nuclear Beams	Y. Tamihata (RIKEN)	1989 First International Conference Applications of linear accelerators in medicine, nuclear physics, and astrophysics
JHP Study Society (Tokyo Univ. Nuclear Research Lab)		Applications in astrophysics
Society for Study of Material Interconnections	Y. Ishida (Tokyo Univ. Production Technology Lab)	Joining materials without adding heat or pressure (semiconductors, etc.)
(Sessions within Optics Society) (1) Optical Devices		Holographic optical devices (one side of which acts as a lens)
(2) Optoelectronics		Optoelectronics (devices)
(3) Precision Machinery Engineering		In the future, applications in servo-systems (noncontact three-dimensional measurements)
(4) Vision Engineering		Elucidating eye fatigue and mechanisms of visual recognition. Neurochemistry of image processing and recognition

[Continuation of Table 2.1.1-1]

Name of study society, workshop, etc.	Key persons (affiliation)	Content
(5) Holography		X-ray holography, miniaturization of X-ray lasers
(6) Optical Computing		Fusion of optoelectronics and neurocomputing
(7) Optical Measurements		Noncontact, high-speed, accurate, nonelectrically-inductive measurements will be possible
(8) Image Processing		Creating images, technology for processing and analyzing moving images
Light Wave Sensing Research Meeting		Optical fiber sensors
Japan Nondestructive Testing Association		Possibility of nondestructive testing using light
Precision Engineering Society		Research of precision measurements using light
Japan Optomechatronics Association		
Optical Production Technology Promotion Association		
Fine Structure Innovation (Academic Promotion 135 Dept. Meetings)	Y. Nanba (Tokyo Univ. of Agriculture & Technology)	Solid quantum structures
Mesoscopic Areas		
Special committees within Electricity Society, 102 newly set up since 1988	M. Okada (Hiroshima Univ. Bioproduction)	
Society for Study of Computer-Aided Materials Design (Japan Metals Society [JMS])	M. Doyama (Tokyo Univ. Engineering Dept.) N. Yukawa (Toyohashi Univ. of Technology	

[Continuation of Table 2.1.1-1]

Name of study society, workshop, etc.	Key persons (affiliation)	Content
Society for Study of High-Temperature Strengthening (JMS)	H. Oikawa (Tohoku Univ. Engineering Dept.) T. Endo (Yokohama National Univ.)	
Society for Study of High-Purity Metals (JMS)	H. Kimura (Tohoku Univ. Metal Materials Lab)	
Fracture physics and chemistry (JMS)	H. Yoshinaga (Kyushu Univ. Graduate School Physics and Engineering Research Dept.) H. Matsui (Tohoku Univ. Metal Materials Lab)	
Bainite Research Meeting (JMS)	K. Tamura (Kyoto Univ. professor emeritus)	
Special Committee on Beryllium Technology Research (Nuclear Power Society [NPS])	S. Ishino (Tokyo Univ. Engineering Dept. Nuclear Engineering Section)	
Special Committee on Muon-Catalyzed Nuclear Fusion Physics and Engineering Research (NPS)	K. Nagamine (Science Univ. of Tokyo Meson Science Research Center)	
Special Research Committee on Limit Fuels Technology (NPS)	T. Iwamoto (JAERI Tokai Lab)	
Nuclear Fusion Plasma Materials Engineering (NPS)	H. Takahashi (Hokkaido Univ. Engineering Dept. Metals Chemistry Research Facility)	
Special Research Committee on Comprehensive Evaluation of Graphite Materials for Fusion Reactors (NPS)	T. Yamashina (Hokkaido Univ. Engineering Dept. Nuclear Engineering Section)	
Special Research Committee on Advanced Fuel Fusion (NPS)	Y. Wakuta (Kyushu Univ. Engineering Dept. Applied Nuclear Engineering Room)	

[Continuation of Table 2.1.1-1]

Name of study society, workshop, etc.	Key persons (affiliation)	Content
Special Committee on Low-Dose Radiation and Safety Evaluations	O. Matsuoka (National Institute of Radiological Sciences)	
(Other) Special Committee on Collected Astronomy Terminology (Japan Astronomy Society)	K. Ishida (Tokyo Univ. Physical Sciences Dept. Educational Research Center)	
Dept. Meetings on Research of Environmental Control of Comfortable Living Spaces, and Solar-Hybrid Energy Systems (Japan Solar Energy Society)	S. Nakahara (Japan Solar Energy Society Research Cooperation Dept.)	
Dept. Meetings on Research of Intelligent Factory Automation (Systems Control and Information Society [SCIS])	M. Abe (Kyoto Univ. Engineering Dept. Electrical Engineering Section)	
Dept. Meetings on Research of Advanced Signal Processing (SCIS)	T. Katayama (Kyoto Univ. Engineering Dept. Mathematical Engineering Section)	
Dept. Meetings on Research of Workstation Applications (SCIS)	S. Maekawa (Kobe Univ. Engineering Dept. Systems Engineering Section)	
The Society of Desert	I. Kobori (Meiji Univ. Dept. of Political Economy)	Formation mechanism of desert Life in desert Desert engineering Dry land farming

[Continuation of Table 2.1.1-1]

Name of study society, workshop, etc.	Key persons (affiliation)	Content
The Japan Society of Mechanical Engineers (Established after 1988: 53 subcommittees, 36 research groups)		
Computer and Education (Information Processing Society of Japan [IPSJ])	M. Ariyama (Univ. of Electro-communications)	
Algorithm (IPSJ)	T. Nishizeki (Thoku Univ., Dept. of Engineering)	
Social Science and Computers (IPSJ)	S. Sugita (National Ethnology Museum)	

2.1.2 Research Themes in Multidisciplinary Areas

Table 2.1.2-1 shows examples of research themes that were obtained by interviewing knowledgeable people.

Table 2.1.2-1 Examples of Research Themes in Multidisciplinary Areas

Research theme	Key persons	Content
(Related to living organisms) Mechanisms of cell cycle control	T. Uno (Tokyo Univ. Applied Microbiology Lab) K. Seno (National Genetics Lab)	Elucidation of mechanisms of cell cycle control
Elucidation of aging genes	F. Hanaoka (RIKEN)	Basic mechanisms of cancer cell generation Predicted to be important after a decade
Eucaryotic DNA synthesis	M. Inuzuka (Fukui Medical School) T. Okazaki (Nagoya Univ. Physics Dept.) H. Yoshikawa (Osaka Univ. Medical Dept.)	Research on DNA duplication, division (Much about eucaryotic cells is unclear)

[Continuation of Table 2.1.2-1]

Research theme	Key persons	Content
Chromosome structure	F. Hanaoka (RIKEN) M. Yanagida (Kyoto Univ.) T. Nishimoto (Kyushu Univ.) T. Shibata (RIKEN)	Research on structure and functions of chromosomes (dynamics of eucaryotic cell chromatin)
Cell cycle, chromosome dynamics	M. Yanagida (Kyoto Univ.)	
Research on genetic recombination	E. Ogawa (Osaka Univ.) H. Ikeda (Tokyo Univ. Medical Research Lab) E. Ohtsubo (Tokyo Univ. Applied Microbiology Lab) T. Shibata (RIKEN)	Elucidation of mechanisms of genetic recombination of chromosomes, and how that relates to proteins
Mechanisms of control in gene expression	T. Ishii (RIKEN)	Elucidation of mechanisms of genetic expression, which is the basis of higher-order life phenomena
Molecular biology in connection with plants	K. Shinozaki (RIKEN)	Elucidation of photosynthesis (substance metabolism), totipotency of differentiation, and environmental response
Roles of iron and oxygen in living organisms	T. Iizuka (RIKEN) T. Ishimura (Keio Univ. Medical Dept.) I. Morishima (Kyoto (Univ.) S. Kanegasaki (Tokyo Univ. Medical Lab)	Elucidation of roles that iron and oxygen play in hemoglobin (a macromolecular complex containing iron) and enzymes that use oxygen
Elucidating interaction between plants and other living organisms	Y. Yamaguchi (RIKEN)	Elucidation of substances involved in interactions between living organisms (substitutes for hazardous agricultural chemicals, etc.)
Botanical biotechnology		Controlling plant-disease-bearing insects without using chemicals

[Continuation of Table 2.1.2-1]

Research theme	Key persons	Content
Basic research on enzyme models	H. Kuzuhara (RIKEN)	Basic research in biomimetics, research on protein-protein and protein-sugar interactions (molecular binding)
Mechanisms of biofunctional stability	T. Sakakura (RIKEN)	Multifunctional cells in form of unit aggregates, e.g., genes and monoclonal antibodies, are stable only in limited functions within tissue (many other functions are wasted). Elucidating mechanisms of what is called cell sociology, i.e., interactions among cells, information transmission among cells, etc.
Sugar chain engineering	S. Ogawa (RIKEN)	Elucidation of mechanisms by which cells recognize friend cells,and interactions between proteins and sugars that relate to the social characteristics of living cells
Relationship between sugar chain engineering and biosystem materials		Research for new materials development, including not only functional and structural analyses, but also structure, production
Fusion of sugar chain and protein engineering	S. Ogawa (RIKEN)	Research on biological information other than genetic information (interactions between sugar chains and proteins are connected with information that governs cell societies)
Physical elucidation in living organisms	S. Aizawa (New Technology Enterprises Group)	Elucidation of mechanisms of ATP energy delivery; genetic-level elucidation of muscles; elucidation of differentiation (what decides form of an organism), interactions between proteins, and photosynthesis
Living organisms and fine structure	Y. Yamaguchi (RIKEN) Y. Aoyagi (RIKEN)	Elucidation of relationship between growth of living organism and cell structure (why does growth stop? why is there directionality?)

[Continuation of Table 2.1.2-1]

Research theme	Key persons	Content
Neurocomputers	Y. Aoyagi (RIKEN)	Development of neurodevice chips (intelligent materials)
(Chemistry-related) Interactions between organisms and inorganic substances (biomimelization)	H. Sasabe (RIKEN)	Elemental technology of biodevices
Science of large molecular aggregate systems (mesoscopic science)	T. Kira (RIKEN)	Middle of the road between chemistry and biology. Elucidation of intermolecular electron transitions (energy exchange), multi-electron process oxidation/reduction, and chemical feedback control mechanisms
Chemical reaction mechanisms	N. Ogata (Sophia Univ. Physics and Engineering Dept.)	Elucidation of chemical reactions that occur in organisms at normal temperatures and pressures (why almost 100% are achieved). Aimed at future molecular configuration control
Chemistry of molecular recognition	"	To study molecular recognition and molecular configuration control during cell differentiation; separation of optical isomers
Chemitronics computer science	Y. Aoyagi (RIKEN) M. Ishiguro (Suntory Biomedical Lab)	Fusion of chemistry and electronics (conceptually) Applications in drug creation using computational chemistry
Physics-Related Processing technology using lasers	H. Toyota (RIKEN)	Fine processing technology Applications in opto-related devices
Short-wavelength laser technology	"	Technology for making lasers and optical devices with shorter wavelengths. X-ray microscopes, X-ray lithography, etc.

[Continuation of Table 2.1.2-1]

Research theme	Key persons	Content
Micromechatronics (Micro machines)	Y. Ikuta (Kyushu Institute of Technology)	Micropumps, microvalves, etc.
Cluster evaluation	K. Takeuchi (RIKEN)	Chemical elucidation of cluster reactions, which are a hindrance in uranium refining
Atomic-order processing	Y. Aoyagi (RIKEN)	Development of technology for controlling materials at atomic level. Elucidation of epitaxial growth mechanisms (computational physics, etc.)
Mechanical engineering and fine structures	Y. Aoyagi (RIKEN)	Ideal surfaces, in connection with friction (atomic-order creation)
Technology using unstable nuclear beams	H. Tanihata (RIKEN)	(1) Tracers: medicine (measuring blood flow in the brain); semiconductors (measuring dispersion) (2) Creation of new elements (3) Astrophysics (elucidating origin of the elements)
Artificial lattice magnetism	T. Shinjo (Kyoto Univ. Chemistry Lab)	By combining insulators and metals, new physical properties expected
Organic ferromagnetic substances	H. Katsumata (RIKEN)	Current manifestation of ferromagnetism at temperatures around that of liquid nitrogen
Biomagnetism	H. Katsumata (RIKEN)	Magnetism of heme proteins and role that plays
Development of rare earth magnets (strong, permanent magnets)	H. Katsumata (RIKEN)	Elucidation of rare earth elements' own magnetism
Relationship between magnetism and high Tc	H. Katsumata (RIKEN)	Theoretical elucidation of high-temperature superconductivity

[Continuation of Table 2.1.2-1]

Research theme	Key persons	Content
Recognition mechanisms of the eye	I. Yamaguchi (RIKEN)	Research that relates structure of eye to functions of eye (measuring psychological phenomenalism, measuring characteristics of eye, etc.)
Neuroscience related to image processing and image recognition	I. Yamaguchi (RIKEN)	Research that relates neurocomputers with image-processing functions (processing moving images, etc.)
Measurements using light	I. Yamaguchi (RIKEN)	X-ray microscopes
Science of holography	I. Yamaguchi (RIKEN)	X-ray holography; making X-ray lasers smaller
Mesoscopic science	M. Takami (RIKEN) T. Kutsu (Technological Univ. of Nagaoka)	Elucidation of the mechanisms of functional manifestation. Technology that uses the selective reactions by solid us s similar to enzymes
Development of ppt-level analysis methods	M. Takami (RIKEN)	Laser resonance ionization methods, radiochemical analysis
Atomic control (atom craft)	M. Aono (RIKEN)	Manipulating atoms one-by-one. Applications in memory and genetic manipulation
Technology for generating extremely high vacuums	M. Aono (RIKEN)	Aiming for vacuum that is 10^{-10}~$^{-11}$ Torr or less
Completely new surface measurement technology	"	Development and evaluation of completely new equipment

2.2 Extraction of Representative Advanced Multidisciplinary Research Areas

As a result of the interview, questionnaire, and documentation surveys described in Chapter 1, we got a grasp on the current state of advanced multidisciplinary research areas in Japan. After taking into consideration global and international needs, we extracted the following nine areas as those representative advanced multidisciplinary research areas that are thought to be important from now on:

1) Intelligent Materials
2) Frontier Measurement and Control Technology
3) New Genetic Manipulation Technology
4) New Neuroscience and Technology
5) Biomolecular S&T
6) Temporal Bioscience and Technology
7) New Global Environmental S&T
8) Recycling S&T
9) Computational S&T

Table 2.2-1 shows how examples of themes in the nine representative advanced multidisciplinary research areas given above relate to global and international needs. Table 2.2-2 shows how those theme examples relate to the S&T areas classified according to the JICST (Japan S&T Information Center) classification table. From these tables we see that there are high global and international needs for the nine multidisciplinary research areas given above, and also that there is a high degree of compositeness of research areas.

2.3 State of Representative Advanced Multidisciplinary Research Areas and Topics

Below we will discuss the current state of affairs and topics in each of the nine representative advanced multidisciplinary research areas that we extracted in the previous section.

2.3.1 Intelligent Materials

(1) Concept of intelligent materials[1,2]

As the target of materials R&D that will open up the 21st century, "intelligent materials" is a new concept in materials design that Japan has advocated. "Intelligent materials" means "new substances and materials that have the capacity to intelligently manifest functions in response to environmental conditions," or, in other words, "not the materials that exhibit functions only under certain conditions, but materials that feel, think, and act on their own." The concept of intelligent materials was built upon the 13th inquiry of the director-general of the Science and Technology Agency (July 1987), and was later consolidated in the form of the report that was in response to that inquiry 1) (November 1989). Below is a summary of that report.

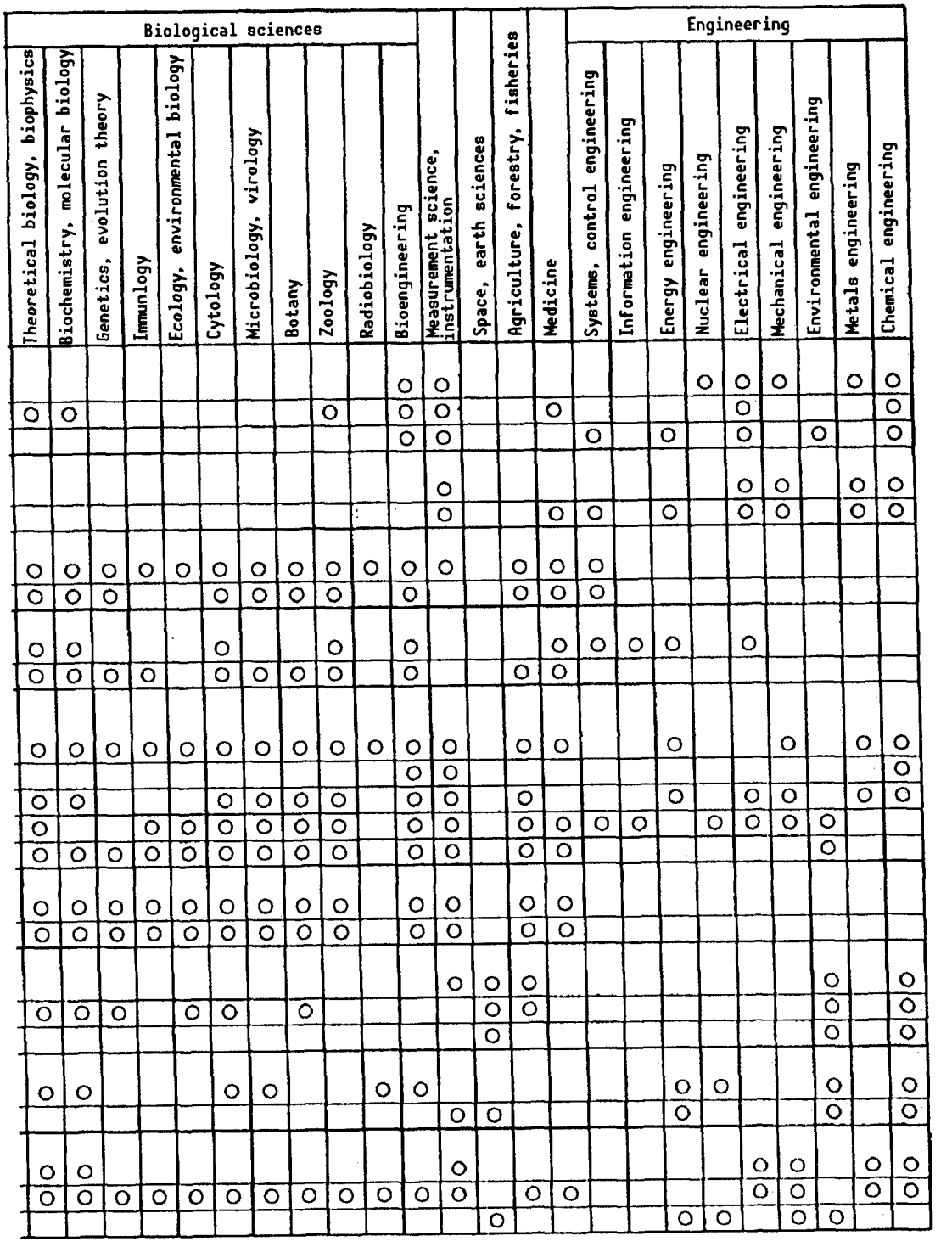
Table 2.2-1 Advanced Multidisciplinary Research Areas and Global, International Needs

Advanced multidisciplinary research areas (sample themes) \ Global, international needs	Global environmental preservation			Health maintenance, promotion			Disaster prevent. safety		Resource problems				Social infras. maint.		Economic activation				
	Preventing desertification	Global warming, acid rain countermeasures	Pollution prevention	Improving medical technology	Comfortable way of life for citizens	Aged society, welfare measures	Disaster forecasting, prevention measures	Improving reliability, safety	Food, plant, mineral resources	Development of new energy technology	Effective resource utilization policies	Solving waste problems	Developing national lands, urban planning	Communications, transportation	Production, processing of new materials	Advances in information, electronics technology	Advances in biotechnology	Improving aerospace technology	Space, ocean development
1 Intelligent materials																			
(1) Structural materials with self-diagnostic, self-recovery functions							○	○							○	○		○	○
(2) Drug carriers, biofunction substitutes and other such medical-use materials				○		○									○	○	○		
(3) Optical materials whose characteristics change according to external conditions					○						○				○	○		○	○
2. Frontier measurement and control tech.																			
(1) Measurement manipulation of individual molecules, atoms															○	○	○		
(2) Micromachining manufacturing tech.				○		○									○	○	○	○	○
3. New genetic manipulation technology																			
(1) Human genome analysis																○	○		
(2) Applications in pharmaceuticals, and treatment of genetic disease				○													○		
4. New neuroscience technology																			
(1) Engineering-type realization of neural circuits														○		○			
(2) Coping with aging, dementia, etc.				○	○	○													
5. Biomolecular S&T																			
(1) In situ nondestructive measurement, control of biofunctions at the molecular level				○													○		
(2) Technology for high-purification of substances that make up living organisms				○											○		○		
(3) High-efficiency energy conversion technology										○	○	○							
(4) Stable prediction systems technology that studies living organisms							○	○											
(5) Environmentally resistant bioengineer.	○								○								○		
6. Biotemporal S&T																			
(1) Elucidation of biorhythms				○	○												○		
(2) Applications in biorhythmical medical treatment				○		○											○		
7. New global environmental S&T																			
(1) CO_2 fixation, separation technology		○								○									
(2) Desert afforestation technology	○																		
(3) New methods of observing hazardous substances in the environment		○	○																○
8. Recycling S&T																			
(1) Searching, utilizing degradable substances, new microbiological organisms					○					○	○	○					○		
(2) High-purity separation technology		○	○																
9. Computer S&T																			
(1) Theoretical establishment and prediction of functional manifestation															○	○	○		
(2) Simulation of biofunctions				○												○	○		
(3) Elucidation of fluidic system theories		○	○				○									○		○	○

Table 2.2-2 Advanced Multidisciplinary Research Areas and S&T Fields

Advanced multidisciplinary research areas (sample themes) \ S&T Field	Mathematics	Physics									Basic chemistry					
		Quantum mechanics, relativity, etc.	Particle, nuclear physics	Atoms, molecules	Fluid body, theory, plasmas, electric discharges	Structure of substances, radiation physics	Mechanical, thermal characteristics	Electronic characteristics	Magnetism	Optical characteristics	Physical chemistry	Analytical chemistry, separation methods	Inorganic chemistry	Chemistry of complexes	Organic chemistry	Polymer chemistry
1 Intelligent materials																
(1) Structural materials with self-diagnostic, self-recovery functions				○		○	○	○	○	○	○	○	○	○	○	○
(2) Drug carriers, biofunction substitutes and other such medical-use materials				○		○	○	○	○	○	○	○	○	○	○	○
(3) Optical materials whose characteristics change according to external conditions				○		○	○	○	○	○	○	○	○	○	○	○
2. Frontier measurement and control tech.																
(1) Measurement manipulation of individual molecules, atoms				○	○	○	○	○	○	○	○	○	○	○	○	○
(2) Micromachining manufacturing tech.					○	○	○									
3. New genetic manipulation technology																
(1) Human genome analysis											○	○			○	○
(2) Applications in pharmaceuticals, and treatment of genetic disease															○	○
4. New neuroscience technology																
(1) Engineering-type realization of neural circuits								○		○						
(2) Coping with aging, dementia, etc.																
5. Biomolecular S&T																
(1) In situ nondestructive measurement, control of biofunctions at the molecular level			○	○		○	○	○	○	○	○	○	○	○	○	○
(2) Technology for high-purification of substances that make up living organisms												○			○	○
(3) High-efficiency energy conversion technology				○		○	○	○		○	○	○				
(4) Stable prediction systems technology that studies living organisms						○	○	○			○	○			○	○
(5) Environmentally resistant bioengineer.																
6. Biotemporal S&T																
(1) Elucidation of biorhythms																
(2) Applications in biorhythmical medical treatment																
7. New global environmental S&T																
(1) CO_2 fixation, separation technology				○		○					○	○	○	○	○	
(2) Desert afforestation technology											○	○	○	○	○	○
(3) New methods of observing hazardous substances in the environment				○		○					○	○	○	○		
8. Recycling S&T																
(1) Searching, utilizing degradable substances, new microbiological organisms															○	○
(2) High-purity separation technology			○	○		○					○	○	○	○	○	○
9. Computer S&T																
(1) Theoretical establishment and prediction of functional manifestation		○		○		○	○	○	○	○	○	○	○	○	○	○
(2) Simulation of biofunctions	○			○		○	○	○	○	○	○					
(3) Elucidation of fluidic system theories	○				○		○									

[Continuation of Table 2.2-2]



The importance and concrete image of intelligent materials, i.e., "materials that feel, think, and act on their own," are as follows. In fields such as aerospace and nuclear power, for example, not only are materials with high reliability in severe usage conditions desired, but also materials that have functions with which to self-diagnose damage and deterioration, inform the outside of that damage, suppress the further development of the damage, and repair themselves (Figure 2.3.1-1). In the fields of medical treatment and welfare, too, intelligent materials for use as drug delivery systems (DDS) (Figure 2.3.1-3) are also desired: e.g., capsule materials that will discharge the required amount of medicine in response to the state of growth and healing, the state of the biofunctional replacement materials that have either grown or decomposed (blood vessels, bones, etc.) (Figure 2.3.1-2), and the state of the body itself (state of the illness, location, etc.). And, in applications such as automotive window glass and variable-focus lenses, optical materials (Figure 2.3.1-4) that can control optical characteristics (index of refraction, transmittivity, reflectance, etc.) in response to changes in electric field, magnetic field, and temperature are also desired.

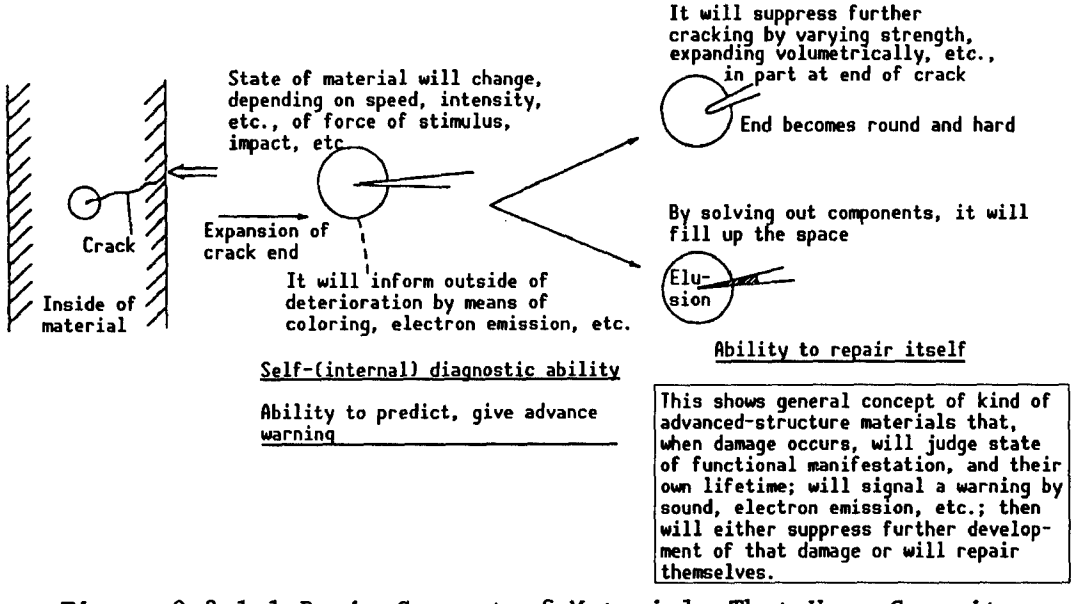


Figure 2.3.1-1 Basic Concept of Materials That Have Capacity for Self-Diagnosis, Warning, and Self-Repair

In the general concept of intelligent materials there are three perspectives: "intelligence from the human viewpoint" (social benefits), "intelligence of the material itself" (intelligent functions), and "basic functions of intelligence" (basic functions). These are organized into a single hierarchal system,as shown in Figure 2.3.1-5.

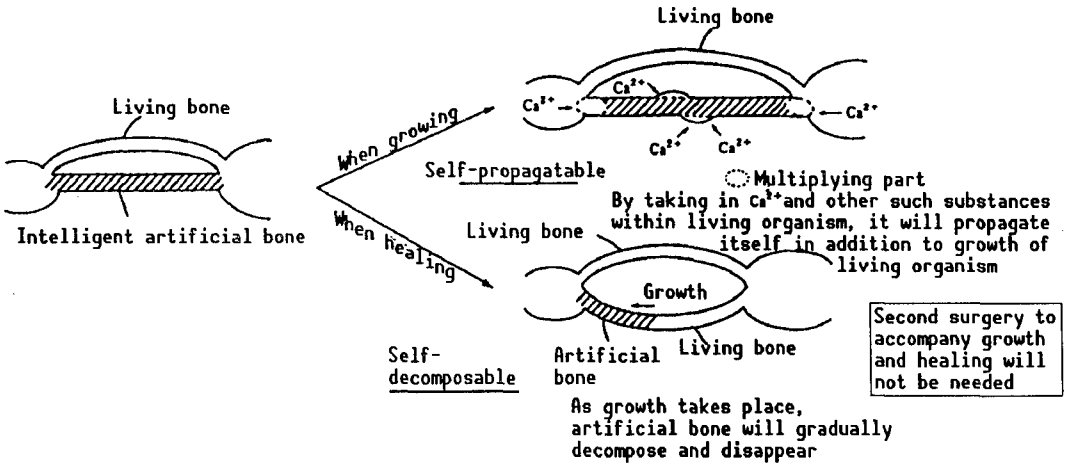


Figure 2.3.1-2. Concept of Intelligent Artificial Bone

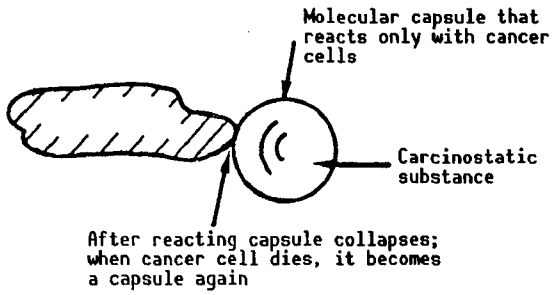


Figure 2.3.1-3 Material That Recognizes Only Cancer Cells and Discharges a Carcinostatic Substance, Then Decomposes When Not Needed

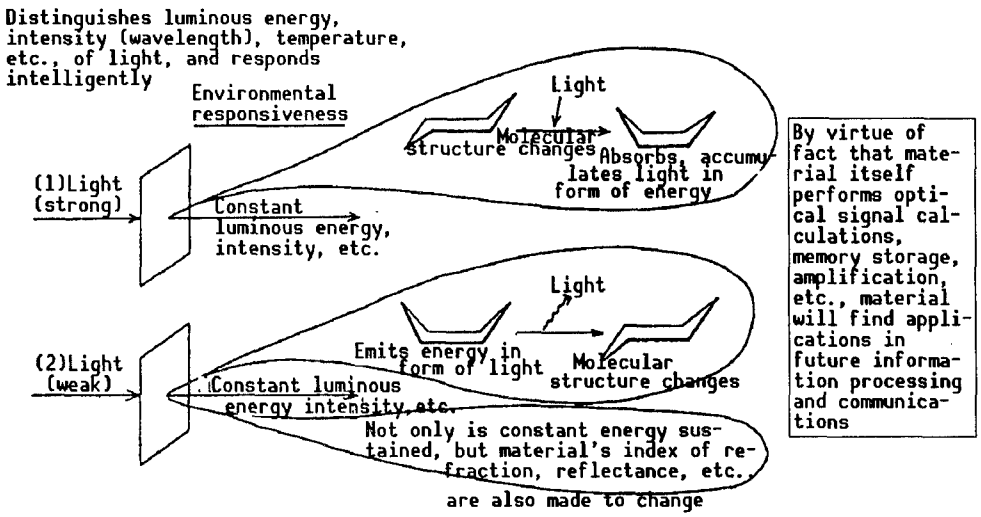


Figure 2.3.1-4 Optical Material With Environmental Response Functions

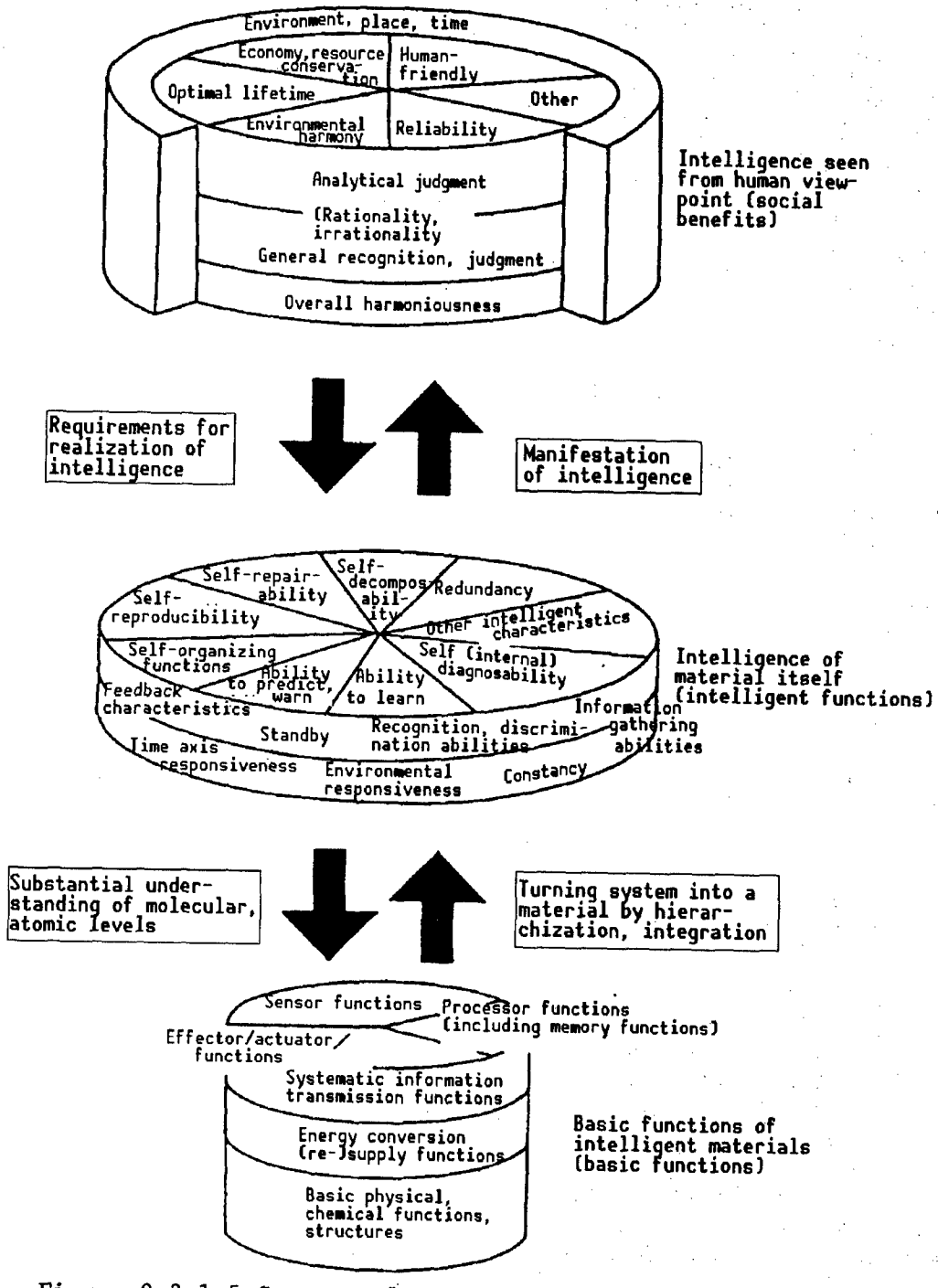


Figure 2.3.1-5 Conceptual Diagram of Intelligent Materials

"Intelligence of the material itself" (intelligent functions) has nothing to do with human assessment or utilization; it is the functions, in the form of individual characteristics, with which the material responds to environmental conditions: self- reproducibility, self-reparability, self-decomposability, redundancy, self-(internal) diagnosability, learning ability, ability to predict and warn, self-organizing functions, etc. To manifest these functions, the materials must have information processing functions, i.e., feedback, standby, recognition and discrimination, and information gathering abilities, that relate to the systematic cooperation of multiple functions. Even more fundamental functions will also be required, i.e., time axis responsiveness, environmental responsiveness, and constancy.

"Basic functions of intelligent materials" (basic functions) are the basic elemental functions that are systematically linked together so that when the material responds to environmental conditions it manifests its intelligent functions. In order for the material to respond intelligently to environmental conditions, there must be systematic cooperation between numerous functions, i.e., the material must detect changes in environmental conditions, transmit and process that information, and, as a result, induce the appropriate functions to go into action. These functions are broadly divided into three basic functions: sensor functions, processor functions (including memory functions), and effector functions (actuator functions). All of the functions act in cooperation through the processor functions. For the manifestation of these three elements of the basic functions, in many cases even more common functions, such as systematic information transmission and energy conversion and supply, must accompany these.

In order to further clarify the aforementioned concepts of intelligent materials, Table 2.3.1-1 shows, for different areas of usage, examples of the concrete forms of intelligent materials that can currently be considered and the kinds of intelligent functions that can be expected.

(2) Current State of, Topics in Intelligent Materials

In a broad sense the research area of intelligent materials overlaps with micro-machine production technology and molecular/atomic-level measurement and manipulation, which are taken up in the next section, "2.3.2 Frontier Measurement and Control Technology." Here we will limit our discussion to the research that is aimed at the original intelligent materials that "feel, think, and act on their own."

Research in intelligent materials starts from building upon the concept of "what is an intelligent material," as discussed above. Now, when scientific and technological creativity is expected of Japan, this research is important in that it is the first case where a new research area that is based on the independent ideas of Japanese has opened. Also, during the process of drawing up the previously mentioned report[1]) the "International Conference on Intelligent Materials" was held in Tsukuba in March 1989. Then again, with this as the turning point, the "US-Japan Workshop on Smart/Intelligent Materials and Systems" was held in Honolulu in March 1990. That the research area has progressed from the stage of building upon a concept to internationalization warrants attention.

Table 2.3.1-1 Concrete Forms of Intelligent Materials That Can Currently Be Considered (Examples for Conceptual Understanding)

Usage area	Example
Structural	•When a crack appears in a strength member under repeated stress, the kind of material that inhibits the development of cracks by producing volumetric changes and exerting compressive stress in the area around the crack as a result of the stress-causing transformations that occur in the end of the crack. (Recognition and discrimination functions, redundancy) •The kind of materials that recognize the loading speed of applied stress, judge whether it is static stress or impact stress, and show great strength in response to impact stress. (Recognition and discrimination functions, redundancy) •When deformation or damage occurs, materials that issue warnings and either suppress that development or recover their original shape in time. (Self-diagnosability; ability to predict, warn; self-repairability) •Materials that can be used in a very broad range of temperatures, from extremely low to super-high temperatures, by virtue of the fact that they are appropriately converted into other substances in response to temperature and to environmental conditions where phase changes and chemical reactions occur. (Heat-resistant materials for use in spacecraft, etc.) (Environmental responsiveness)
Electrical, electronic materials	•The kind of varistors that supply oxygen to repair themselves as a result of their having detected the degree of deterioration or the amount of oxygen vacancies when a pulsed voltage repeatedly operates on the material. (Self-repairability) •By changing the value of their resistance in response to temperature changes, etc., the kind of very-weak-constant-current-generating materials whose resistance changes in a very sensitive manner so as to maintain a constant current. (Constancy)
Optical materials	•The kind of optical materials that, according to the objectives and to their environment, allow an optimum amount of light to pass through them, no matter how much light is incident upon them. (Materials used for sunglasses, glass for automobile and residential windows, etc.) (Recognition and discrimination functions)

[continued]

[Continuation of Table 2.3.1-1]

Usage area	Example
[continued Optical materials]	•The kind of materials that change optical characteristics as a result of changes in electric field, magnetic field, temperature, etc.; materials that control their index of refraction, transmittance, reflectance, etc. (Variable focus lenses for autofocus cameras, etc.) (Environmental responsiveness)
Bio-materials, medical materials	•The kind of materials that are implanted within living organisms and can grow or decompose as the need arises when the living organism grows or undergoes medical treatment. (Artificial bones, etc.) (Self-repairability, self-reproducibility) •The kind of medical materials that discriminately adsorb cancer cells, and in response to that state gradually release carcinostatic substances. (Materials for carcinostatic microcapsules) (Recognition and discrimination functions, standby characteristics)
Other	•The kind of gas-sensing materials that can recognize the amount and type of gas that was absorbed; when the amount of gas goes above a certain constant, materials in which current flows at different levels that correspond to the gas. (Recognition and discrimination functions) •Adhesive materials that maintain constant adhesive power during the time they are being used, but once that time has passed they make a judgment on their own and can be easily peeled off. (Time-axis responsiveness) •The kind of materials whose permeability, heat transmission, etc., change according to internal and external temperature and humidity conditions. (Clothing materials, insulating materials for residential use) (Feedback characteristics, environmental responsiveness) •The kind of packaging materials with functions for controlling, without accelerating, the ripening of vegetables and other produce by regulating the transmittivity of ethylene gas; materials that indicate that the produce is just ripe enough for eating. (Environmental responsiveness)

We can say that the "First Intelligent Materials Symposium"[3]) that was held in Tokyo in March 1991 gave a complete survey of the current, most advanced research in Japan in this area. Thus, summarizing the contents of the lectures from this symposium will give a summary of trends in namely that research area.

At present, materials for use in drug delivery systems (DDS; discussed later in (a) of this section) are thought to be where research is progressing the most in the original meaning of intelligent materials, i.e., materials that are equipped with sensor, processor, and effector functions. Research that attempts to add local deformation and crack-sensing functions to structural materials (discussed later, in (b) of this section) is the first step towards intelligent materials, but because it is at the stage where researchers are trying to add only a single function, the sensor function, to structural materials, it is still quite a ways from intelligent materials that ""feel, think, and act on their own." Attempts at applying the concept of fractals in order to make materials intelligent are innovative and interesting ideas, too, but at present they are lacking in substantiality.

Below we will discuss the current state of and topics in intelligent materials with respect to several research themes in that area.

(a) Research on Intelligent Materials for Drug Delivery Systems

In drug delivery systems (DDS), which control the dosage of drugs, targeting (having functions for efficiently delivering the drug only to the focus of the infection or illness) and control release (having functions for controlling a fixed amount of the drug for a fixed period of time) have been regarded as problems for quite a while. In addition, in recent years there have also been requirements such as functions for perceiving changes in the external environment and then automatically controlling the release and permeation of the drug. These functions are for the purpose of realizing the kinds of systems that provide drug treatment only during an illness and then automatically stop releasing the drug when there is no need for it, and systems in which the drug is released only in an environment where the treatment can be carried out effectively. Because of these objectives, intelligent materials for DDS that can "feel, think, and act on their own," as mentioned above, are being widely researched.[4,5,6]

(i) Drug Release Systems That Control Drug Release by Means of Temperature Changes[4,5,6]

As for on/off control of drug release by means of external temperature changes, gels that reversibly exhibit low-temperature expansion and high-temperature contraction in response to temperature changes have already been synthesized. Owing to this, drug release systems that are on at low temperatures and off at high temperatures[4,5] have become a reality. The synthesis of gels that reversibly exhibit low-temperature contraction and high-temperature expansion in response to temperature changes are making possible low-temperature-off, high-temperature-on drug release systems.[6] In the former, an N-isopropylacrylamide (IPAAm) and alkylmethacrylate (RMA) copolymer gel was used.[4,5] In the latter, an inter-penetrating polymer network (IPN) made from polyacrylamide (PAAm) and polyacylate (PAAc) was used.[6]

The growth of this kind of research may lead to the realization of systems in which a de-heating agent is released only when there is heat, and drug release stops when the heat lowers; and systems that release anti-cancer agents at temperatures above 42.5°C, when cancer cells are easily damaged.

As mentioned in this section, in order to use the changes in swelling for on/off control of drug release or permeation, it is important to grasp the dynamics and non-equilibrium states of the changes in swelling; from now on, developments in research in this direction will be important.[4]

(ii) Microcapsules Whose Permeability Change In Response To External pH

Microcapsules whose permeability change reversibly according to external pH have already been produced on a trial basis.[7,8] The microcapsule is a polyacrylate/polyethylenimine-polyion complex capsule whose particle diameter is 6 mm; it is known that the when p-toluene sulfonic acid and phenylethylene glycol are used as the permeating substances, the permeability depends a great deal on the pH (when the pH is small, the permeability is large).

Because the pH of cancer cells is lower than that of normal cells, if, in the future, microcapsules with diameters on the order of 10 microns are possible, then it may tie in with the development of intravenously used drugs that release anti-cancer agents only in places where there are cancer cells.

The development of tiny microcapsules made from membranes that are permeable to drugs in response to external stimuli will be anticipated. The microcapsules would be superb in terms of biocompatibility, biodegradability, and safety.

(iii) Glucose-Responsive Intelligent Permeation/Release Devices

For the purpose of using intelligent materials as artificial pancreases in the treatment of diabetes, there are vigorous attempts being made to develop systems, in the form of intelligent materials, that release insulin in response to glucose concentrations. Polymer membranes that change their insulin permeability in response to external glucose concentration are being formed[9,10]; glucose-responsive insulin- release gels are being produced[11]; glucose-responsive insulin- release protein devices are being synthesized[12]; and so forth.

(iv) Drugs Carriers With Targetability

Targetability is one of the important qualities sought after in drug delivery systems. If targetability can be achieved, it will be possible to treat only abnormal cells, without affecting normal cells (side effects will be reduced). The use of polymer micelles as drug carriers that target liver cells has been reported.[13] These polymer micelles, which are polystyrene derivatives with galactose in their side chains (PVLA), are effective because they bind selectively and strongly with liver parenchyma, and their drug inclusion functions are also excellent.

In the future, by carrying out molecular design that involves, for example, changing the molecular weight and comonomer components in this cell-recognizing polymer-micelle-type drug carrier PVLA, it will be desirable to endow the PVLA with environmental responsiveness and thereby bring about further growth in intelligent medicines.

(b) Research On Adding Deformation- and Crack-Sensing Functions to Structural Materials

Much of the damage in structural materials starts out with the occurrence of local deformation on the surface, then progresses into microscopic cracks. As the first step for adding self-diagnostic functions to structural materials, it is reported that materials have been given deformation-detection functions by coating the surface of the material with a piezoelectric polymer to utilize the piezoelectric polymer's sensitivity to deformations.[14] Trial versions are being made of systems that, by applying a probe, measure the amount of electrical charge that is generated as a result of deformation occurring in the material (the charge is proportional to the amount of deformation). Scientists also observe areas of deformation by observing the voltage contrasts occurring in SEM (scanning electron microscope) secondary electron images that are due to the electric charge caused by the deformation. At the present stage, however, the materials only have sensing functions, and so are quite far from intelligent materials.

(c) Polymer Gel Actuators[15,16]

Because polymer gels can be made to have nearly the same water content as that of living systems, and because they are superb in terms of flexibility, there is ongoing research that attempts to add environmental-response functions to polymer gels and thereby realize polymer gel actuators.[15,16] Okuzaki, et al.[16] clarified that highly efficient deformations could be realized when an electric field is applied to an electrolytic polymer gel in a micelle solution; they are making actuators that walk along a rail at a speed of 14 cm/minute. It is an intelligent material in the sense that it moves in a reaction to an electric field, but we have to say that, with the need for a rail in a micelle solution, and so forth, the material is in a first-step stage.

(d) Ceramic Sensors With Molecular-Recognition Functions[17]

Conventional ceramic sensors do not have molecular-recognition functions; they do no more than monitor the changes in the amount of oxygen adsorption that accompanies gas combustion reactions of oxide surfaces. Nakamura et al are focusing on the phenomenon of electron transition in special reaction sites on ceramics called hetero-contacts; they are investigating the possibility of applications in ceramic sensors with molecular- recognition functions.[17]

(e) Intelligent Molecular Materials Using Protein Hybrids[18,19]

By hybridizing information-reception proteins and effector proteins, as shown in Figure 2.3.1-6 [not reproduced], Aizawa, et al., are pursuing the creation of molecular-specific intelligent materials in which information cooperation will be possible.[18,19] Actually, they are using calmodulins (CaM; proteins whose structures change as a result of C^{2+} within cells, and which control the functions of various oxygens and structural proteins) as the information-reception proteins, and hosujusterase (PDE) as the effector proteins; they hybridize the CaM and PDE by means of carbodimide, and are assessing the information cooperation within the hybrid molecules.[19]

(f) Attempts To Apply New Concepts Such As Fractals To Make Materials Intelligent

There are proposals to try to apply new concepts such as fractals,[20] three-dimensional quantum structures,[21] and quasi-crystals[22] in order to make materials intelligent. At present all are lacking in concreteness; future developments in this field are anticipated.

References

1. Council for Aeronautics, Electronics and Other Advanced Technologies, report (November 1989) in response to "About the Promotion of Comprehensive R&D in Connection with the Creation of New Substances and Materials Having the Capacity To Intelligently Manifest Functions In Response to Environmental Conditions" (Inquiry No 13).

2. T. Shirao, Survey of Intelligent Materials, Mitokagaku Gijutsu Kyokai, September 1990, p 3.

3. First Symposium on Intelligent Materials (Tokyo, March 1991), collection of lecture summaries, Mitokagaku Gijutsu Kyokai, 1991.

4. A. Okano, Survey of Intelligent Materials, Mitokagaku Gijutsu Kyokai, September 1990, p 22.

5. R. Yoshida, et al., First Symposium on Intelligent Materials (Tokyo, March 1991), collection of lecture summaries, Mitokagaku Gijutsu Kyokai, 1991, p 24.

6. H. Kamitono, et al., Ibid., p 26.

7. F. Tabata, et al., Annual Meeting of the Polymer Society (May 1990) preliminary manuscript collection, 39, 443 (1990)

8. T. Takagishi, et al., Proceedings from the Joint Conference of Sub-Area B, "Synthesis and Functional Control of Biofunctional Materials" (Kyoto, December 1990) of the Ministry of Education's Scientific Research Expenditures Important Area Research "New Functional Materials: Design, Production, Control of Properties," 1990, p 100.

9. S. Kitano, et al., First Symposium on Intelligent Materials (Tokyo, March 1991), collection of lecture summaries, Mitokagaku Gijutsu Kyokai, 1991, p 32.

10. K. Ito, et al., Ibid., p 34.

11. T. Shiino, et al., Ibid., p 30.

12. K. Ito, et al., Ibid., p 36.

13. A. Goto, et al., Ibid., p 38.

14. M. Egashira and K. Shintani, Ibid., p 6.

15. M. Suzuki and D. DeRossel, Ibid., p 20.

16. H. Okuzaki and S. Nagata, Ibid., p 22.

17. S. Nakamura, et al., Ibid., p 12.

18. M. Aizawa, Survey of Intelligent Materials, Mitokagaku Gijutsu Kyokai, September 1990, p 14.

19. T. Miwa, et al., First Symposium on Intelligent Materials (Tokyo, March 1991), collection of lecture summaries, Mitokagaku Gijutsu Kyokai, 1991, p.22.

20. K. Ishikawa, Ibid., p 4.

21. Y. Sakaki, JOURNAL OF THE ELECTRONIC INFORMATION AND COMMUNICATIONS SOCIETY, 72, 1404, 1989.

22. J. Tanaka, Survey of Intelligent Materials, Mitokagaku Gijutsu Kyokai, September 1990, p 57.

2.3.2 Frontier Instrumentation and Control Technology

Owing to the advances in instrumentation and control technology, measuring and controlling fine, molecular- and atomic-order structures is continuing to become more possible. Technology for manipulating atoms one by one (atomic manipulation) is especially gaining attention as the key technology for realizing extremely small, atomic-scale devices. Intelligent micromachines are also sought after for use in medical treatment, and research for the purpose of producing micromachines is also expanding. In this report we call these "frontier instrumentation and control technology."

Below we will give an overview of several fields of research in frontier instrumentation and control.

(1) Technology for Measuring and Manipulating Atoms Individually

In recent years, atomic-scale measurement using a scanning tunnel microscope (STM) is gaining attention as a new way to evaluate materials. Technology for manipulating atoms one by one is also gaining attention as a way to produce new materials and new atomic-scale devices.

(a) Atomic-Scale STM Measurements of Surface Contours

An STM is an experimental technique for analyzing the structure of a sample's surface: it scans a metallic needle extremely close to the surface, and the quantum mechanical tunneling current that flows between the atoms in the tip

of the needle and the atoms on the surface of the sample is used as a probe. The STM was developed in 1981 by Binning and Rohrer at the IBM Zurich Lab; the results of their first surface observations were reported in 1982.[1,2] Figure 2.3.2-1 shows the principles of STM operation.[3] If we sacrifice rigor to a certain degree and explain the principles of STM operation in a way that is easy to understand, we get the following. Because the amplitude of the tunneling current varies exponentially with respect to the distance between the needle and the surface, when the position of the probe is controlled so that a constant tunneling current, I, is maintained while the probe is scanned across the surface, the probe will move up and down as it follows along the undulations of the surface (strictly speaking, along the equilocal state density surface[4]). The STM is equipment that measures the undulations of the surface by electrically detecting the movement of this probe. The resolution of an STM that is perpendicular to a surface is very high, 0.1 nm.[4] As a consequence of this high resolution, it has become possible to directly observe the arrangement of individual atoms. As an example, Figure 2.3.2-2[3] shows an STM image of a silicon (111) surface. As a result of atomic-scale (nanometer-scale) surface observations becoming possible due to the appearance of the STM, research in surface science is rapidly evolving.

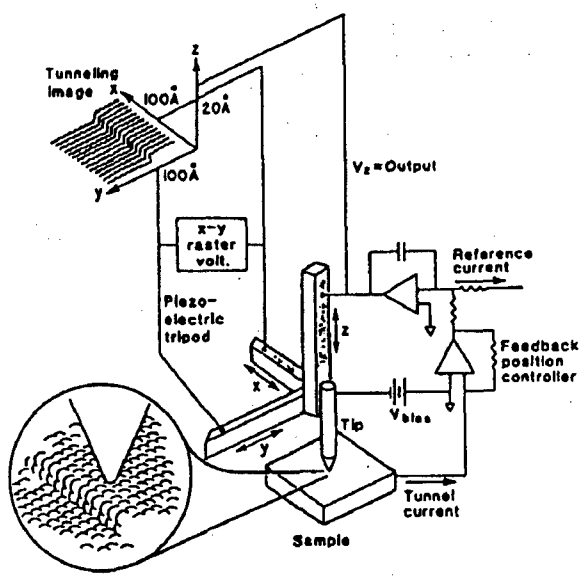


Figure 2.3.2-1. Schematic Illustration of the Tunneling Microscope
The tunnel current from tip to sample, induced by V_{bias} is maintained constant by an electronic feedback system (right), which controls the tip position normal to the sample surface via the z leg of the piezoelectric tripod. A record of the z-leg feedback voltage, as the x-y tripod legs raster scan the tip laterally, constitutes a tunneling image, which is a kind of replica of the sample surface (inset at bottom). The sample, tip, and tripod are maintained in a vacuum chamber.

The STM described above cannot be applied in measurements of insulator surfaces because of the necessary condition that a tunneling current flows. Binning, et al., taxed their ingenuity to create a device called the atomic force microscope (AFM), with which they measured insulator surfaces. The unique feature of the atomic force microscope is that its probe is set up with a small "cantilever." The repulsive force (inter-atomic force) that acts between the electric clouds of the electrons in the tip of the probe and the electric clouds of the electrons on the sample surface bends the "cantilever"; measuring this bending inversely determines the inter-atomic force. From the information about the inter-atomic force that accompanies the scanning of the sample, information about the insulator surface is obtained. In recent years, research on atomic force microscopes has continued to flourish.

Other kinds of microscopes that have evolved from the STM are the laser force microscope (LFM), a precision microscope that uses the interference phenomenon of the laser light rays to capture the changes in the position of a probe; the magnetic force microscope (MFM), which uses a magnetic probe; the electrostatic force microscope, which captures the charge distribution of the sample surface; the thermal sensitivity microscope, which captures extremely small temperature changes; and the scanning ion conduction microscope, whose probe is a glass microbit, that can be used to observe living organisms while they are alive. Including the STM and AFM, a new field called "scanning probe microscopes" is evolving.[6]

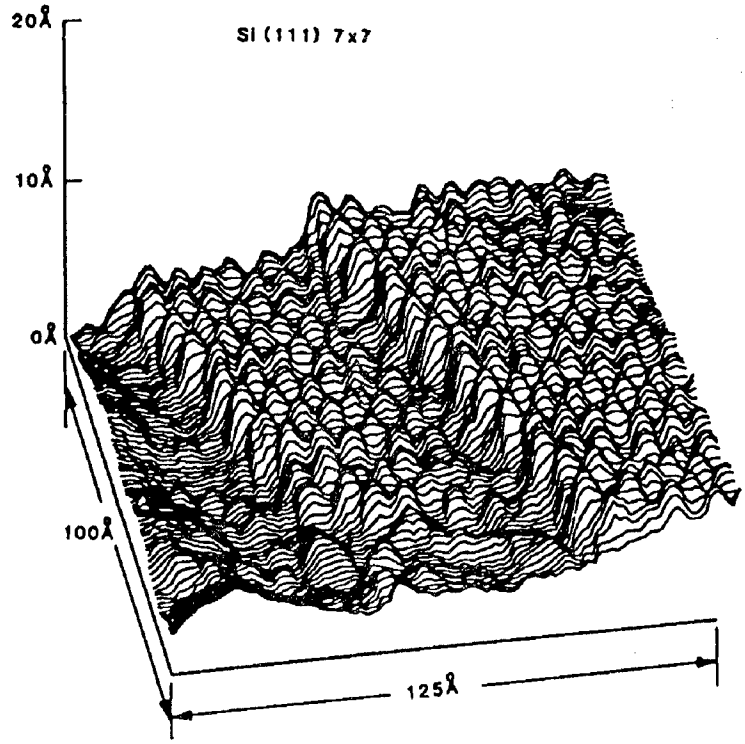


Figure 2.3.2-2 Tunneling Image of Silicon (111) Surface That Shows the 7x7 Atomic Reconstruction on Terraces Separated by Atomic Steps

(b) Measuring a Surface's Electron States by Means of Scanning Tunneling Spectra

The tunneling current in an STM primarily provides information about the density of states of a sample's surface electrons. This original nature of the STM has been used not only to measure surface contours but also to measure the state density distribution in the surface levels of metals and semiconductors, and in the vicinity of quantum flux in superconductors. If we scan the voltage V that is applied to the probe, and then measure the differential conductance, dI/dV, of the tunneling current, I, as a function of V, dI/dV is proportional to the density of states, and a density of states spectrum, D(E), is obtained. This kind of spectral method that uses an STM is call a scanning tunneling spectrum (STS). Density of states spectra that are measured by means of conventional methods are normalized over a macro area, whereas if an STS is used, local—at the atomic scale—density of states spectra will be obtained. Thus, if an STS is used, the position dependence of the density of states spectrum within a very small area can be measured.

Here we will take up as an example of a scanning tunneling spectrum the STS measurements of the quantum flux periphery of a type-II superconductor.[7,8]

Figure 2.3.2-3[7] shows the differential conductance, dI/dV, of the tunneling current, I, plotted against the applied voltage, V, for $NbSe_2$, a type-II superconductor, with a zero magnetic field and a temperature of 1.45 K. That is, this is a density of states spectrum of $NbSe_2$ at 1.45 K and with no magnetic field. From Figure 2.3.2-3, a value of 1.11 meV is obtained as the gap energy, del, at 1.45 K. The temperature dependence of the gap energy, del(T), was obtained by plotting the gap energies that were determined from STS measurements at several other temperatures, as shown by the white circles in the diagram inserted into Figure 2.3.2-3. This del(T) that was determined from experiments fits the temperature dependence of del that is given by the Bardeen-Cooper-Schrieffer theory of superconductivity.

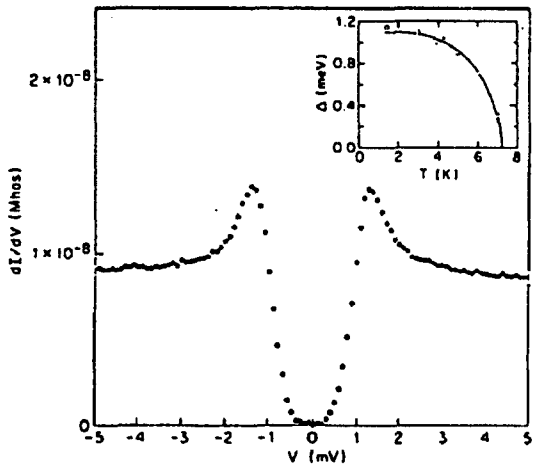


Figure 2.3.2-3 dI/dV Vs V for $NbSe_2$ and 0-T Applied Magnetic Field Used To Determine the Gap at 1.45 K. Inset: The gap vs. temperature and the corresponding BCS fit.

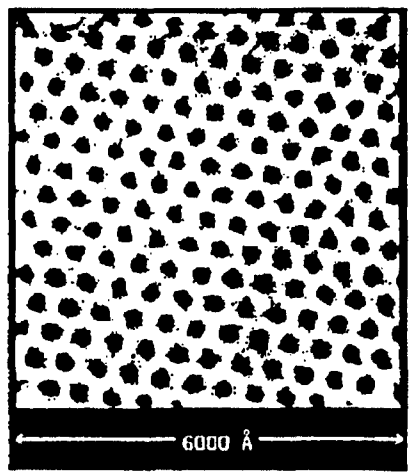


Figure 2.3.2-4 Abrikosov Flux Lattice Produced by a 1-T Magnetic Field in $NbSe_2$ at 1.8 K The scan range is about 6000 Å. The gray scale corresponds to dI/dV ranging from approximately $1x10^{-8}$ mho(black) to $1.5x10^{-9}$ mho(white).

Figure 2.3.2-4[7] shows the results of using an STM to observe an Abrikosov flux lattice when a 1-T magnetic field is applied in $NbSe_2$ (1.8 K), a type-II superconductor. With the applied voltage, V, set to 1.3 mV (the peak positions in Figure 2.3.2-3) while scanning the probe position, the differential conductance, dI/dV, was monitored under the condition of a constant tunneling current, I. When a magnetic field is applied to a type-II superconductor, the density of states will be modulated by the flux lattice. That is, in the area of a vortex's normal conduction states, dI/dV at V = 1.3 mV will be smaller than in the area of the superconduction state where dI/dV exhibits a peak. The dark areas in Figure 2.3.2-4 are the regions of normal conduction states where the values of dI/dV are small; the light areas are the regions of superconduction states where the values of dI/dV are large.

Figure 2.3.2-5[7] shows dI/dV vs V for NbSe2 (1.8 K) with a 0.02- T magnetic field applied, taken at three positions: 1) on a vortex, 2) about 75 Å away

from a vortex; and 3) a central position between the three closest vortices (a position 2000 Å away from each vortex). The dI/dV–V curve in a superconducting region, the third from the top, resembles Figure 2.3.2–3 where the magnetic field was zero. In the regions of normal conduction of a vortex, a flat dI/dV–V curve is expected, but, contrary to expectations, in the top curve in Figure 2.3.2–5 dI/dV increases into a peak shape at V = 0 (zero bias). And, the second curve from the top in Figure 2.3.2–5 has a shape in which the zero-bias peak mentioned above is superimposed onto the superconduction gap.

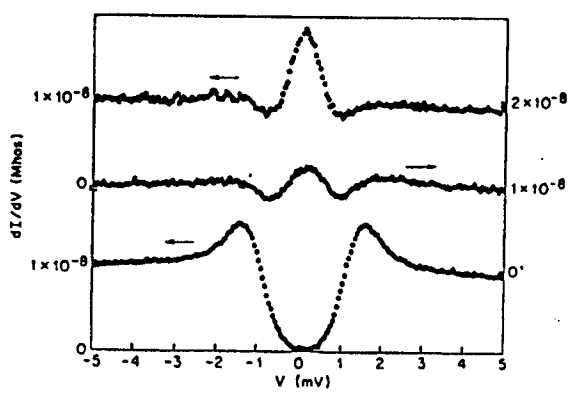


Figure 2.3.2–5 dI/dV Vs V for $NbSe_2$ at 1.85 K and a 0.02–T Field Taken at Three Positions: on a Vortex, About 75 Å From a Vortex, and 2000 Å From a Vortex
The zero of each successive curve is shifted up by one quarter of the vertical scale.

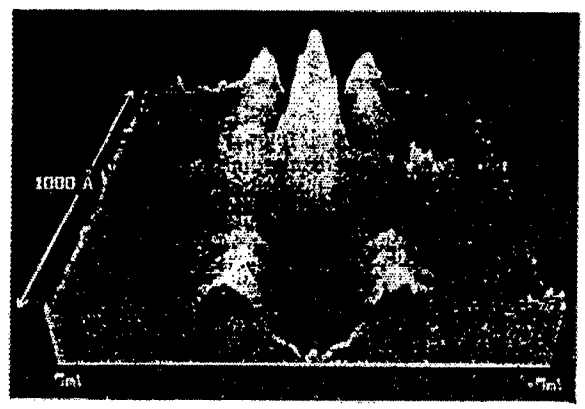


Figure 2.3.2–6 Perspective Image of dI/dV Vs. Tunneling Voltage (horizontal axis) and Position Along a Line That Intersects a Vortex (vertical axis)

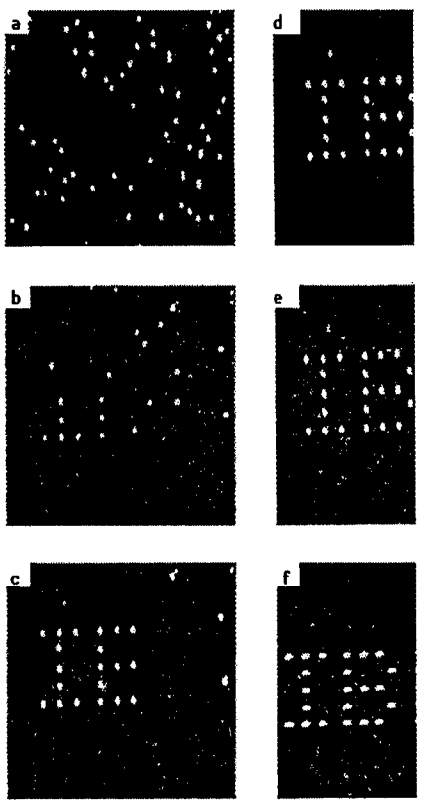
In order to understand in more detail the spatial changes of the dI/dV curve mentioned above, Figure 2.3.2–6[7] shows a perspective image of the dI/dV vs V curve ($NbSe_2$, T = 1.8 K, B = 0.03 T) at 128 equally-spaced points along part of a 1000 Å line that intersects a vortex. Research on the zero-bias peaks seen in Figures 2.3.2–5 and 2.3.2–6 is once again being advanced.[8] This kind of STS measurement of the quantum flux periphery of superconductors is given a position at the forefront of research that approaches the true nature of superconductivity.

As discussed above in the examples of state density distribution of the quantum flux periphery of superconductors, the scanning tunneling spectra (STS), as an application of the STM is a new and powerful experimental method for investigating the physical properties of surfaces; with the STS, the local electron states of a surface can be measured.

(c) Manipulation of Electrons One By One Using an STM

Electronic devices, starting with semiconductors, are steadily getting smaller; the limits of miniaturization are supposed to reach as far as the

atomic level. As an atomic-level device, for example, memory comes to mind: a single atom is one bit. In order to realize atomic-level devices, technology to manipulate atoms one by one (atomic manipulation) is essential. Starting from this kind of background, there have been numerous attempts in recent years to use an STM as a pair of tweezers that picks up atoms. The feature of using an STM in atomic manipulation is that the tip of the probe, which is a means of measurement at the same time as it is a means of manipulation, can be positioned directly above the very locations of individual atoms that the STM sees.



←Figure 2.3.2-7 Sequence of STM Images Taken During Construction of a Patterned Array of Xenon Atoms on a Model (110) Surface
Gray scale is assigned according to the slope of the surface. The atomic structure of the nickel surface is not resolved. The $(1\bar{1}0)$ direction runs vertically. a) The surface after xenon dosing; b-f) Various stages during the construction. Each letter is 50 Å from top to bottom.

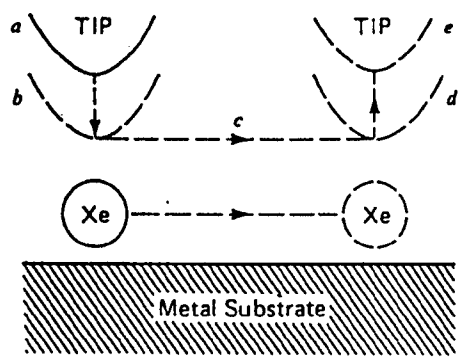


Figure 2.3.2-8 A Schematic Illustration of Process for Sliding Atom Across a Surface
The atom is located and the tip is placed directly over it (a).

Atomic manipulation using an STM was first carried out by Eigler and Schweizer of the IBM Almaden Research Center.[9] They wrote alphabetical letters that were 50 Å high, as shown in Figure 2.3.2-7[9], by using the tip of an STM to move xenon atoms, one at a time, that were sparsely adsorbed on a nickel (110) surface, then fixing the xenon atoms to the positions they wanted on the nickel substrate. Figure 2.3.2-8[9] is a schematic illustration of the process by which xenon atoms are moved with the tip of the probe. The tip is lowered from directly above a xenon atom to a height where gravity appears to act between the tip and the xenon atom; by keeping the tip at that same height (in a state where gravity is acting) and moving it to the desired position, the adsorbed atom is made to move; then, as a result of making the height of the tip such that gravity no longer acts between the tip and the xenon atom, the

xenon atom is fixed onto the desired position on the nickel substrate, with a precision of 0.2 Å.

In 1990 and 1991 the research results of atomic-scale picture- drawing were announced[10-14] one after another by many Japanese companies who had been motivated by the report of Eigler and his colleagues. In Table 2.3.2-1 we put together summaries of the contents of these announcements, including the research of IBM's Eigler that was mentioned above.

Table 2.3.2-1 Atomic-Scale Processing Using an STM

Method		Research organization	Document	Sample (deposited atoms/substrate)	Temperature	Processed line width
Electric field vaporization		Hitachi	10)	-/Molybdenum disulfide	Room temp.	Single atom
		JEOL, Ltd.	11)	-/Silicon	Room temp.	2 n m
Adatom movement		I B M	9)	Xenon/Nickel	4 K	Single atom
Gas	Etching	N T T	12,13)	-/Silver-selenium compound	Room temp.	3 n m
Surface reaction	Deposition	NEC	14)	Tungsten/Silicon	Room temp.	1 0 n m

With atomic manipulation using an STM, not only will atomic-scale device fabrication be possible, but it will also be applicable in creating new functional materials with artificially arranged atomic configurations. Research is expected to further evolve in the future.

(2) Micro-Capsule Manipulation Technology by Means of Lasers

Research is also being carried out on technology that uses laser light in place of tweezers to manipulate microcapsules, whose diameters are on the order of a micron, either one by one or many at one time.[15,16] When laser light hits microcapsules that are dispersed throughout a liquid, a pressure differential of the light arises because of the difference between the refractive indexes of the capsule and the liquid around the capsule. This causes a force that acts on the capsules, and the capsules can be picked up and moved around (Figure 2.3.2-9[15]). The aims of this research are applications in technology for carrying out chemical experiments in micro-areas, with the microcapsule replacing the test tube; and applications in micro-machines, which are discussed in the next Sub-Section (3).

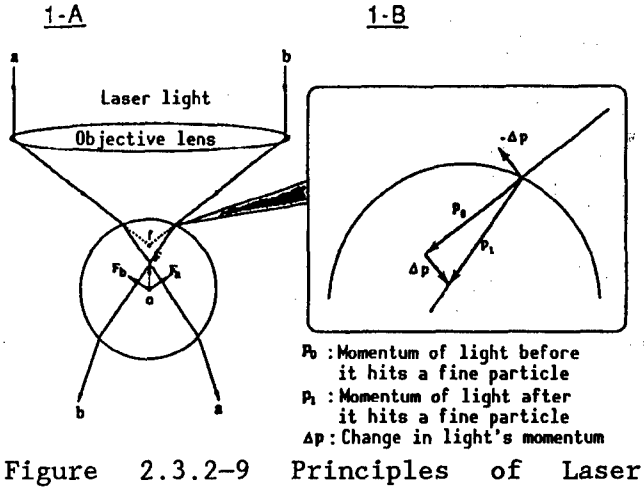


Figure 2.3.2-9 Principles of Laser Capture

(3) Technology for Producing Micromachines

Intelligent micromachines for use in medical treatment and other fields are sought after, and research for the purpose of producing micromachines continues to flourish. There is a close connection between the intelligent materials discussed in Section 2.3.1 of this chapter and micromachines, in the sense that intelligent materials can become the materials for producing micromachines and their smaller versions, which should be called nanomachines.

The world of micromachines is one where the basic parts of the machines have dimensions that range from 10 nm to 1 mm, as seen in Figure 2.3.2-10.[17] Some applications of micromachines that come to mind are in medical treatment; within post-assembly precision machinery; and in cases where fine work must be done in special kinds of environments where there are high pressures, high vacuums, and so on, as in the ocean or in space. But the use of micromachines in medical treatment is thought to be the most concrete application area.

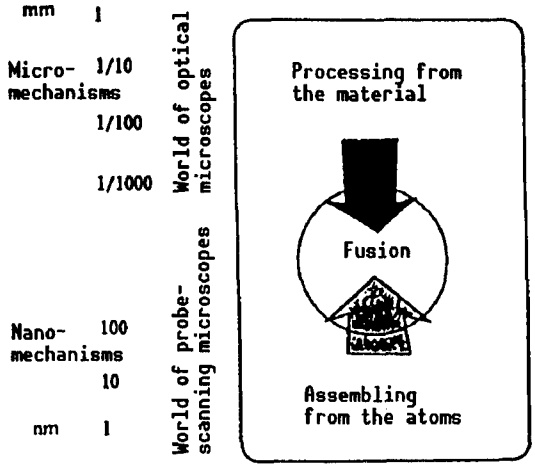


Figure 2.3.2-10 Areas Where Micromachines Exist

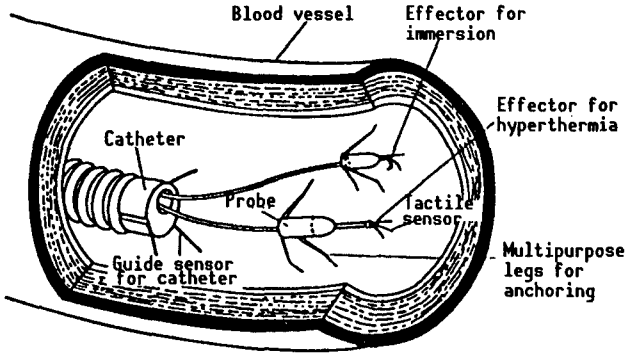


Figure 2.3.2-11 Micro-Robot Moving in a Blood Vessel

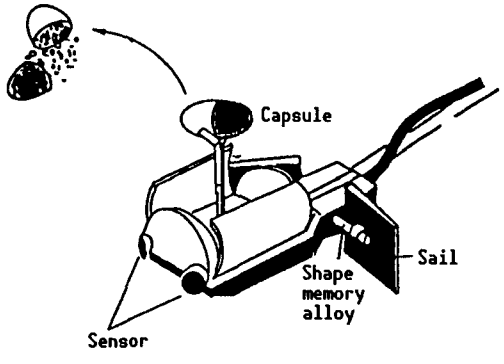


Figure 2.3.2-12 Drug Transport Vehicle in a Blood Vessel (Moves to the required position, then releases drugs)

Figures 2.3.2-11[18], 2.3.2-12[17], and 2.3.2-13[17] show concrete images of cases where micromachines are used in medical treatment. When drugs are given for treatment, with most drugs it is acceptable to focus them on only one part of the body, but in conventional medical treatment, the entire body gets the dose, whether the medicine is given orally or in the form of an injection. As a result, when a medicine that has a strong effect on the body is given, it sometimes becomes toxic; and, in fear of that, the doctor sometimes limits the

use of the medicine. To solve this problem, research on drug delivery systems (DDS) is being carried out. Also described in "2.3.1 Intelligent Materials," drug delivery systems, which deliver drugs in appropriate ways, then bring out the effects of the drugs in specific places and only for specific lengths of time, are a typical example of micromachine applications (Figures 2.3.2-11,[18] 2.3.2-12[17]). In conventional surgery, the affected area is reached after cutting through undamaged skin and tissue, the diseased part is removed, then the opened section is roughly closed. Because of this the side effects are very great. In contrast, if advances are made in micromachine technology, it will be possible, as shown in Figure 2.3.2-13, to go through tubular cavities such as blood vessels, the spinal cord cavity, etc., to insert a tiny laser endoscope into the diseased part and then a small manipulator attached to the end of the endoscope will cut out only as little as necessary of the diseased part of the body. If advances are made in micromachine technology, there will also be dramatic progress in miniaturization, flexibility, and functions of the artificial organs that currently exist.

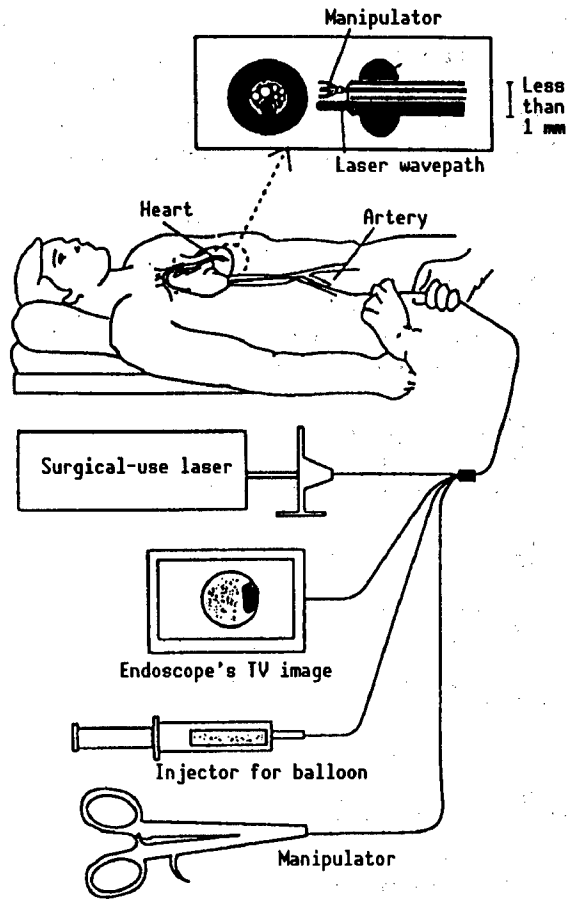


Figure 2.3.2-13 Future Surgery by Means of Laser Endoscope

The problems that arise in micromachine design technology as a result of the machines becoming so small are the marked increase in friction resistance, viscous resistance, and surface resistance, and the noticeable decrease in chronic strength. In this connection, the central idea of the design must change to the concept of learning about the body,[17] and, in the actual design, rigorous computer simulation and careful consideration are necessary.

As for "micromachining," the technology for producing micromachines, in addition to applying the fine processing technology used to produce semiconductors,[19-21] methods that involve using protein engineering and atomic manipulation to assemble molecules and atoms together will also be needed.[17]

As a recent example of micromachine production technology, there is the trial manufacture of cantilever-beam-type actuators that mimic the ciliary movement of living organisms. Figure 2.3.2-14 shows the operational principles of a ciliary movement system, and Figure 2.3.2-15 shows an SEM photograph of cantilever actuators that were actually created. Each of these actuators

consist of a cantilever made from two kinds of polyimides that have different rates of thermal expansion, and a metallic resistance wire sandwiched between two polyimide sheets. As shown in Figure 2.3.2-15, in their initial state the cantilevers curve up about 250 microns from the substrate because of the residual stress. When current flows through the resistance wire,

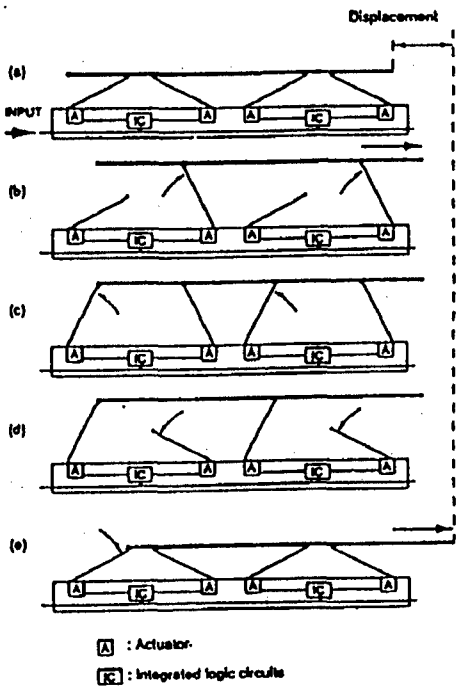


Figure 2.3.2-14 Operational Diagram of a Ciliary Movement System

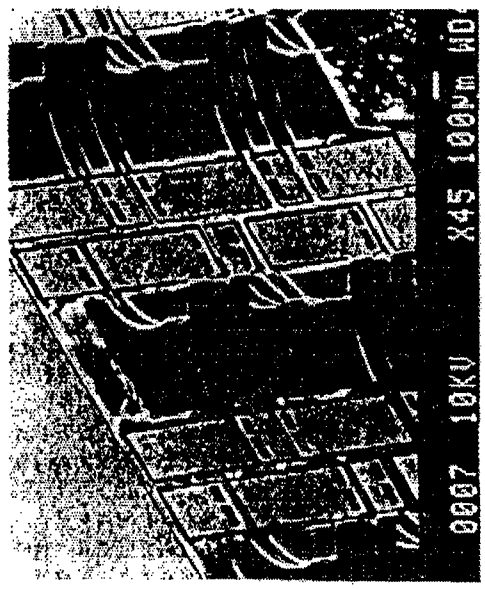


Figure 2.3.2-15 SEM Photograph of Cantilever Actuators

Joule heating heats up the cantilevers and, like a bimetal, they bend down to the substrate. By distributing many of these actuators over the surface of a material, the material surface can be endowed with transport functions, and a tiny carrier machine can be realized.

Research on bacterial flagella to find a model for micromachines in living organisms is energetically carried out.[23] Flagella use protein molecules as parts, and are what is referred to nature's smallest "molecular motors"; to a bacteria, they play the role of a screw. Recently it was reported that experiments to freely control the rotational speed of flagella were successful.[24] The success was the discovery that the rotational speed of the flagella of Salmonella bacteria, which were fixed in a nutrient medium on the tip of a glass tube 1-μm in diameter, was proportional to the voltage that was applied between two electrodes set up on the inside and outside of the tube.

In view of the importance of micromachine production technology, the New Energy Development Organization (NEDO) has taken up "Micromachine Technology" as a new theme, starting in 1991, in the large MITI-AIST projects (the Large Industrial Technology R&D System). Given the plans to promote this R&D for a ten-year period, with about ¥25 billion in investments, from now on progress is anticipated in this field.

References

1. G. Binning, H. Rohrer, Ch. Gerber, and E. Weibel, APPL. PHYS. LETT., Vol 40, 1982, p 178.

2. G. Binning, H. Rohrer, Ch. Gerber, and E. Weibel, PHYS. REV. LETT., Vol 49, 1982, p 178.

3. J.A. Golovchenko, SCIENCE, Vol 232, 1986, p 48.

4. R. Sakurai, DENKI KAGAKU, Vol 56, 1988, p 601.

5. G. Binning, C.F. Quate and C. Gerber, PHYS. REV. LETT., Vol 56, 1986, p 930.

6. H.K. Bikkramishing, SAIENSU, December 1989, p 90.

7. H.F. Hess, R.B. Robbinson, R.C. Dynes, J.M. Valles, Jr., and J.V. Wasczak, PHYS. REV. LETT., Vol 62, 1989, p 214.

8. H.F. Hess, R.B. Robbinson, and J.V. Wasczak, Ibid., Vol 64, 1990, p 2711.

9. D.M. Eigler and E.K. Schweizer, NATURE, Vol 344, 1990, p 524.

10. S. Hosoki, First Symposium on Intelligent Materials (Tokyo, March 1991), collection of lecture summaries, Mito Kagaku Gijutsu Kyokai, 1991, p 10.

11. NIKKAN KOGYO SHIMBUN, 8 November 1990, p 1.

12. Y. Utsugi, NATURE, Vol 347, 1990, p 747.

13. NIHON KEIZAI SHIMBUN, 7 January 1991.

14. NIKKAN KOGYO SHIMBUN, 18 December 1990.

15. H. Mizawa, Creative S&T Promotion Enterprises' 1990 Conference (Tokyo, December 1990), 4th collection of lecture summaries, Shingijutsu Jigyodan, 1990, p 35.

16. NIKKEI SANGYO SHIMBUN, 6 December 1990.

17. M. Fuji, Kyoi no Iryo Kikai Maikuromashin (Miracle Medical Machines: Micromachines), Kodansha, 1990.

18. H. Nakajima

19. M. Esashi, OOYO BUTSURI, Vol 60, 1991, p 227.

20. M. Esashi, DENKI GAKKAI SHI, Vol 110, 1990, p 203.

21. H. Fujita, Ibid., p 289.

22. H. Takeshima, A. Omotaka, and H. Fujita, First Symposium on Intelligent Materials (Tokyo, March 1991) collection of lecture summaries, Mito Kagaku Gijutsu Kyokai, 1991, p 8.

23. H. Takatani, Creative S&T Promotion Enterprises' 1990 Research Report Meeting (Tokyo, December 1990), 3rd collection of lecture summaries, Shingijutsu Jigyodan, 1990, p 1.

24. NIHON KEIZAI SHIMBUN, 20 May 1991, p 19.

25. NIKKAN KOGYO SHIMBUN, 12 December 1990, p 13.

2.3.3 New Genetic Manipulation Technology

Since long ago human beings have been improving the breeds of domestic animals by using natural cross-breeding to make selective improvements upon desired characteristics.

In recent years, in addition to the "classical genetics" mentioned above, "molecular genetics" has advanced along with genetic engineering, where the genetic substance itself is directly manipulated. Because DNA recombination and the chemical synthesis of genes has become possible, stocks of genetic characteristics that can be used on any living organism have increased tremendously.

Now, genetic manipulation that centers mainly on microorganisms is becoming practical. Applications of this technology to microbiologically more complex plants and animals, where it is difficult to introduce genes into their cells and to manipulate those genes, is seen as needing a little more time.

In this section we will discuss the research topics related to genetic engineering, and application examples of the genetic manipulation using microorganisms that is becoming practical.

(1) Principles of Genetic Manipulation

In genetic manipulation, there is the case where full-length DNA is used, and there is the case where parts of the DNA having special functions are snipped and used. We will give general overviews of both below.

(i) Ways To Handle Full-Length DNA

Oxygen-type DNA Amplification (Polymerase Chain Reaction) Method

The PCR method involves repeating template DNA thermal conversion, primer combination, and primer extension reactions in an isothermic reaction tank. Figure 2.3.3-1 shows a full-length cDNA (complimentary-DNA) amplification method by Kogara and others.[1] By amplifying and determining the base sequences of, in succession, the central section, a three-prime side region, and a

five-prime side region, and then linking the three together, the entire sequence is obtained.

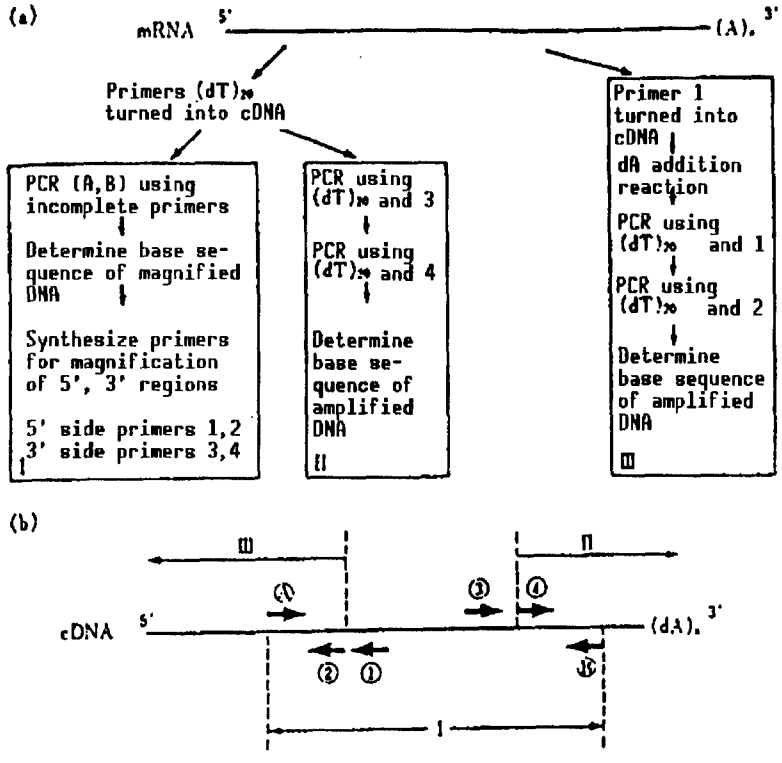


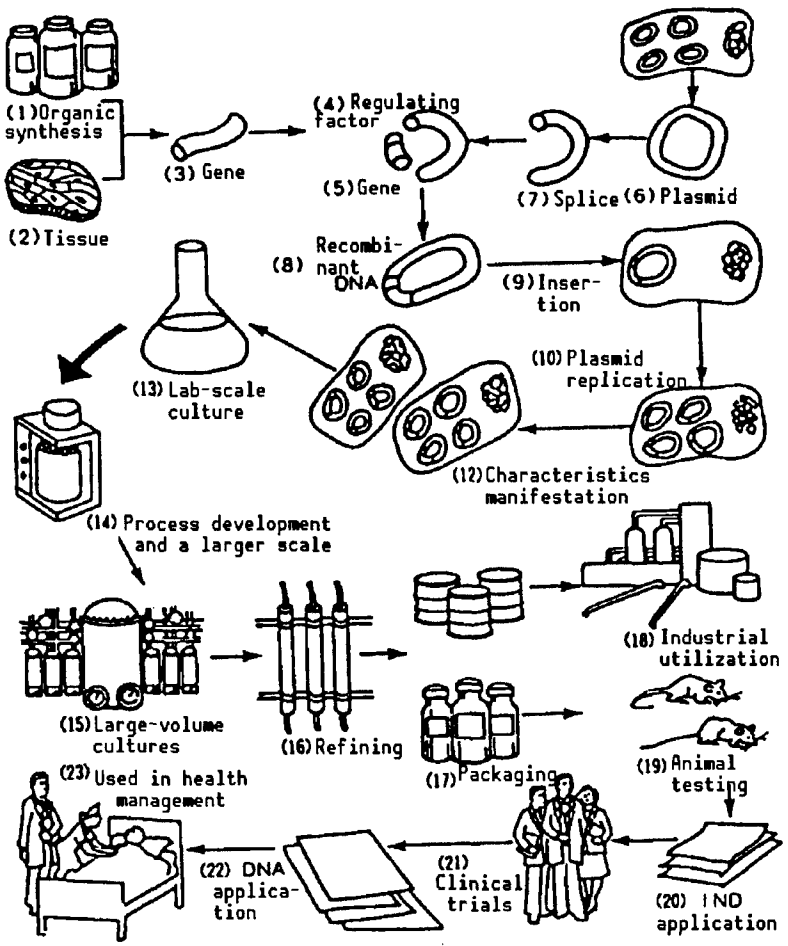
Figure 2.3.3-1 Full-Length cDNA Amplification in Three Steps
(a) shows how the central section (I), a three-prime side region (II), and a five-prime side region (III) are amplified. Usually steps (II) and (III) are done in parallel after step (I).

(b) shows the positional relationship on the primer (A, B, 1-4) cDNA structure shown in (a). The direction of the arrows indicate three-prime. The primers shown above the line that indicates the cDNA have sequences of sense strands; the primers shown below the line have sequences of anti-sense strands. Lastly, the base sequences of the I, II, and III regions are combined, and the structure of the entire cDNA can be obtained.

A special feature of the PCR method is that, even if the primers that are used contain many mismatches, they can hold up in the use. This feature demonstrates its power in cases where there is only a tiny amount of the sample, or when a valuable archeological sample must be handled.

Genetic manipulation is also being vigorously fused with other related technologies, e.g., attempts to make the automatic analysis sequence more efficient by incorporating the PCR in automatic reaction equipment that is based on the dideoxy method (Sanger's method) of DNA sequencing (Soeda, et al.,[2]).

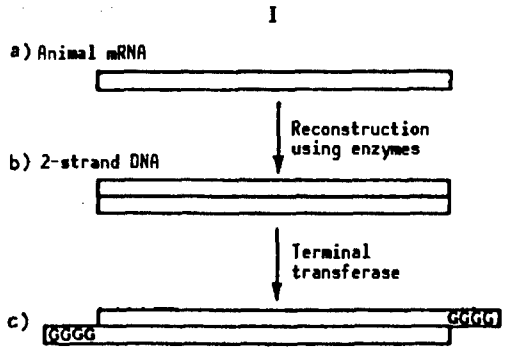
Figure 2.3.3-2 The Genetic Engineering Process

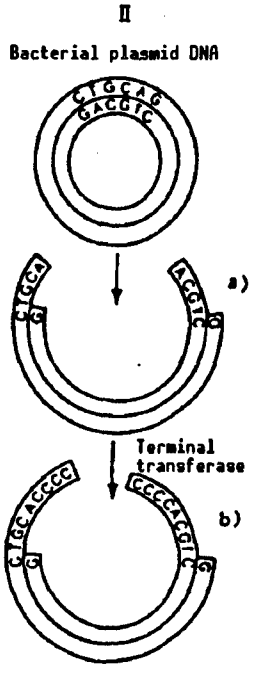


The development process starts by getting DNA from either organic synthesis (1) or from samples like tissue taken from a living organism (2). The DNA obtained is then re-adjusted in order to create the basic gene (3) containing the genetic information that codes the target substance, e.g., human interferon, insulin, etc. The section that contains the regulating factor (4) is then added to this gene (5). Ring DNA, called plasmids (6), from microorganisms such as *E. coli* is isolated and then the plasmid basic gene and the regulating factor are spliced together, (7) and (8), to produce recombinant DNA. This DNA is then introduced into a host cell (9). The recombinant plasmid replicates itself many times within the cell (10). The information incorporated into the plasmid is translated into the target substance by a process called characteristics manifestation (11). The cell divides (12) and transfers the same genetic information as that of the original parent cell to the grandchild. The microorganism culture produced by genetic engineering is at first done in a flask (13); then on a small scale (14) for the purpose of determining the conditions for large-volume cultures; and finally in a large-scale tank (15). The cell extracts obtained from the culture process are separated and refined (16), packaged (17), and are turned over for industrial utilization (18) or for use in health management.

To investigate the pharmacological effects and safety of the product so that it can be used for health management, it is first tested on animals (19). In the U.S., an application for an investigational new drug (IND) is made (20) so that clinical trials are conducted to prove the efficacy and safety of the drug. The results of the clinical trials (21) and a new drug application (NDA) are submitted to the FDA. The FDA investigates the drug again; after approval it will first go on the market in the U.S. (23). (Material from Genetech)

I First target gene must be removed and reconstructed.
a) RNA (mRNA) that carries information about the targeted protein is isolated.
b) Two strands of DNA are reconstructed, oppositely from mRNA.
c) Lastly, after allowing terminal transferase to act, two ends of DNA are extended with short chains made of the same bases (in this case, four quanines).





II Plasmids that are small ring DNA of bacteria serve as transporters for introducing the new gene (obtained in step 1) into a bacterium.
a) Ring plasmid is sliced by means of suitable restriction enzyme.
b) After allowing terminal transferase to act, two ends of open-ring plasmid are extended with chains made of the same bases (in this case, four cytosines, which complement the quanines that extended the gene in step 1, are linked onto the plasmid).

III Finally, a bacterial plasmid that contains a new gene is obtained. This plasmid is then inserted into a bacterium and allowed to replicate and synthesize the target protein.
a) The gene obtained in step I and the plasmid DNA obtained in step II are mixed together; both combine through formation of complementary base pairs.
b) Enzymes of bacteria work to fill in spaces between plasmid DNA and inserted DNA; a complete ring plasmid containing the new gene is made.

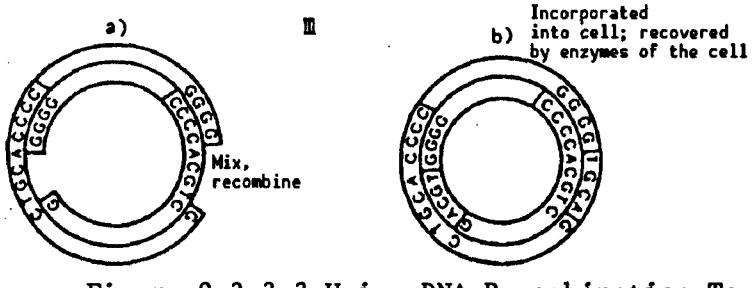


Figure 2.3.3–3 Using DNA Recombination To Introduce a Gene Into Bacteria

(ii) Ways To Handle Specific DNA Sequences

a) Use of Plasmids

Figure 2.3.3–2[3] shows the process of synthesizing mass volumes of specific proteins by manipulating the genes of *E. coli*. Figure 2.3.3–3[4] shows the details of steps (3) to (8) in Figure 2.3.3–2.

The feature of this kind of genetic manipulation is that it uses plasmids (units of DNA that are capable of self-replication in bacterial cells) that exist in extrachromosomal parts of bacteria. That is, when plasmids (even if they are of different species) move from one strain of bacteria to another, they make the bacteria where they move to form proteins according to the information that they bring, so they can be used as vectors in gene introduction. Also, because a plasmid that was inserted one time replicates during cell division, if a culture is made of bacteria that have recombinant plasmids, specific proteins can be obtained in mass volumes.

This method is now often used in cases where information is registered in cDNA libraries and where known proteins are obtained in mass volumes.

b) Use of Bacteriophages

On the other hand, for DNA that is completely unknown, bacteriophages are often used as vectors. There are two kinds of phages that are used differently according to the objective: the virulent phage that begins to propagate (solve out) immediately after infection, and the temperate phage that lies dormant within the chromosomes of bacteria for a fixed period of time (lysis), then begins to propagate when it receives a stimulus. The former is used like plasmids. As for the latter, after as many as ten or more genes are incorporated into one kind of phage, they can be made to propagate all at once by adding an external stimulus, so this kind of phage is used in cases where several enzymes are efficiently produced.

2) Other Methods

a) Artificial Synthesis Methods

Because the nucleotide sequence of a gene can be inferred from the amino acid sequence of the protein it produces, it is possible to artificially synthesize genes.

Furthermore, the methods can be adapted to genetic manipulation in any kind of living organism. If accompanied by advances in peripheral technologies, such as improvements in the information processing speed of computers, the preparation of genetic information libraries, and so on, artificial synthesis methods will become the central technique of genetic manipulation in the future.

However, in the present situation where not enough progress has been made in the aforementioned peripheral technologies, there is a problem with these methods: as the molecular weight of the protein gets larger, synthesis becomes more difficult. This state of affairs can be understood from the example of somatostatin synthesis: to synthesize a protein such as this, which has only 14 amino acids, DNA that consists of 42 nucleotides must be synthesized (because three nucleotides correspond to one amino acid).

b) Shotgun Method

This is a method where an entire gene is cleaved by means of a restriction enzyme, and the resulting fragment is combined with some vector and then introduced into bacteria; it is an attempt to select from among those bacteria those that will form the targeted protein.

In the past, the gene fragments obtained only had six bases, but in recent years the variety of restriction enzymes that can be used has increased; eight-base and ten-base-long gene fragments can now be obtained. With this, the variety of proteins that can be generated has also increased, and the degree of freedom in research has improved.

(b) Research Trends Involving Genetic Manipulation

As seen in (a) above, methods that involve splicing and then using the natural materials that living organisms generate by themselves are now central to genetic manipulation technology, more so than pure synthesis methods by human hands. This is because DNA replication by a living organisms is extremely accurate and efficient. Radman and Wagner explained the mechanisms of error correction in each process of DNA replication in *E.coli*.[5] According to them, the rates of error occurrence in replication processes are 1) 1 in 100,000 (base pairs) in the nucleotides of the main DNA strand that will become the template, at the stage where complementary nucleotides are checked; but are 2) reduced to 1 in 10 million by correction of the errors that arose in the aforementioned processes; and are 3) reduced as low as 1 in 10 billion in the final process where a one-time error in the DNA strand is discovered and cut out, then the correct base sequence is rearranged.

It was confirmed that these error correction mechanisms are maintained by three kinds of oxygen reaction systems, but there are still only hypotheses about the actual correction mechanisms. At present, there is a high error-occurrence rate, about one in a hundred, when genes are synthesized without oxygen; elucidating the highly precise mechanisms of living organisms' error correction is essential to the future progress of artificial gene synthesis.

Furthermore, in experiments where they used *E. coli*, Cox and Pikoki confirmed that in severe environments stocks with a high mutation rate become more dominant (epistatic) than normal stocks.[5] In other words, there is the possibility that living organisms control the rate of error occurrence according to the environment that surrounds them. When an incorrect base sequence is left alone without modification and that base is combined with a correspondent base (an incorrect base pair is made), and then the base without a partner is removed, the living organism has several mutation generating processes; much about the mechanisms awaits future elucidation. Neverthe-less, if this kind of research progresses further, genetic characteristics may become freely controllable, including the generation of mutated varieties that correspond to the environment and the objectives.

(2) Application Areas of Genetic Manipulation Technology

As a general survey of present-day genetic manipulation technology, genome analysis comes to mind. The human genome is a gigantic molecule that is made up of about 3 billion base pairs; a considerable amount of time is thought to still be needed until the human DNA library is complete. And, hardly anything is known about why there are parts, which account for 95% of the DNA library, that are not directly related to protein synthesis (intron, spacers, repeating sequences, etc.)

As a result of cleaving and modifying DNA, genetic manipulation technology will first shed light on the entire image of DNA, and will be intensively applied for the purpose of elucidating the meaning of the existence of DNA. After that, the originally intended "manipulation," e.g., the production of artificial DNA, will begin.

Human genome analysis projects are now carried out in many countries.[6] According to the data of the Investigative Committee on Human Gene Analysis of Japan's Science Council,[6] the significance of human genome analysis is summarized in the following points:

1) promoting the understanding of life phenomena from the viewpoint of the natural sciences

2) an opportunity for innovative developments in bioscience

3) the creation of new academic fields (by the fusion of information science, engineering, physics, chemistry, etc.)

4) the diagnosis and treatment of diseases

5) elucidating development, differentiation, high-order functions, etc.

6) understanding chromosomes and evolution

7) international contributions in scientific research

Of these, items 2), 3), and, indirectly, 7) are thought to be about all that will receive attention from the perspective of multidisciplinary research areas. The time for these to be realized is predicted to be a long ways off, and, at any rate, the realization will be conceptual.

Below we give the benefits that already result from genetic manipulation techniques; focusing on the diagnosis and treatment of disease, we will discuss the current state of affairs.

(a) Applications in Medical Drugs

In several categories related to this field, products based on genetic manipulation technology are already being put to practical use.

(i) Hormones

The following is a broad classification of the hormones that are thought to be useful from a medical viewpoint:

- peptide hormones like insulin
- the group of plant hormones represented by cytokinins
- somatostatin and other such hypothalamic factor hormones
- opioid peptides such as enkephalins, endorphins, etc. (morphine-like substances within the brain)
- steroid hormones such as sex hormones, glucocorticoid, etc.
- amino varieties such as catecholamine, serotonin, etc.
- others; for example, thyroid gland hormones (amino acids) and prostaglandins (fatty acids)

Table 2.3.3-1 Large Human Polypeptides Where Biosynthesis Is Potentially Attractive

	Number remaining bases in amino acid	Molecular weight
Prolactin	198	
Placental lactogen	192	
Growth hormone *	191	22,005
Nerve growth factor	118	13,000
Parathyroid hormone (PTH)	84	9,562 (cow)
Proinsulin	82	
Insulin-like growth factor (IGF-1 and IGF-epithelial growth factor)	7,067	7,649 7,471
Insulin *	51	5,734
Thymopoiethyne	49	
Gastric-secretion-inhibiting polypeptide (GIP)	43	5,104 (pig)
Adrenocortitropic hormone (ACTH) *	39	4,567 (pig)
Cholecystokinin (CCK-39)	39	
Big gastrin (BG)	34	
PTH activation fragment	34	4,109 (cow)
Cholecystokinin (CCK-33)	33	3,918 (pig)
Calcitonin *	32	3,421 (human)
Endorphin	31	3,465
Glucagon *	29	3,483 (pig)
Thymocan-α_1	28	3,108
Vascular-acting intestinal polypeptide (VIP)	28	3,326
Securethyne *	27	
ATH activation fragment *	24	
Mochilin	22	2,693

* Now used in medical practice.

Table 2.3.3-1[7] lists the hormones from those above that are thought to be especially attractive. In the present state of affairs, small hormones with up to 32 amino acids that are produced by means of genetic manipulation technology can compete with those that are obtained from conventional biologically extracted sources.

Because both have only seven amino acids, genetic manipulation is also possible with melanocyte stimulating hormone (MSH) and a kind of adrenocorticotropic hormone (ACTH4-10), which are thought to enhance memory and the ability to concentrate. Perhaps genetic manipulation technology will be used to develop "drugs that make you smarter."

(ii) Proteins

The typical subject of research in this category is antigens (vaccines) as immune proteins. At present, most vaccines are live viral/bacterial vaccines whose direct hosts are living organisms; several problems with respect to supply and safety have been pointed out. For this reason expectations are growing for genetic manipulation technology that will selectively extract only the targeted functions and will enable the mass production of vaccines. In connection with vaccines for influenza, pneumonia, and foot and mouth disease in livestock, joint government-private projects centered on the U.S. Department of Agriculture are being promoted.[7]

Meanwhile, in connection with the AIDS treatment methods that are the focus of current research, treatment methods using proteins that are produced by means of genetic manipulation have been proposed. AIDS is an illness where the HIV virus invades helper-T-cells, a kind of lymphocyte, in the blood, then propagates and destroys the immune mechanisms of the human body. Because the surface form of the HIV changes from moment to moment, creating a vaccine is thought to be difficult. Dr. Harrison of Harvard University and others clarified the three- dimensional structure of CD4, a protein located on the helper-T-cell surface noticed to which HIV attaches; they noticed that, because HIV invades cells from there, the parts on the HIV surface that distinctively bind with CD4 do not change in shape.[8] Building upon these results, there is now ongoing research throughout the world on the so-called "missile treatment," which involves using genetic manipulation techniques to artificially produce a protein whose structure is very similar to CD4, and then combining it with a cytotoxin.Conventionally used substances in AIDS treatment have been shown to have severe side effects, e.g., the decrease in leukocytes with AZT treatment. Because there are no side effects with "missile treatments," where the virus attaches to toxins on its own and self-destructs, the expectations are great.

It is predicted that viruses whose surface shapes change frequently, as well as other viruses such as influenza, hepatitis-C, herpes, and so on, can be the effectively treated by the same kind of process.

(iii) Enzymes

The enzyme urokinase that is used to remove thromboses (blood clots), which cause apoplexy, myocardial infarction, pulmonary infarction, etc., is induced from *E. coli* by Abbot Labs.[9] And, the use of genetic manipulation to produce TPA (Tissue Plasminogen Activator), as the substance that is equivalent to urokinase, is being researched by both governmental and private groups.[10]

(iv) Other

In addition to these, there is also research on the application of genetic manipulation in the production of antibodies, interferon, etc. For typical examples, refer to Table 2.3.3-2 for the diseases and the corresponding drugs that were obtained by means of genetic engineering methods.

Table 2.3.3-2 Diseases That Are Given Drugs Produced in the Pharmaceuticals Industry by Means of Genetic Engineering

Disease, State of Health	Drugs that can be produced by genetically engineered organisms
Diabetes (a)	Insulin
Arteriosclerosis	Platelet-derivative growth factor (PDGF)
Viral Diseases	Interferon
Influenza	
Pneumonia	
Poliomyelitis	
Herpes	
Common cold	
Cancer	Interferon
Hodgkin's disease	
Leukemia	
Breast cancer	
No ovulation	Human placental gonadotropic hormone
Dwarfism (a)	Human growth hormone
Pain	Enkephalins and endorphins
External injuries and burns	Human growth hormone
Inflammation, rheumatism	Adrenocorticotropic hormone (ACTH)
Bone abnormalities like Padget's disease (a)	Calcitonin and parathyroid hormone
Nerve damage	Nerve growth factor (NGF)
Anemia, hemorrhages	Erythropoietin
Hemophilia (a)	Coagulation factors VII and IX
Blood clots (a)	Urokinase
Shock (a)	Serum albumin
Immunological abnormalities	Cytokinin

(a) indicates illnesses that are currently treated with the drugs shown in this table.

(b) Treatment of Genetic Illnesses By Means of Genetic Modification

Because the technology for making copies of specific genes has advanced, there are also attempts to return modified genes back to cells and thereby alter the functions of the cells. Of these, antisense RNA and DNA are noteworthy. Using short RNA molecules that bind to specific mRNA (messenger RNA), this is a technique that masks the RNA in such a way that the message is not transmitted; this can hinder the production of specific proteins.

France's National Institute of Health and Medical Research already succeeded in inhibiting division of the Trypanosoma parasite that causes sleeping sickness, although it was in vitro.[11]

By means of this technology, treatments can be expected for genetically caused incurable diseases such as Down's syndrome, muscular dystrophy, and Alzheimer's disease. Researchers at the Tokai University medical department succeeded in impeding the central nerves' production of structural proteins with antisense RNA, and artificially produced mice that have genetic diseases.[12]

There are also reports that the same kind of technique can be used to treat viral diseases and to improve agricultural crops: a group at Hollands' Vriji University improved the color of petunias and tobacco by means of antisense DNA.[12]

References

1. O. Ohara, TAMPAKU KAKUSAN KOSO, Vol 35, 1990, p 2319.

2. NIKKEI BIOTECH, 24 April 1989, p 2.

3. Idenshikogaku no Genjo to Tenbo I: Baitekunoroji (Current State of Genetic Engineering and Outlook I: Biotechnology), Nikkei Saiensu Co., 1982, p 15.

4. Ibid., p 43.

5. Idenshi no Hatsugen to Seigyo (Genetic Expression and Control) science supplement, Nikkei Saiensu Co., 1988, p 52.

6. S. Ishihara, SEIKAGAKU, 61, 407 (1989).

7. Idenshikogaku no Genjo to Tenbo I: Baitekunoroji (Current State of Genetic Engineering and Outlook I: Biotechnology), Nikkei Saiensu Co., 1982, p 15.

8. For example, NIHON KEIZEI SHIMBUN, 1 December 1990, p 13.

9. Idenshikogaku no Genjo to Tenbo I: Baitekunoroji (Current State of Genetic Engineering and Outlook I : Biotechnology), Nikkei Saiensu Co., 1982, p 16.

10. NIKKEI BIOTECH, 28 August 1989, p 4.

11. NIKKEI BIOTECH, 10 October 1988, p 9.

12. NIKKEI BIOTECH, 29 August 1988, p 2.

2.3.4 New Neuroscience and Technology

(1) The Engineering of Neurocircuits

In this section we will touch upon the characteristics of the human brain and then will discuss the results of recent engineering attempts to imitate the circuitry of the brain and nervous system.

(a) Characteristics of the Human Brain

A rough classification of the various functions of the human brain that can be replaced by machines gives: 1) computation, 2) inference, 3) control of organs and functions, 4) recognition, 5) creation, 6) learning, 7) self-organization, and 8) highly-parallel abilities.

In the current state of affairs, the computational functions of the brain can be completely replaced by machines; and inference, the control of organs and functions, and recognition can be partially replaced. From the viewpoint of ethics as well as the technical difficulties involved, creative functions will have to stay in the brain. How to realize the remaining functions—learning, self-organization, and highly-parallel abilities—will be major research topics from now on.

In particular, self-organization is a high-order, refined function that first becomes possible in the form of the "soft" structures of living tissue. Conventional devices based on inorganic materials, which do not lose their structure once configured unless something drastic happens (rather the structure is made that way), do not quite make it. Starting with this self-organization, reorganization of a structure in order to enable learning and highly-parallelness can be done without disturbing the system.

(b) Construction of Neurocomputing Models

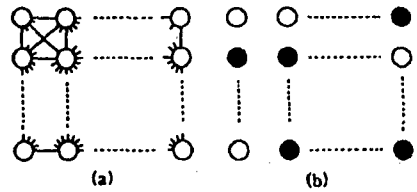
We will discuss the research concepts in both the software and hardware aspects of what is needed in order to realize the human brain in a machine.

(i) Software

To discuss the construction of neuromodels, we can go back to the neuron model by McCulloch and Pitts in 1943. In this section we will talk about the general concepts of two representative models that are the basis of present-day neuromodels.

1) The Hopfield Model

A pioneering effort in neurotechnology was the model proposed by Hopfield et al during the latter half of the 1980s. Figure 2.3.4-1 shows the general concept of this model. These men connected several hundreds of neurons to build a system with the following features.



(a) Hopfield neuronetwork model
○: show neuron cells; unbroken lines show connection between neurons. With the latter, though, to keep the diagram simple, only a few are shown.
(b) That activity potential generation pattern
●: show neurons that fired
○: show neurons that did not fire

Figure 2.3.4-1 Hopfield Model

- As the action patterns of all the neurons, content-addressable memory within the network (unlike the currently popular memory that is prescribed by physical addresses, this memory can be read by the information content) can be formed.
- Character and voice recognition is possible.
- The model can be implemented in hardware.

The Hopfield model is praised for its hardware implementation of an information processing model that is unlike anything else before it, and because, using that model, the recognition mentioned above and problems that are considered tough for computers, e.g., the "traveling salesman problem," can be processed.

The important function of learning, however, was unfortunately not incorporated into that model.

(2) The Back Propagation Model

"Back propagation learning rules" and the back propagation model proposed by Rumelhart et al in 1986 added learning functions to the Hopfield model. Figure 2.3.4-2 shows the model.[2] This model has, separate from the signals flowing from inputs to outputs, "teacher signals"; the "teacher signals" compare the input with the output and provide feedback that reinforces the transmission of the neurons that form the answer patterns. With this feedback, the rate of correct answers gradually rises.

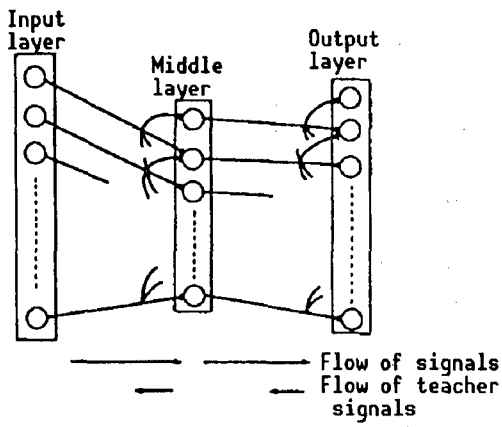


Figure 2.3.4-2 Neural Network Model That Uses Back Propagation Learning Rules

An example of an application of this model is the famous "NETalk" that was developed by Saikovski et al. With this system, when the spelling of English words is input, the corresponding pronunciation symbols are output. The input of about 10,000 words resulted in the system being able to output pronunciation symbols with a correct-answer rate of almost 100%.

(c) Hardware Implementation of Neurons

To imitate neurons in hardware, three general ways come to mind. The first is to use a conventional von Neumann computer to simulate a neural network. Next is the method of multiply-linking general-purpose microcomputers and DSPs (digital signal processors) to form a neural network. The third way is to design a special-use LSI. The first two ways "substitute" equipment with different architecture that was created for a different purpose; these ways are thought to be approaching the limits of the actual structures involved.

However, with regard to systems that are partially based on digital devices, multiprocessor-type accelerators, in which conventional processors are connected in a ring shape, are being developed at Fujitsu Labs[3] and other places. Because this is basically a neural network doing matrix calculations, it is a method that involves summing the products of input values multiplied by weights, converting them with functions, and then outputting the values. In this case, the ring-type bus is used for data exchange between processors. But such a structure is indispensable to the execution of learning algorithms in a back propagation model. Nevertheless, with this kind of method, the overall system inevitably gets too large, and consequently applications will be limited. Actually, in recent years many neural systems are implemented in a form that calls for the development of special-use LSIs. With the hardware development itself, it is thought that hardware can be adapted to neural systems by extending the existing semiconductor technology, and that neural control will have a wide range of application fields in industry. Therefore the fact that development by private firms is quite vigorous deserves special mention. Below we will talk about major neurochip development efforts.

(i) Digital Chips

Because present-day computers are digital, digital neural chips are where there is the most technical proficiency; their completion is also regarded as being the fastest.

Hitachi produced a trial version of a wafer-scale-integration neurochip4) in which it integrated 576 neurons on a five-inch wafer. The processing speed of this chip is 820 megaconnections per second. Toshiba is aiming for 2 giga-connections per second in its MULTI-NEURO that is currently under development.[5]

Overseas, a U.S. venture firm, HNC Co., is developing a 320-megaconnection-per-second chip.[5]

(ii) Analog Chips

Basically, analog methods are better suited to neurochips: the necessary number of devices per neuron is smaller, and parallel processing of all the neurons is possible. Because analog voltage values can also be input, using them together with sensors is also convenient.

However, despite these kinds of merits, analog neurochips that are close to being practical have not yet been developed. That is due to the following three technical barriers, which we will explain below: maintaining the strength of the synaptic connections in analog circuits, guaranteeing the homogeneous actions of all neurons when the chip is highly integrated, and keeping temperature-dependent characteristics from changing.

As for the first problem, the usual solution is to get the strength of the synaptic connections from the magnitude of the resistance or the charge that accumulates in capacitors. The U.S. Jet Propulsion Lab and Matsushita Electric use this method,[7] but, like DRAMS, the chip must be periodically refreshed, and this is a barrier to higher integration. On the other hand, Intel keeps the strengths of the synapses in EEPROM cells, which do not need refreshing. However, unlike normal binary data, many-valued data must be accurately controlled in order to sequentially hold the synaptic strengths that change as learning takes place. In the current state of affairs, although four-bit control is the limit, Intel's ETANN analog chip[8] is also equipped with inter-neuron feedback connection mechanisms that can be applied in both Hopfield and back-propagation models; in combination with improvements in many-valued-bit control, future development trends will be watched.

In connection with the second and third problems, together with coping on the hardware side with the homogeneous action of neurons and suppressing the deviations in temperature-dependent characteristics, coping with the problems from the software perspective is also thought to be essential, i.e, the development of learning programs that execute in the case where neurons with some deviations are connected.

(iii) Optical Chips

In comparison with electrical circuits, optical circuits are superb in terms of their parallelness. Taking the Hopfield model as an example, the number of synapses must be the square of the number of neurons. For example, to integrate 100 neurons, an electrical circuit will require 10,000 connections. In contrast, optical circuits do not need connections; as long as there is space for the light to pass through, information can be transmitted. Optical circuits are suitable for high-integration neurochips whose basic characteristic is super-parallelness.

Devices in which synaptic strength is fixed are already being produced on a trial basis. Figure 2.3.4-3 shows a 32-neuron optical chip developed by Mitsubishi Electric's central research lab.[9] The light that emerges from an array of linearly-integrated light-emitting diodes passes through a grid-structured spatial modulation matrix, and then arrives at the photodiode

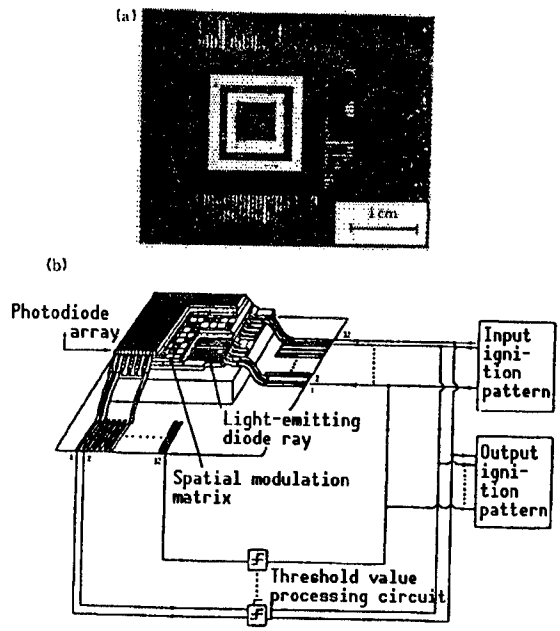


Figure 2.3.4-3 Optical Neurochip Implementation of Hopfield Model

(a) external view, (b) structure

(Photograph (a) provided by Dr. Kuma of Mitsubishi Electric's Central Research Laboratory. (b) is taken from Ota's, Takahashi's, Shinda's, Tai's, Akie's, and Kuma's preliminary draft of the National Spring Conference of the Electronic Information and Communication Society proceedings (1989), 4-437)

array. Each of the squares in the grid of the spatial modulation matrix are given a different transmittance beforehand, so the grid mimics synaptic strength by the differences in transmittance.

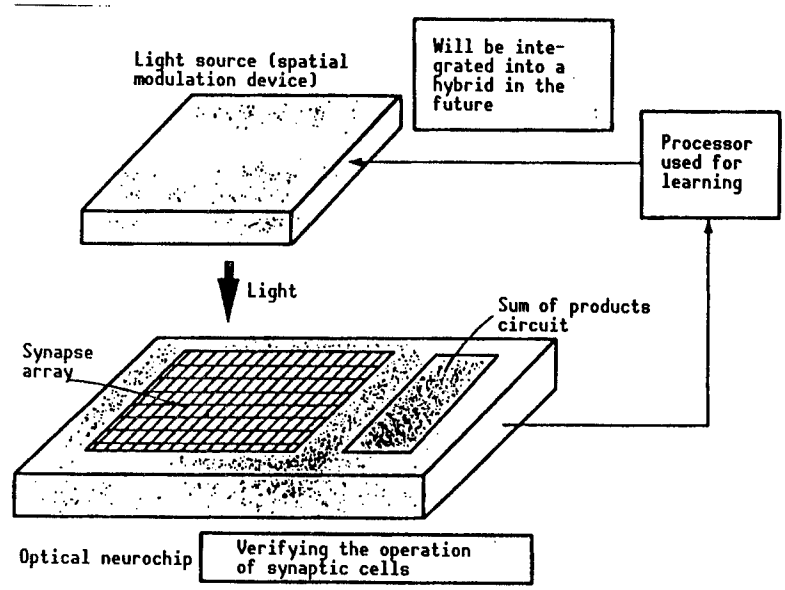


Figure 2.3.4-4 Current State of Optical Neurochips[12]

It has reached the level where synaptic arrays composed of photoconductive devices have been fabricated into chips. The number of neurons is on the order of 32. The next topic is to superpose and integrate onto the synaptic cells a spatial modulator for altering supply strength.

The light-emitting diode and photodiode arrays are also mutually orthogonal; the light from a single light-emitting diode passes through each square in the grid of the matrix and is transmitted to every photodiode. In other words, the output from one neuron is transmitted with a different intensity to every neuron on the receiving side. It was confirmed that this chip can distinguish three kinds of alphabetical letters (O, P, T) that contained mistakes.

On the other hand, AT&T's Bell Labs developed a type of chip that is programmed by applying light from the outside (Figure 2.3.4-4). Unlike Mitsubishi Electric's chip, synaptic strengths can be sequentially modified, so the chip can also be adapted to back propagation models.

From now on the topic will be how to hybridize the spatial modulation devices that are external to the chip. National and private research pertaining to the development of this kind of three-dimensionally structured device is slow in comparison with one time; it is still thought that quite some time is needed to perfect neurodevices to the point where learning functions are on a chip.

(iv) Outlook for the Future

As seen above, the current state of affairs is one where attempts are being made to reproduce the human neural-net structure in a form such as a chip. But, as long as humans input from the outside the synaptic strength and the competing values that determine that strength, the systems will do nothing more than provide parallel processing according to the commands that they are given.

If neurotechnology is to truly imitate the human brain, which learns and evolves, then the series of the brain's processes from recognition to its self-organization of intelligence must be mechanized up to a certain level. Therefore, the promotion of research on the actual recognition process of the brain and the process of its self-generation of intelligent networks is essential.

(2) The Elucidation of Aging Mechanisms

An important topic when discussing neuroscience is research on the human brain. The human brain, as mentioned in the previous section, is such a complicated and precise system that its total content cannot be understood with the current level of technology, but there are also biological weak points. Given the brain's fragility as a system that originates in soft structures made from organic substances, and the weak points manifest themselves in the phenomenon called aging. In contrast with the lack of strong reverse flexibility in inorganic-based rigid structures, biological organs are more unstable and are better suited for autonomous changes. Regular body cells multiply and maintain redundancy in their systems. Brain cells, however, do not reproduce and are very likely to show damage over time as the body ages.

In recent years, a number of noteworthy reports have been written about the causes of aging. Below we will describe research relating to the brain and nerves.

In order to consider the correlation between life activity and the nervous system, the correlation between the degree to which neurons decreased in mice and their death rates was investigated. Both were in a parallel relationship.[11] Likewise, in humans too, it is common knowledge that brain-damaged patients generally have short lifespans. However, even if it is a sweeping statement about the neurons of the brain, the degree to which they decrease is

considerably different depending on where they are located. That is, in the cerebral and cerebella cortex there are areas where the number of neurons decrease to half by the age of 90, whereas neurons in the brain stem do not decrease very much at all. Indeed this is expressed in the summary of functions shown in Table 2.3.4-1,[11] but very little decrease is seen in the functions that contribute to central functions and whose decline is as fast as peripheral functions.

Table 2.3.4-1 Decline in Psychoneurotic Functions Due To Aging

The higher-order functions of the brain are not likely to deteriorate, even with advancing age. According to investigations into the mental and neural functions that change between the ages of 25 and 75, there are considerable differences in the degrees to which each function weakens. At the head of the list is the test that involved standing on one foot with eyes closed; the weakening of hand and foot functions was great. On the other hand, functions related to the high-order centers of the brain hardly declined at all. Although neural functions weaken with age as much as peripheral functions, surprisingly the central functions do not decline. (By Katzman and Terry)

Little change	Vocabulary, information, understanding, memorization of numbers
	Sense of touch in the fingers and toes
	Distinguishing two spots on a finger
Less than 20% decline	Tying a string, closing a safety pin
	Reaction time, clapping, manual dexterity
	Tapping, skipping
20~40% decline	Using one's hands and rising from a chair
	Putting on a shirt
	Handwriting speed
	Reading and understanding numerical shapes
	Bending over and touching feet
	Standing on one leg with eyes open
40~60% decline	Sensing vibration in upper limbs
	Bending legs
More than 60% decline	Sensing vibration in lower limbs
	Standing on one leg with eyes closed

Nevertheless, in the brain stem, too, there is a high rate of decrease depending on the location, as shown in Figure 2.3.4-5.[11] The decline of the substantia nigra in the midbrain, where there are many neurons that take part in muscle relaxation, is thought to be deeply related to Parkinson's disease, a typical geriatric illness (accompanied by shaking, muscle contraction, and difficulty in walking). The decline of the blue group nucleus of the pons is also thought to be deeply related to the occurrence of insomnia and dizziness. These have much greater effects than the "forgetfulness" that is caused by the decline of the cortex.

- Geriatric disabilities arise when the brain's neurons decrease.

  The decline in the brain's neurons is greatest in the *substantia nigra* and the blue group nucleus of the midbrain. Neurons related to muscle tension are concentrated in the substantia nigra. With Parkinson's disease, which occurs in many older people, the muscles often become hard, the hands shake, and the patient slows down; it is thought to be deeply related to the decrease in the neurons of the *substantia nigra*. The blue group nucleus regulates blood flow in the brain and sleep. So when the neurons of the blue group nucleus decline, dizziness and sleeping problems occur. Thus, neurons in specific areas of the brain lead to geriatric disabilities.

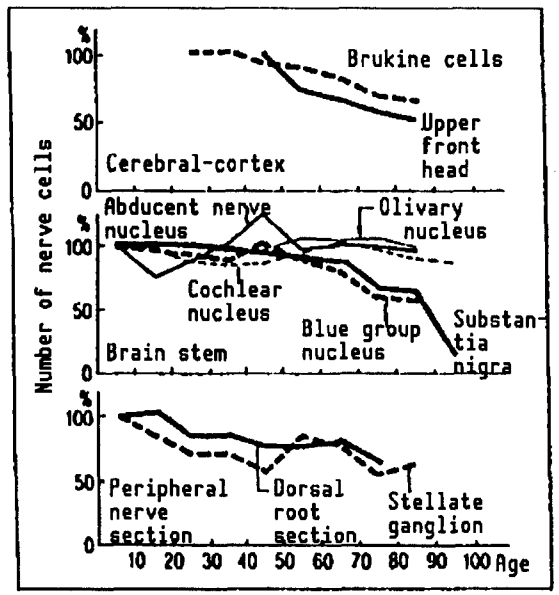


Figure 2.3.4–5 Changes in Numbers of Neural Cells Due to Aging

(a) Attempts To Inhibit the Decline of Brain Cells

Fascinating research is being conducted on the correlation between oxygen and aging, as a clue to inhibiting the decline of the brain's cells. The oxygen that is taken into human lungs is eliminated in a form that is 90% water, and the remaining 10% contributes to direct oxygen reduction reactions. When this takes place, free oxygen radicals that become cytotoxins form. These oxygen radicals, which oxygenate the lipids that are the main substances in cell membranes, cause cellular functions to decrease and cells to die. Normally, however, oxygen SOD (Super Oxide Desmutase) acts to capture the free oxygen radicals and render them powerless, so we can carry on our life activities without any problems.

Figure 2.3.4–6[12] shows the relationship between SOD activation and the lifespans of various animals. We see that the higher the SOD activation, the longer the lifespan of the animal. From this table by Cuttler it is also apparent that lifespan is proportional to body size (because animals with larger bodies can get by with less surface area with respect to cubic volume, their heat efficiency is better). There is also a sense of danger in discussing the effects that simply taking out SOD activation would have on lifespan. On the other hand, however, it is also known that alpha-tocopherol (vitamin E), which exhibits an anti-oxidation effect, extends the lifetime of nematodes; there seems to be no doubt that oxygen and lifespan have a close relationship.

- The higher the ability to process harmful oxygen, the longer the lifespan

  Harmful activated oxygen is produced as a result of oxygen metabolism in the bodies of animals. It was understood from investigations that animals in which there is high activation of the SOD enzyme, which captures this activated oxygen and renders it harmless, have longer lifespans. The diagram is the result of investigating the relationship between lifespan and the activation of the SOD enzyme in the livers of animals. Both are in proportion, and humans top the other animals. The relationship is the same for the brain and myocardium. This indicates the strong relationship between oxygen and lifespan. The SOD activation of the vertical axis is taken as an equivalent ratio with respect to the basic metabolic rate. (By Cuttler)

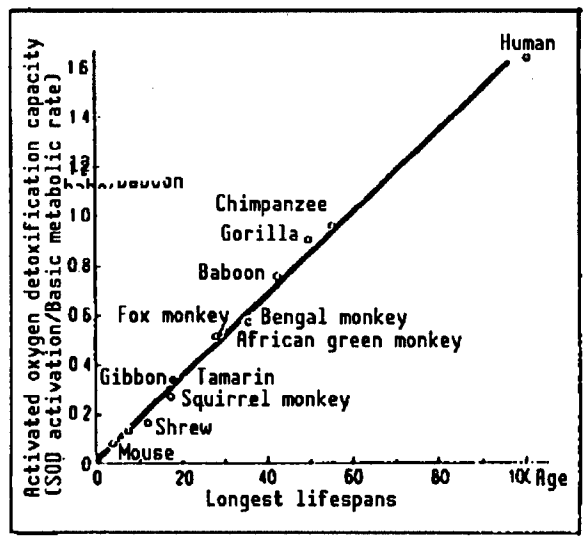


Figure 2.3.4-6 Relationship Between the Capacity To Render Activated Oxygen Harmless and Lifespan

(b) Tackling the Challenges Relating to Brain Cell Redundancy

Like myocardial cells, brain cells come under the division termination cell group (cells that do not regenerate once they die). However, there are individual differences in the memory and intelligence retention levels among elderly people of the same age. As the reason for this it is thought that there are individual differences in the speed at which brain cells die and decrease in number, owing to factors such as the differences in SOD activation that was mentioned above. Recently, though, another explanation was proposed: the degree of aging seems to be determined by the quality of redundancy in the brain as a bodily organ.[11] That is, perhaps brain cells, which gradually die and decrease in number, retain the arrangement of their neural circuitry by growing more axons, in much the same way that a bypass line is used to connect an electrical wire that had been cut. Actually, it was already proved that axons regenerate in even aged brain cells. When the brains of elderly people who were extremely active up to an old age were investigated, reports came out that back up the explanation given above. In one of those reports[11] the remarkable growth of axons was recognized in the hippocampus area, which is thought to play a part in memory and learning.

Currently there is a great deal of research on pharmaceutical development that centers on the treatment of Alzheimer's disease (a disease where the neurons of the brain die).[13]

Thus, in connection with aging there is ongoing research in both 1) maintaining neural network redundancy, which centers on the development of drugs for making the axons of aged cells grow more, and 2) attempts to inhibit the decline of brain neurons.

References

1. S. Shiono, Nyuro Konpyuta e no Chosen (The Challenge of Neurocomputers), Agune Shofusha, 1990, p 5.

2. Ibid., p 20.

3. H. Kato, H. Yoshizawa, H. Ichiki and K. Asakawa, Proceedings of the International Conference on Neural Networks, 1990 (IJCNN 90), p 47 (1990).

4. NIKKEI ELECTRONICS, 2 October 1989, p 86.

5. Ibid., 5 March 1990, p 170.

6. S. Eberhardt, T. Doung and A. Thakoor, Proceedings of the International Conference on Neural Networks, 1989 (IJCNN 89), II- p 183 (1989).

7. T. Morishita, Y. Tamura and T. Otsuki, 1990 IEEE Inter- national Solid-State Circuit Conference, paper no TPM 9.2, 1990.

8. M. Holler, S. Tam, H. Castro and R. Benson, Proceedings of the International Conference on Neural Networks, 1989 (IJCNN 89), II- p 191 (1989).

9. J. Ohta, M. Takahashi, Y. Nitta, S. Tai, K. Mitsunaga and K. Kyuma, OPTICAL LETTERS, Vol 14, 1989, p 844.

10. C.F. Neugebauer, A. Agranat and A. Yaliv, Proceedings of the International Conference on Neural Networks, 1990 (IJCNN 90), II- p 64 (1990).

11. M. Asanaga, KAGAKU ASAHI, September 1989, p 20.

12. I. Suzuki, Ibid., p 24.

13. E.g., NIKKEI BIOTECH, 28 March 1988, p 12.

2.3.5 Biomolecular S&T

Elucidation of life phenomena from the molecular level is essential to the utilization, either directly or indirectly, of the elaborate and advanced functions of living organisms. On the other hand, there is also ongoing research that attempts to close in on life phenomena by getting a hold of cell groups and elucidating the inter-cellular networks and the mechanisms that govern the cell groups.

In order to actually utilize the functions of living organisms, researchers already use, or plan to use, many technologies such as genetic recombination, cell fusion, mass cell culture, biofunctional imitation, and so on, in fields such as medicine, engineering, energy, and agriculture, forestry, and fisheries.

In this section we will discuss the most recent research trends in "biomolecular S&T," which we define as the S&T that relates to the elucidation of these life phenomena from the molecular level and the utilization of biofunctions.

(1) Elucidation of Life Phenomena

(a) The Approach From the Viewpoint of Molecular Biology

Molecular biology starts out from the point where light is shed onto how genetic phenomena depend on the workings of nucleic acids. In connection with procaryotic cells, a considerable part of that life phenomena is said to have been clarified. The developments in technology that uses procaryotic genes (genetic engineering) are astounding and are being applied in a variety of fields. Here we will present examples of the latest efforts in understanding life phenomena from the molecular level, including research in which genetic engineering is utilized.

(i) The Cell Cycle

Cell propagation is a cyclic process. Figure 2.3.5-1 depicts the general concepts of the cell cycle. The cell propagation period consists of the DNA synthesis stage (S stage), the cell multiplication stage (M stage), and two intermediate stages (the G_1 stage and the G_2 stage); then there is a separate state where no cell propagation takes place (the G_0 stage). In the cell cycle, there is a deep connection between development and differentiation. In a mono-cellular organism, control of self-propagation is the control of the cell cycle; in a multicellular organism, the cell cycle is controlled in a complicated manner by means of the connections between cells. Thus, elucidation of the mechanisms that control the cell cycle can be said to form the basis of the research on

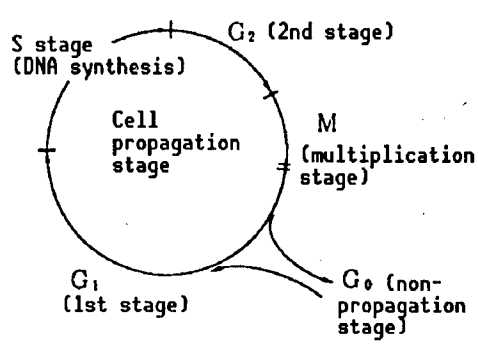


Figure 2.3.5-1 Abbreviated Diagram of the Cell Cycle

cancer, regeneration of tissue after injuries, aging, and so on. Below we will discuss the trends in research on control of the cell cycle.

Until the 1950s, research centered on morphological observations in connection with cell multiplication, and, consequently, only the M phase was regarded as important. After the 1950s, i.e., since DNA replication started to gain attention, the S stage (DNA replication stage) and the G0 stage, which is not part of the cell propagation stages, were discovered.

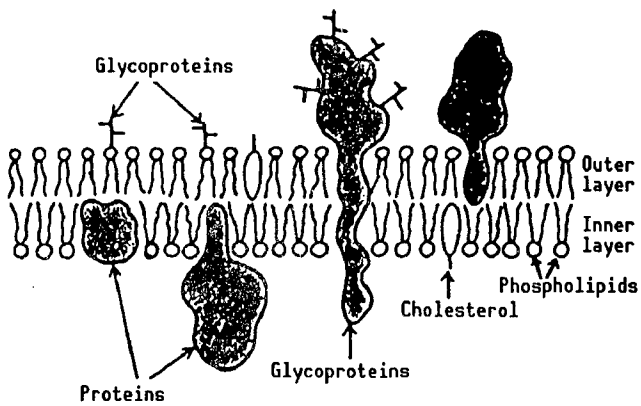
The discovery of cell propagation factors is essential to advances in research on cell cycle control. By means of a genetic approach, numerous genes that have unique functions during each period of the cell cycle have been detected. Furthermore, these genes are being cloned, one after another, as a result of recombinant DNA experiments, and their structures and mechanisms are being clarified. From the approach that emphasizes the functional aspect, it is reported that various protein kinase (the kind of enzymes that phosphorylate proteins), such as cyclic AMP and cyclic GMP, participate in regulating the cell cycle.

As future research topics, there is the need to know about the hierarchy among genes that relates to control of the cell cycle; and in research on the G_1 (the first interval) stage, G_2 (the second interval) stage, and M stage, in-vitro reconfiguration systems must be developed.

(ii) Sugar Chain Engineering

The functions of sugars in living organisms are broadly divided into 1) the recognition of substances and information, 2) the source of energy, and 3) support of living organisms

The sugar chains that exist in the forms of glycoproteins and glycolipids in the cell membranes of living organisms (Figure 2.3.5-2[2]) are thought to play an important part in recognition functions. Although these sugar chains are seen as one of the substances that governs super-cell groups, which we will discuss later, there is still much that is unclear, e.g., only a few of the parts of the DNA that produces these sugar chains have been determined, and there are many expectations for future research.



After the changes that biomembrane models went through, e.g., Daniel Dobson's model (1935), Robertson's unit model (1960), Benson's model (1966), etc., Singer announced the fluid mosaic model (1972).

Figure 2.3.5-2 Structure of Cell Membrane

The sugar chains that are used as a source of energy are the simple sugar glucose and polysaccharides such as starches and glycogen. After being broken down into pyruvic acid by various enzymes in the body of a living organism,

these sugars react with oxygen in the mitochondria and are broken down into carbon dioxide. In this process ATP is produced and becomes a source of energy for the body's activities. In muscles, for example, when ATP is broken down and kinetic energy is obtained, the conversion efficiency is about 50%, which is high in comparison with engines (whose conversion efficiencies range from 10 to 20%). As research that utilizes this high efficiency, basic research on biomolecular systems (bionic systems) is promoted. This research started with biomotors (Figure 2.3.5-3[3]) that used proteins that make up muscle tissue (actin and myosin).

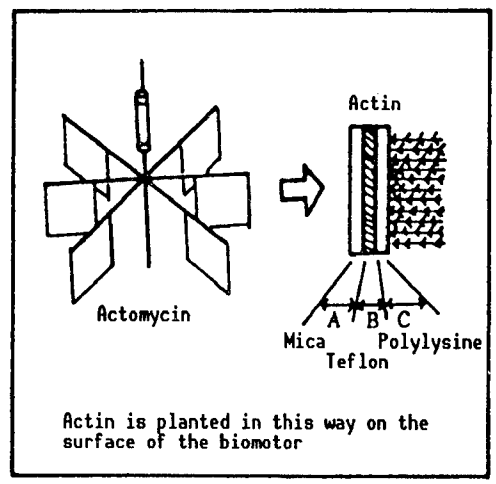


Figure 2.3.5-3 Biomotor (From Mietekita 21 Seiki (21st Century Seen) by W. Jogi, Tokyo, p 152)

The sugar chains that provide support in living organisms are collagen (the largest part of animals), cellulose (plants), and chitin (crustaceans, insects, etc.). Of these, chitin and the chitin inducer, chitosan, are especially getting a great deal of attention lately. The range of applications that are expected is very broad: flocculants, ion exchangers, oxygen-fixing agents, cosmetics, medicines, medical materials, food products, soil- improving agents, etc. However, there are only a few fields where there have been actual applications of these substances. That is, when using chitin and chitosan as materials, technology for processing the materials as fiber or film compacts is essential, but in the case of chitin, dealing with its greatest characteristic, i.e., that it does not dissolve or melt, is difficult. On the other hand, chitosan can be readily processed because it dissolves easily in hydrogen-oxygen solutions. But because of that it is weak in water, and its limited range of applications becomes a problem. Therefore in research from now on, the development of chitin compacts, which is now considered to be extremely difficult, is thought to hold the key.[4]

(iii) Biomagnetism

Topics pertaining to biomagnetism can be classified under one of three categories: 1) the effects of magnetic fields on the body, 2) magnetic fields that are emitted from the body, and 3) body images using magnetic fields (NMR imaging).

1) Effects of Magnetic Fields on the Body

When the magnetic field changes periodically, the effects on the body are thought to be the same as those due to electric fields because eddy currents are produced in the body, which is an electric conductor. For example, when the head is exposed to an alternating-current magnetic field, there is a phenomenon called magnetic flashing that is visually recognized. One possible interpretation of this phenomenon is that the eddy currents generated in the head because it is exposed to an A.C. magnetic field stimulate the retina.

Table 2.3.5-1 shows examples of the body's reactions against a varying magnetic field such as an A.C. magnetic field. Heart pacemakers that stimulate the heart and nerves with a magnetic field, bladder pacemakers, methods for treating high blood pressure, and so on have been proposed as attempts to actively apply in medical treatment the eddy currents arising from varying magnetic fields.

Table 2.3.5-1 Reactions of the Body to Varying Magnetic Fields

Biophenomenon	Flux density	Frequency or pulse width	Area stimulated	Cross section flux penetrates	
Magnetic flashing (retinal stimulation)	AC magnetic field 10 mT	20 Hz	Part of head or front of head	$1.0 \times 10^{-3} m^2$	Note 1
Fluctuations in blood flow (dermal receptor stimulation)	AC magnetic field 32 mT	3.8 kHz	Palm of hand	$6.0 \times 10^{-3} m^2$	Note 1
Neural stimulation	Pulsed magnetic field 0.25 T 0.5~1.5 T	0.1 ms 1.0 ms	Sciatic nerve in Ringer's solution	$8.0 \times 10^{-4} m^2$	Note 2
Myocardial contractions	Pulsed magnetic field 0.1 T 1.0 T	0.1 ms 1.0 ms	Chest and torso	$1.2 \times 10^{-1} m^2$	Note 1

Note 1: Value from experiments on humans
Note 2: Value from experiments on frogs

On the other hand, the influence that static magnetic fields have on the body has yet to be clarified. That the substances involved in the important life processes (oxidation mechanisms within the body) are paramagnetic materials, despite the fact that much of the body is diamagnetic material, is getting attention as a clue in the elucidation of the effects of static magnetic fields. Oxygen and hemoglobin are examples of oxidation-mechanism-related substances within the body that are paramagnetic materials; and in the electron transmission systems in the oxidation processes within the body, there is a period of time that goes along with electron transfer when cytochromes can become paramagnetic material. Figure 2.3.5-4[6] shows the possibilities of clinical applications of magnetic phenomena, including both varying and static magnetic fields; research oriented towards practical applications is being carried out.

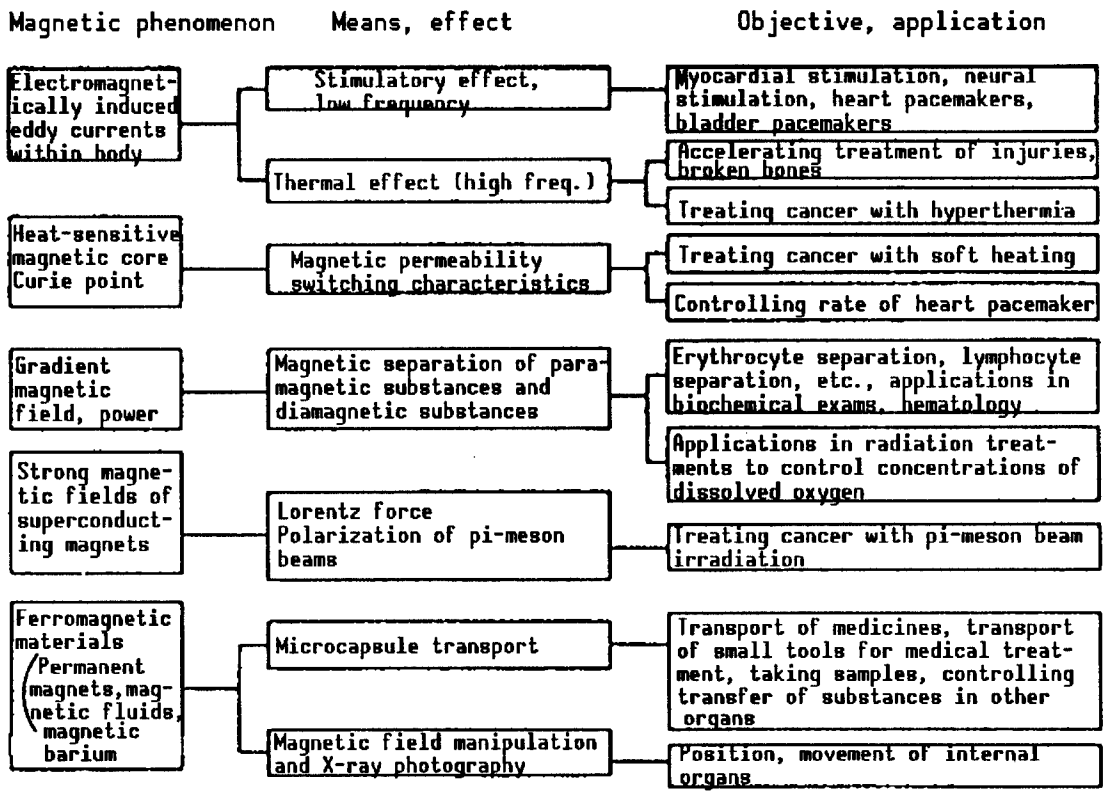


Figure 2.3.5-4 Magnetic Phenomena and Possibilities for Clinical Applications

2) Magnetic Fields Coming From the Body

Measuring the very weak magnetic fields that arise from the body became popular in 1969 when the SQUID (Superconducting Quantum Interference Device) flux meter was developed (Figure 2.3.5-5[7]). For example, the magnetic fields coming from the human body, as shown in Figure 2.3.5-6[8], are very weak; a method that uses a magnetic shielding room and a method called the negation method are used.

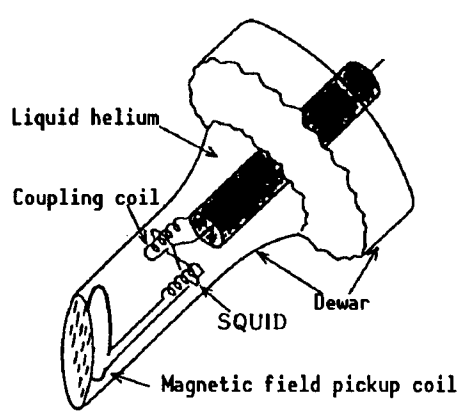


Figure 2.3.5-5 Detector Section of a SQUID Flux Meter

There are two kinds of magnetic fields that arise from the body. One kind of magnetic field generates outside of the body as a result of the electrical currents that in turn result from the action potentials that occurring in parts of the body. The other kind is a magnetic field that arises from the magnetization of magnetic substances deposited in the lungs and stomach. Examples of clinical applications of the first type of magnetic field are the magnetocardiogram, with which to obtain electrical information about the heart that cannot be found with an electrocardiogram; and measurements of the brain's magnetic field with which to infer the areas of magnetic brain wave

occurrence in epilepsy patients. The second type of magnetic field is used in measurements of the lungs' magnetic fields; this can lead to the early detection of pneumoconiosis. In addition to these, applications are considered in magnetic images of the eye, measurements of illnesses where iron accumulates abnormally in the liver, and so on. But, in order for there to be further advances and dissemination, the development of high-performance, low-price, and easy-to-use measurement systems is desired.

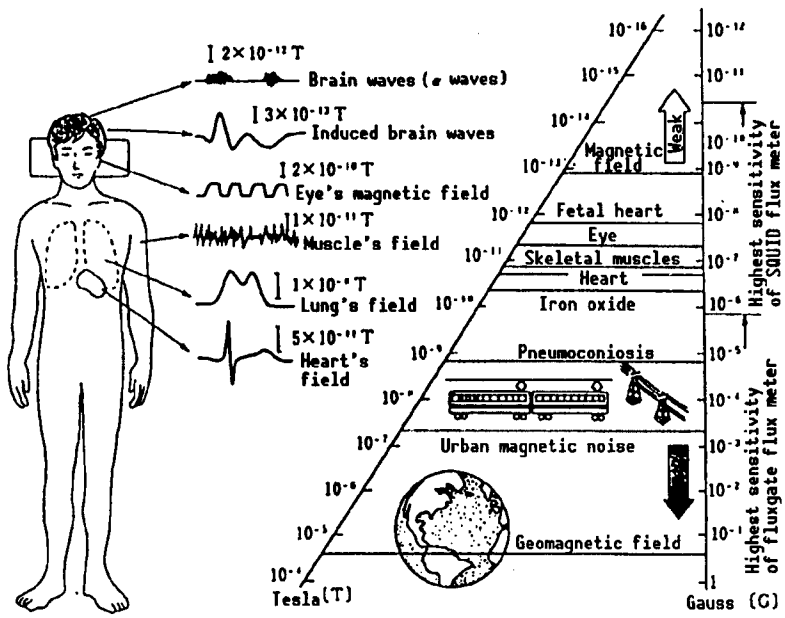


Figure 2.3.5-6 Magnetic Fields Arising From Parts of the Human Body and Sizes of Waveforms

3) Body Images Using Magnetic Fields (NMR Imaging)

NMR (nuclear magnetic resonance) imaging is a way to make visual images of the information within the body that is invisible. Also called NMR-CT and MRI (magnetic resonance imaging), it utilizes the phenomenon of resonance in the magnetism of the atomic nuclei in the molecules and ions that make up the body. The strongpoint of NMR imaging, when compared with X-ray-CT and ultrasonic imaging, is that it can depict physical information as well as information about biochemical processes. In the past, it was used mainly for measuring protons in the human body for the purpose of obtaining images with morphological information. Lately, though, it has come to used in the spectroscopy of various nuclear species, as shown in Table 2.3.5-2, for the purpose of obtaining metabolic and other such biochemical information.

New types of NMR imaging are being developed, e.g., chemical shift[10] and blood flow imaging,[11] and NMR microscopes and TMR (topical magnetic resonance).[12] The broad application of these in research on the physical properties of heterogeneous systems is expected.

(b) Elucidation of Substances, Tissue That Govern (Super) Cell Groups

The term "cell sociology" emerges as an approach to understanding the body as groups of cells; clarifying what it is that governs these super-cell-groups; and, in turn, elucidating the mechanisms of cancer, memory, and the origins of life. The following systems are thought to be clues in that elucidation:
1) the internal substance system (hormones, body fluids); 2) the immune system (takes part in the elimination of abnormal cells); and 3) the nervous system (participates in recognition).

Table 2.3.5-2 Major Nuclei Observed With NMR

Nucleus	Resonant frequency at 1 T (MHz)	Natural occurrence (%)	Detection of sensitivity relative to ^1H		Spin I (*)
			Constant magnetic field	Constant frequency	
^1H	42.577	99.9844	1.0	1.0	1/2
^2D	6.536	1.56×10^{-2}	9.64×10^{-3}	0.409	1
^{13}C	10.705	1.108	1.59×10^{-2}	0.251	1/2
^{14}N	3.076	99.635	1.01×10^{-3}	0.193	1
^{15}N	4.315	0.365	1.04×10^{-3}	0.101	1/2
^{17}O	5.772	3.7×10^{-2}	2.91×10^{-2}	1.58	5/2
^{19}F	40.055	100	0.834	0.941	1/2
^{23}Na	11.262	100	9.27×10^{-2}	1.32	3/2
^{25}Mg	2.606	10.05	2.68×10^{-3}	0.714	5/2
^{27}Al	11.094	100	0.207	3.04	5/2
^{29}Si	8.460	4.70	7.85×10^{-2}	0.199	1/2
^{31}P	17.235	100	6.64×10^{-2}	0.405	1/2
^{35}Cl	4.172	75.4	4.71×10^{-3}	0.490	3/2
^{39}K	1.987	93.08	5.08×10^{-4}	0.233	3/2
^{43}Ca	2.865	0.13	6.39×10^{-3}	1.41	7/2
^{55}Mn	10.553	100	0.178	2.89	5/2
^{63}Cu	11.285	69.09	9.38×10^{-2}	1.33	3/2

With respect to the internal substance system, elucidating the mechanisms of receptors when hormones and other such substances act on genes will be the key; sugar chains, as described in 2.3.5 (1)(a)(ii), are getting attention as the substances that play a part in the functions of these receptors. Because sugar chains exist on the cell surface and differ according to the type of cell, the possibility that they are the central dogma in cell sociology is also considered.

(2) Applications of Structures, Functions

(a) Biodevices

Figure 2.3.5-2 shows the "fluid mosaic model" of a biomembrane that was proposed by Singer and Nikolson. Quite important functions of a biosystem, e.g., the active transport of nutrients and ions, the recognition of biologically activated substances, secretions, etc., are found to be located in biomembranes. Although these functions are thought to depend on the complex interactions of the proteins, lipids, and sugars that make up biomembranes, much is still unclear. Furthermore, research that actively uses the functions of biomembranes is just beginning in Japan. In current research, attention is especially focused on biosensors in which molecular recognition functions are applied.[2]

On the other hand, there is also research being carried out on biosensors that use man-made thin films, rather than materials of living organisms. In a normal environment, these films are very durable and safe, and they are easy to handle. Table 2.3.5-3[13] shows candidate biosensor materials. LB (Langmuir Blodgett) films are getting attention as a technology for making artificial

Table 2.3.5-3 Materials That May Be Usable in Biosensors

Type of material	Uses	Examples of corresponding materials
Proteins	Electron transport, switching	Cytochrome C, C_3
	Molecular identification	Enzymes, antibodies
	Movement and energy supply	Movement proteins, ATP supply system
	Matrix components	Collagen, tubulin
Pigments	Photo-energy supply	Photoelectric-conversion pigments and photochromic pigments
	Optical information output	Fluorescent dyes
Lipids	Matrix components	Phospholipids, fatty acids
Electron transfer substances	Electron energy transfer	Quinone, viologen
Macromolecular materials	Selective permeability	Permeable membranes
	Information conversion, transfer	Piezoelectric membranes, red-ox macromolecular membranes, conductive macromolecular membranes
	Matrix components	Carrier macromolecular membranes

(From the FY 1984 Survey of Next-Generation Industrial Base Research)

thin films from these materials (Figure 2.3.5-7[14]). The biodevices using man-made thin films that are being put into practical use fastest are not surprisingly, biosensors (Figure 2.3.5-8[15]). In the past it was hard to get direct electrical signals from proteins, so biosensors measured the amounts of oxygen and methane consumed by converting them to electrical signals, but new oxygen sensors are emerging. Proposed by Aizawa,[16] these biosensors have molecular interfaces so that the electron transfer between proteins and the electrical conductors is smooth. Research is also being carried out on immune sensors

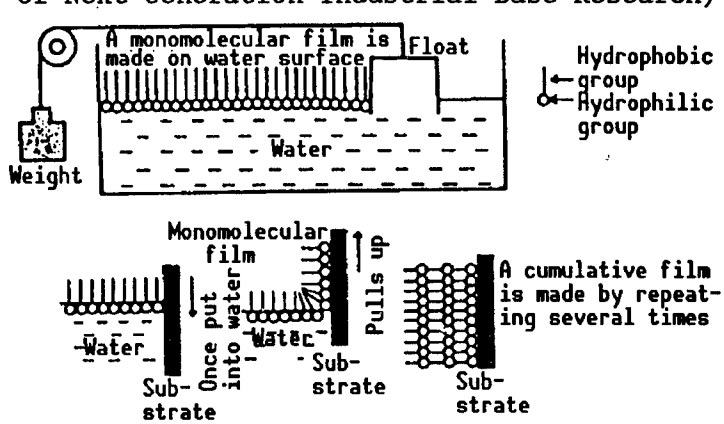
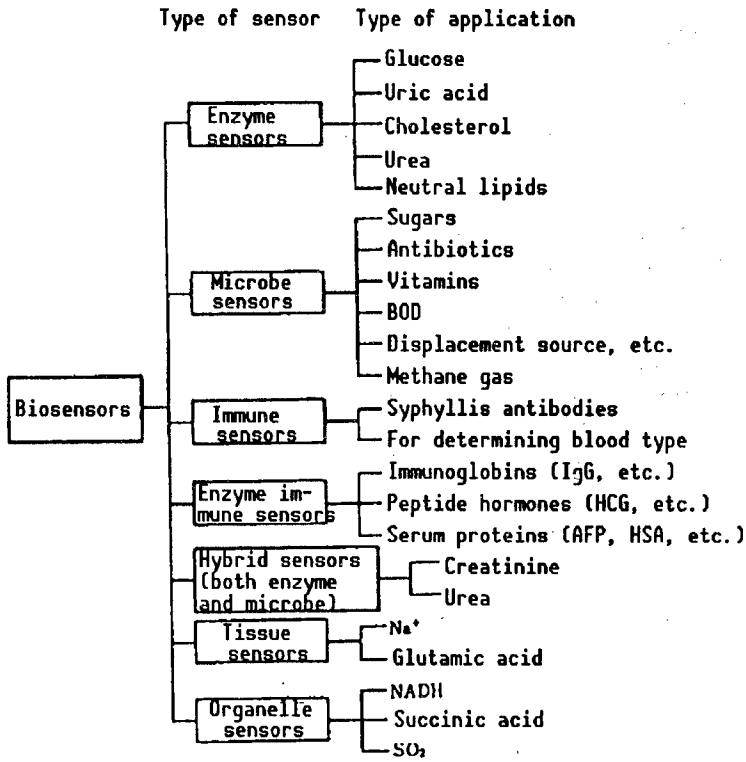


Figure 2.3.5-7 Ways To Produce Monomolecular Films and Cumulative Films by Creating LB Films

that use functions for molecular recognition of antibodies, and super-high-sensitivity immune sensors based on the chemical amplification of enzymes.



(From Molecular Electronic Devices, a basic survey from FY 1984 on new devices, compiled by the New Functional Devices R&D Association.)

Figure 2.3.5-8 Types of Biosensors and Application Areas

(b) Bioreactors

By using them as catalysts, bioreactors are systems that apply the biochemical reactions ruled by enzymes in tasks such as producing useful substances, breaking down environmental pollutants, analyses, medical treatment, and so forth. There is on-going research on the use of catalysts other than enzymes, e.g., organelles, microbial fungi, animal and plant cells, etc. In order to continuously obtain the desired chemical compound, biocatalysts such as enzymes must be fixed inside the reactor. As a result of this fixation, though, the instability of the biocatalyst can improve. Furthermore, to construct an excellent bioreactor, in addition to preparing an excellent fixation biocatalyst, the following conditions are necessary: 1) searching for excellent biocatalysts, cultivation by means of mutations or gene recombination, and then mass production of the biocatalysts; 2) establishment of systems for regenerating bio-energy substances, like ATP, and oxidation-reduction coenzymes; 3) simulation of the enzyme systems needed for controlling the reactions and making them more efficient; 4) development of functional molecules and selective molecular membranes; 5) the design of bioreactors that are suited to the reaction system, etc. In particular, setting up systems for

economically regenerating ATP and coenzymes is seen as necessary in order for bioreactors to take further root as a general-purpose technology.

(3) Measurement Technology

Measurement technology, for probing into how the complex and high-order functions of living organisms are manifest, is indispensable in biomolecular S&T.

The characteristics of living organisms are that, by always carrying out metabolism, they maintain many different systems of their own in parallel, and they manifest complex functions. Because they are structures that are based on protein macromolecules, three-dimensional profiles have an extremely important meaning. Therefore, measuring the functions of living organisms must certainly be non-destructive; in-situ and in-vivo methods are desirable. Here we will present, as a line-up of such measurement methods, techniques that are applications of various kinds of microscopes.

(a) Techniques That Are Applications of Optical Microscopes

Optical microscopes are the simplest and most general microtechnique. In recent years, microtechniques in which proteins are stained with fluorescent dyes so that individual molecules can be observed continue to be put into practical use (fluorescent microtechniques).

Kinoshita, et al.,[19] used fluorescent dyes that are sensitive to voltage potentials to observe changes in the potentials inside and outside of cells immediately after holes had been punched in the cells by means of electric perforation. It was confirmed that flash pictures with exposure times of a microsecond or less could be taken by using a pulse-laser fluorescent microscope with this method. It is expected that with this method researchers can observe how cells and supermolecules react to changes in their external environments.

(b) Techniques That Are Applications of Electron Microscopes

Electron microscopes are thought to be unsuitable for observing living organisms because, theoretically, the sample must be placed in a vacuum and because the living organism can be damaged by the electron beam. However, in addition to over 40 years of advances in microtome methods, new sample-processing technology has progressed in recent years, e.g., the cold replica method, the cold replacement method, the critical-point drying method, etc. With these advances, electron microscopes can now be used to observe ultrafine structures on the order of 20 Å.[20]

(c) Techniques That Are Applications of Raman Spectroscopy

Figure 2.3.5-9[21] shows the princi-ples of a Raman spectroscopy apparatus. With this measurement technique, incident photons from a laser interact with the lattice-vibrators of the molecules in the sample, then the photons that underwent state changes are emitted from the apparatus. Information about

molecular structure and so forth is obtained from the spectrum of this outgoing light's energy. Because the sample to be measured can be an aqueous solution, a gel, or a solid, the method is oriented towards the measurement of various kinds of biomaterials. Because the process of Raman scattering is extremely fast, i.e., a picosecond or less, there is also the advantage of being able to trace the changes in molecular structures during a chemical reaction.

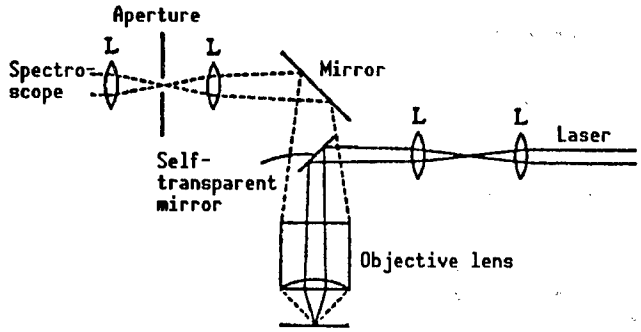
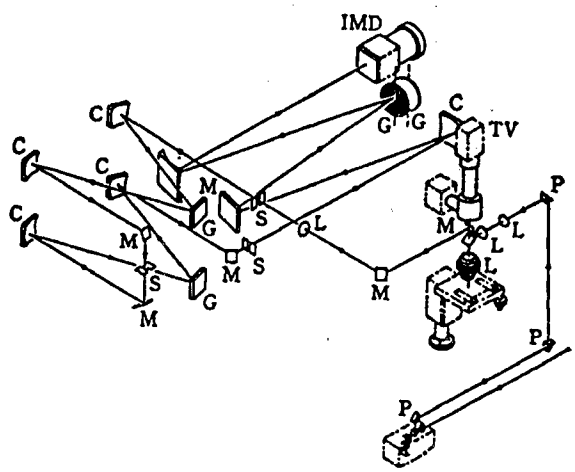


Figure 2.3.5-9 Principles of Raman Spectrum Microscope

Although there is the fear that irradiation with laser light will damage the sample, Nishimura, et al.,[21] developed an apparatus with which sufficient sensitivity is obtained even with low-output lasers (Figure 2.3.5-10).



P: prism; L: lens; M: mirror; TV: television monitor camera; S: slit; G: grating; C: concave mirror; IMD: individual-photon-counting multi-channel detector
(Y. Nishimura, T. Ikeda, and H. Kume, Proceedings of the 11th International Conference on Raman Spectroscopy, John Wiley & Sons, 1988.)

Figure 2.3.5-10 Full Diagram of a Raman Spectrum Microscope

(d) Scanning Tunneling Microscope (STM) Applications

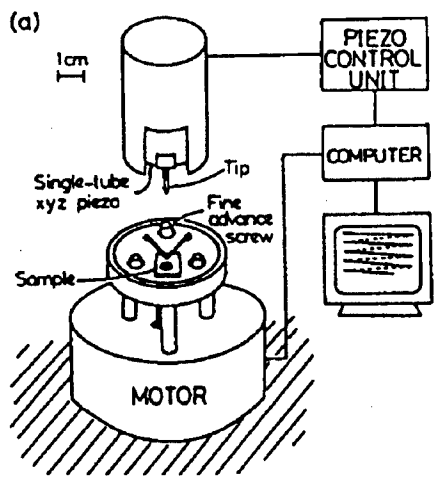


Figure 2.3.5-11[12] summarizes the STM. A system in which an insulator is sandwiched between two electrodes, the STM utilizes the fact that electrons tunnel through a potential barrier and flow between the electrodes.

←Figure 2.3.5-11 General Diagram of STM
(a) Overall structure, depicits only one direction in the x direction
(b) Expanded view between the probe and sample

In essence, this measurement technique is for atomic-order observation of the contour of the sample's upper surface. However, it was shown that the STM could be used to observe samples in solutions such as water or oil,[23] and there

is growing expectation that the STM can be used to observe biological samples that are alive. Recent results[24,25] include observations of the structure of the DNA helix; it was confirmed that, depending on the types of molecules, observations of samples that are in a live state, even very microscopic structures, is possible. For example, the transfer of proteins and the deformations that take place in cell membranes are two-dimensional movements; observing these kinds of life activity is thought to be a lively field for the STM. In connection with three-dimensionally-structured samples like biopolymers, however, the tunneling current flows from places other than those that were targeted, and it is hard to get an accurate image. Because the STM, which was announced by Binning, et al.,[26] in 1982, is a relatively new measurement method, there are other problems too, as shown below, whose solutions may be issues in the future.

- Stability of the apparatus itself
- Fluctuations in resolution due to the shape of the probe

As problems specific to the observation of biosamples, the problems involved in making the sample are also considered.

- Biological tissue is not very conductive and charges up easily
- Types of bases and adhesion methods
- Contamination of the base surface and the short probe by foreign materials in the air and water
- Observations must be at low concentrations, and without periodic structure over a wide range

References

1. T. Uno, TAMPAKU KAKUSAN KOSO, Vol 34, 1989, p 1024.

2. Research and Development Corp. of Japan's Life Sciences Research Group, Raifusaiensu Nyumon (A Guide to the Life Sciences), Ohmusha, 1987, p 130.

3. Ibid., p 10.

4. H. Kifune; Kichin, Kitosan no Oyo, Kichin, Kitosan Kenkyukai Hen (Applications of Chitin and Chitosan, Chitin and Chitosan Conference proceedings), Hihodo Shuppan, 1990, pp 99-100.

5. Joint editing by K. Atsumi, M. Kotani and T. Uno, Baiomagunetoronikusu Nyumon (A Guide to Biomagnetronics), Ohmusha, 1986, p 34.

6. Ibid., p 75.

7. Ibid., p 97.

8. Ibid., p 96.

9. Ibid., p 138.

10. Ibid., pp 200–206.

11. Ibid., pp 206–208.

12. Ibid., pp 208 210.

13. Research and Development Corp. of Japan's Life Sciences Research Group, Raifusaiensu Nyumon (A Guide to the Life Sciences), Ohmusha, 1987, p 119.

14. Ibid., p 117.

15. Ibid., p 118.

16. M. Aizawa, OYOBUTSURI, Vol 59, 1990, p 1320.

17. A. Tanaka, Baioriakuta (Bioreactors), Kodansha, 1985, pp 1–8.

18. Research and Development Corp. of Japan's Life Sciences Research Group, Raifusaiensu Nyumon (A Guide to the Life Sciences), Ohmusha, 1987, pp 112, 126.

19. H. Takaratani and K. Kinoshita, Genkai wo Koeru Seibutsu Kenbikyo—Mienai Mono wo Miru (Biomicroscopes That Go Beyond the Limits—Seeing Things That Cannot Be Seen), Gakkai Shuppan Center, 1990, p 61.

20. K. Yada, SEIBUTSU BUTSURI, Vol 35, 1990, p 2761.

21. Z. Nishimura, TANPAKU KAKUSAN KOSO, Vol 35, 1990, p 2979.

22. Y. Kato and H. Miyamoto, SEIBUTSU BUTSURI, Vol 30, 1990, p 165.

23. R. Sonnenfeld and P. Hansma, SCIENCE, Vol 232, 1986, p 211.

24. T.P. Beebe, Jr., T.E. Wilson, F. Ogletree, J.E. Katz, R. Balhorn, M.B. Salmeron, and W.J.R. Siekhaus, SCIENCE, Vol 243, 1989, p 370.

25. D.D. Dunlap and C. Bustamante, NATURE, Vol 342, 1989, p 204.

26. G. Binning, H. Rohrer, Ch. Gerber and E. Weibel, APPL. PHYS. LETT., Vol 40, 1982, p 178.

2.3.6 Chronobiology

From single-celled algae to human beings, living organisms carry on their life activities with fixed rhythms. In human beings, heartbeat, respiration, depth of sleep, and menstruation are some examples of those. There have been invigorated efforts in recent years to elucidate these kinds of rhythms that are inherent in living organisms, and to apply them in medical treatment and other such fields. In this section we will roughly divide biorhythms into circadian rhythms, which are the most noticeable when it comes to governing physiological functions, and the other rhythms that involve longer periods of time than circadian rhythms.

(1) Circadian Rhythms

(a) Summary

Most living organisms have a rhythm that is like the period of the earth's rotation, i.e., 24 hours, and their temperature, degree of activity, food intake, and so forth fluctuate in time with this rhythm. A special point about this rhythm is that, even if there are no changes in cyclical stimuli from the outside (differences in light, temperature), the rhythmic cycle is sustained (free periodicity). However, under conditions where there are no external stimuli, the cycle often deviates as much as four hours more or less than the interval of about 24 hours. It is thought that living organisms can change their daily-prescribed physiological parameters and thereby adapt to the environment on earth by supplementing their own 24-hour-long rhythm with the fluctuations of external stimuli, which serve as minute adjustments. Halberg called this "circadian rhythms," a word he created from two Latin stems (Circa=about + Dian=day).

(b) Mechanisms of Circadian Rhythms

The circadian rhythms described above have been confirmed in many living organisms other than man; in several living organisms the locations in the brain or in the nervous system that are thought to be the sources from which the rhythm is telegraphed have already been determined (Table 2.3.6-1[2]). That the places related to sight (photoreception) tie in deeply with the transmission of circadian rhythms is especially interesting.

Although knowledge has been gained about the places that play a part in circadian rhythms, much is still unclear about the actual mechanisms. Various hypotheses about what determines the rhythmic cycles have been put forth in recent years, e.g., the theory that the RNA synthesis system plays a part; the theory about ion permeability changes in biomembranes due to protein transfer in the membranes; and the theory that 24-hour cycles are created as the Fourier-series-like "sum" resulting from the mutual control that several metabolic systems conduct over each other.[1] None of these have yet been proven to be correct, and are undeniably hypotheses only. If the level of research in molecular biology advances from now on, it is predicted that the true character of circadian rhythms will become clear.

Table 2.3.6-1 Examples of Biorhythm-Transmitting Areas

Name	Rhythm-transmitting area	Remarks
Cockroach Cricket	Optic lobe (Part of the nerve linking the brain with the eyes)	Controls nocturnal activities and dietary behavior
Seahorse	Eyeball	
Sparrow	Pineal body (In the midbrain; functions like a retina in fish and living creatures. In birds and mammals, photoreceptive functions are lost, but it secretes melatonin and stimulates progesterone formation.)	Controls diurnal activities and dietary behavior
Rat	Optical crossover nucleus (Part of the thalamus, located above the part where the optic nerves intersect. It is known that cells of this area are activated when a stimulus is applied to the optic nerve.)	Controls nocturnal activities and dietary behavior

Circadian rhythms are also being approached from the microscopic perspective. At the genetic level, the gene that participates in the circadian rhythms of the fruit fly was determined (Konopka, Benzer, 1971), and analyses were later continued by Young, et al., (1987) and Rosbash (1987). It is now known that there are at least six genes in the yellow fruit fly that play a part in circadian rhythms; the one being researched the most is the per gene that is located on the end of the X chromosome.[3] In the mutations that originate in that gene, which bases get changed around in the cases of 1) the total absence of a circadian-rhythmic cycle, 2) an abnormally long cycle, and 3) an abnormally short cycle have been confirmed. This kind of genetic approach is thought to further accelerate the elucidation of the mechanisms of circadian rhythms at the cellular level.

(2) Long-Term Biorhythms

Living organisms have other rhythms with periods that are longer than the 24-hour-long circadian rhythms described above. Examples of these are menstruation in human beings, animals' shedding and growing of hair, plants' and animals' breeding seasons, etc. One cycle may range over a month (strictly speaking, 28 days), a season, a year, and so on.

In clinical medicine, attention is focusing on biorhythms for the purpose of treating autonomic ataxia and psychoses that are synchronized with the menstrual cycle, and depression and insomnia that appear seasonally. Recent

research confirms that there is a definite relationship between changes in the hours of sunlight over the year and the number of suicides.[4]

There also seems to be more research on the correlation between long-term and short-term biorhythms. There is a report, for example, that proposes that the "Monday-morning blahs" are caused by the sudden shifting of stress to the weekend because of the 24-hour-long cycle of social lifestyle, even though the normal human circadian rhythm is 25 hours (Mitsubishi Chemical Industries' Science Lab).[5]

Like with circadian rhythms, external stimuli such as lightness/darkness, temperature, and so on play an important part in long-term biorhythms, too. At the present stage, though, the correlations between these stimuli and the parameters of life activity in plants and animals are being compiled by means of statistical methods; research has not yet reached the point where scientists are determining the origins of rhythm transmission or modeling the transmission mechanisms.

(3) Spillovers From Biorhythms Research

Knowledge about biorhythms may have purely scientific significance, i.e., to close in on the root of life activities, but it is also expected to provide great contributions in the realm of clinical medicine. Below we give examples of major applications in recent years and the future outlook.

(a) Utilization of Circadian Rhythms

(i) Applications in Cancer Treatment

Various methods of cancer treatment are being investigated and moved into actual use, but when doctors try to get the greatest effect in a short period of time, there is often the problem of accompanying side effects. Tamura, et al.,[6] noticed that there are circadian rhythms in the activity of cancer cells and adopted a method of treatment that is based on biorhythms: they concentrated treatment during the periods when the cancer cells were the most active (the high-temperature phase) and ceased the treatment when that activity stopped. The results in both the tumor size and percentage of recurrence confirmed that such treatment is very effective in comparison with the group that was treated during times other than the high-temperature phase (Figure 2.3.6-1).

(ii) Applications in the Treatment of Depression

"Light-pulse therapy" is known to be effective in improving psychotic illness and sleeping disorders in depressive states such as seasonal emotional disorder. Because this therapy does not have any serious side effects, it is thought that it will be used more and more in the future. Although there are as many different theories as ever about why this therapy is effective, e.g., the melatonin production suppression theory, the photon theory, the phase shift theory, the neurobiological theory, etc., none have yet been proven to be correct.

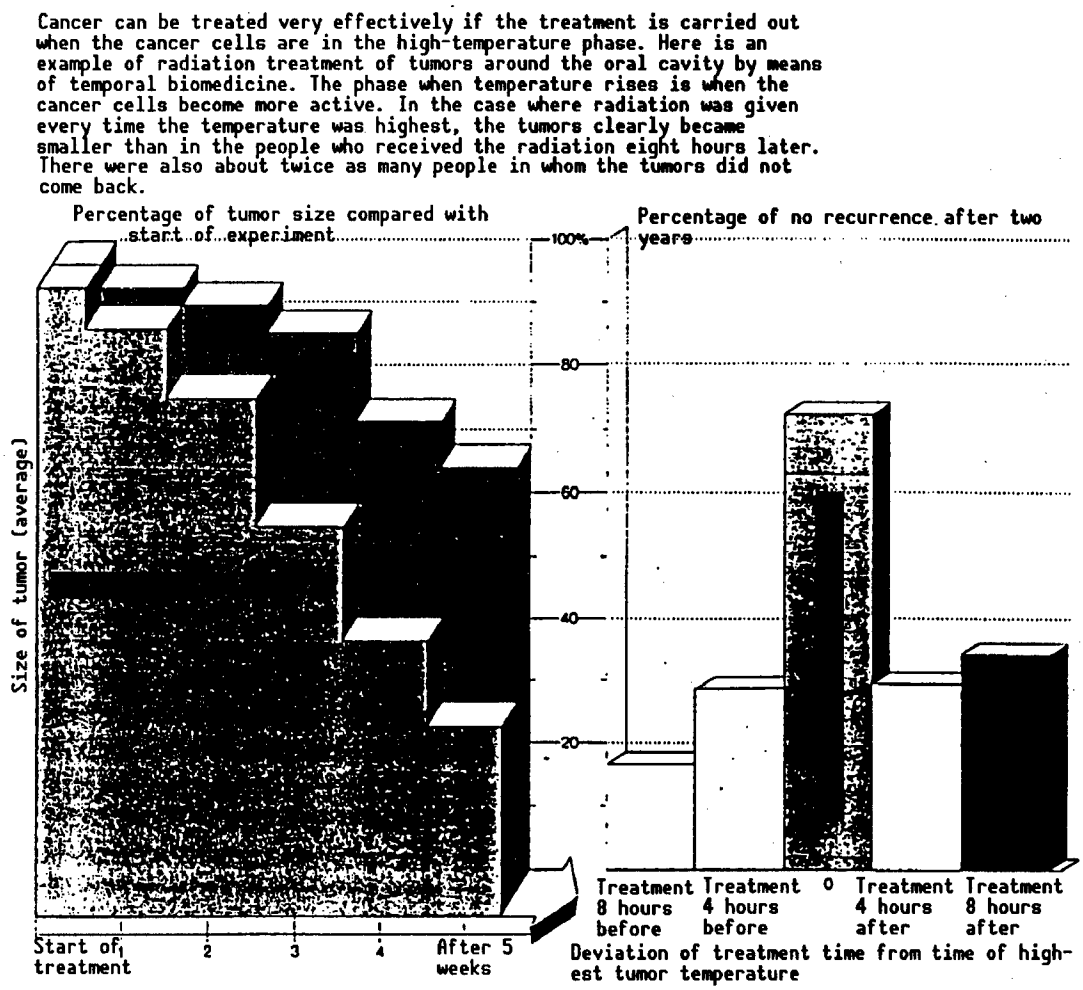


Figure 2.3.6-1 Effects When Cancer Cells Are Treated During High-Temperature Phase

Figure 2.3.6-2 shows the treatment equipment of Asano.[7] In this example, light with an illumination of 5,000 lux is shown for three hours from 6:00 until 9:00. Figure 2.3.6-3 shows the data obtained from the treatment of a 29-year-old patient with seasonal emotional disorder; improvements were observed in the patient's feelings of depression, decline in activity, over-intake of sugar, and oversleep.

It was confirmed that light-pulse therapy can also be applied in the conditions that relate to biorhythms, such as winter insomnia[8] and seasonal pre-menstrual emotional disorders (Parry, 1987).[7] This kind of therapy is also getting attention because of its wide range of applications.

On the other hand, however, symptoms are also known to worsen again when this treatment is interrupted. An approach that involves natural treatment is also thought to be necessary; it would heighten peoples' ability to help themselves during their daily lives, without the use of special facilities, by deepening their understanding of biorhythms.

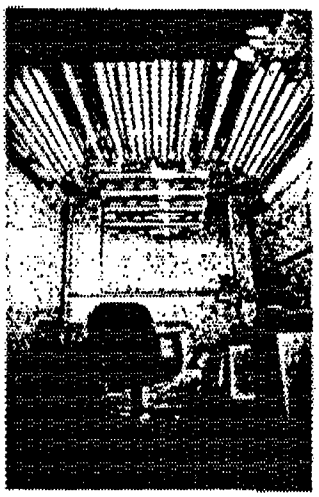
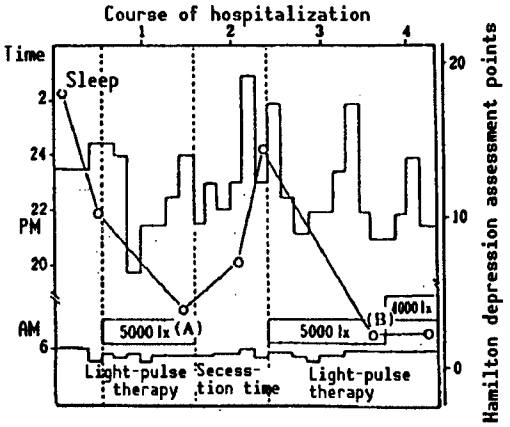


Figure 2.3.6-2 Light-Pulse Therapy Room



The shaded part shows the time when the patient was awake, the white circles show the Hamilton depression assessment points. With the light-pulse therapy (A), improvements were observed in the patient's feelings of depression, decline in activity, over-intake of sugar, and oversleep. Because the symptoms got worse when the therapy was interrupted, the effectiveness of the therapy was reconfirmed when it was tried a secod time (B). After leaving the hospital, the patient used a portable light-therapy device.

Figure 2.3.6-3 29-Year Old Woman, Seasonal Emotional Disorder

(iii) Applications in Conditions Caused by Abnormalities in Hormone Secretions

In the field of internal medicine as well, applications of biorhythms are considered in the treatment of conditions that are due to abnormalities in hormone secretion. Because many of the fluctuating hormonal rhythms are affected by the natural environment, living habits, and so forth, it is difficult to characterize them all together and make use of biorhythms in treatment. If the patterns of individual patients can be understood, however, applications such as optimizing the timing of drug doses are possible. Already a number of insulin-reinforcement methods are being tried in the treatment of insulin-dependent diabetes: in order to suppress early-recoil blood sugar (the phenomenon where blood sugar rises until about eight in the morning, regardless of whether a meal was eaten or not), continual subcutaneous insulin injection, intermediate insulin doses before bedtime, continual insulin dose before supper, etc.[9]

Applications of this method are not only anticipated in the treatment of conditions caused by abnormalities in hormone secretions, but also in drug therapy for other biorhythms- related conditions such as hypertension. Depending on the results, it may create quite a stir in the present-day "drug pickling" system of medicine.

(b) Utilizing Long-Term Life Rhythms

(i) Results From the Elucidation of Hibernation Mechanisms

Hibernation is also a kind of biorhythm. In the physiology of mammals during hibernation, centering on rodents such as squirrels, there are several characteristics that are thought to be useful to mankind as well.[10]

Representative of these are resistance to viral/bacterial infection, functions that suppress increases in sarcomas, and the fact that resistance against lethal radiation increases. These are all physiological phenomena that can have an impact on the prevention of infectious diseases and cancer, and on radiation treatment. The mechanism for withstanding low temperatures during hibernation is also thought to have applications in low-temperature surgery and the preservation of organs and other such body parts. Thus, as knowledge about hibernation deepens, information that is useful in mankind's health maintenance is expected to be gained.

References

1. S. Takahashi, K. Takahashi, and K. Honma, Rinsho Jikan Seibutsugaku (Clinical Temporal Biology), Asakura Shoten, 1990, p 3.

2. M. Ito, No no Sekkeizu (Design Diagrams of the Brain), Chuo Koronsha, 1989, p 138.

3. Z. Chiba, KAGAKU ASAHI, August 1989, p 18.

4. K. Egashira and K. Abe, NISSEI KISHI, Vol 25, 1988, p 97.

5. For example, NIHON KEIZAI SHIMBUN, 27 April 1988, p 14.

6. Y. Tamura, KAGAKU ASAHI, June 1990, p 104.

7. S. Takahashi, K. Takahashi, and K. Honma, Rinsho Jikan Seibutsugaku (Clinical Temporal Biology), Asakura Shoten, 1990, p 183.

8. T. Hansen, T. Bratlid, O. Lingjaerde et al, ACTA PSYCHIATR. SCAND., Vol 75, 1987, p 428.

9. S. Takahashi, K. Takahashi, and K. Honma, Rinsho Jikan Seibutsugaku (Clinical Temporal Biology), Asakura Shoten, 1990, p 292.

10. N. Kondo, KAGAKU ASAHI, March 1990, p 35.

2.3.7 New Global Environmental S&T

Global environmental problems that are thought to be caused by the increase in human activities are big problems for the entire world. Science and technology that aims for ongoing development while continuing to be harmonious with Nature is seen as necessary. Here we will discuss the trends in the S&T for preserving and improving the global environment, and about the observational techniques that will become basic technology.

(1) Technology for Countering Global Warming

Due to the increase in water vapor, carbon dioxide, and other such greenhouse gases, more than necessary amounts of infrared light, which should be

reflected back from the earth's surface into space, are absorbed by these gases, and global warming occurs as a result of the rise in the temperature of the earth's surface. As shown in Table 2.3.7-1,[1] the gas that has the greatest effect on global warming is carbon dioxide. As ways to keep carbon dioxide emissions in check, an extremely diverse array of R&D efforts are being made. Some of the major areas are: 1) energy technologies, starting with nuclear power and fusion, that generate little carbon dioxide; 2) high-efficiency energy conversion technologies that generate small amounts of carbon dioxide per unit volume of heat, e.g., fuel cells, compound power generation that uses coal gasification, etc.; 3) technology that utilizes natural energy, e.g., solar cells, geothermal power, etc.; and 4) high-density power storage technology, e.g., high-density storage batteries, superconducted power storage, etc.

Table 2.3.7-1. Concentrations of Greenhouse Gases, Amount of Infrared Radiation From the Earth That Is Absorbed (Ω), and Increase in the Amount of Absorption (ΔΩ)

Greenhouse gas	Pre-industrial revolution concentrations	1985 concentration (rate of temperature increase)	2050 concentrations	Ω_{1985} a) (Wm^{-2})	$\Delta\Omega_{pre.}$ b) (Wm^{-2})	$\Delta\Omega_{1985}$ c) (Wm^{-2})
CO_2	275ppm	345ppm (0.4%)	400~600ppm	~50	1.3	0.9~3.2
CH_4	0.7ppm	1.7ppm (0.9%)	2.1~4.0ppm	1.7	0.6	0.2~0.9
O_3	0~25%	10~100ppb (~1%)	15~50%	1.3	0.0~0.2	0.2~0.6
N_2O	285ppb	304ppb (0.25%)	350~450ppb	1.3	0.05	0.1~0.3
CFC12	0.0ppb	0.38ppb (5%)	0.7~3.0ppb	0.12	0.12	0.6~1.4
CFC11	0.0ppb	0.22ppb (5%)	2.0~4.8ppb	0.06	0.06	0.23~0.7
Total	—	—	—	—	~2.2	2.2~7.2

a) Net change in the amount of radiation in tropopause when the respective greenhouse gas is removed
b) Change in the amount from pre-Industrial Revolution times until 1985.
c) Change in the amount from 1985 to 2050

Source: K. Akimoto, Global Warming and Greenhouse Gases, ANZEN KOGAKU, Vol 28, 1989, pp 270-278.

In addition to carbon dioxide, there are other greenhouse gases such as methane, dinitrogen oxide, and CFCs (chlorofluoro-carbons). Of these, methane and dinitrogen oxide are not just generated by industrial activities; because they can also originate in farmland, livestock, waste processing, marshes, and so on, an investigation of the actual state of affairs is late. For this reason there are plans to elucidate the sources and mechanisms of generation by developing new measurement equipment and by conducting field surveys.[2]

(2) Technology for Countering Desertification

The world's deserts are said to be expanding at a rate of 60,000 km^2 every year. Furthermore, they are at the root of extremely severe conditions, e.g., 18% of the world's population is concentrated in this kind of arid land. Therefore the problem of desertification should be taken up as a global-scale problem. Japan, which has no deserts of its own, is also being asked to deepen its view of deserts and to contribute internationally to the prevention of desertification and the afforestation of deserts.

There are various types of deserts—sand deserts, gravel deserts, and rock deserts—and there are great differences among regions and deserts, such as the differences in the conditions under which sand is formed. Therefore, measures for preventing desertification or for afforestation that are suited to each region are necessary. Before that, though, with the lack of data on the weather conditions in the deserts, and so forth, even if simulation and modeling is done, the accumulation of data for each area is seen as necessary.[3]

Technologies for ensuring water and for preventing sand movement are indispensable in desert afforestation.

1) First, as applications of traditional technology, technology must be developed for mechanical excavation and pipeline management of *kanato* (groundwater lines for irrigation that are seen mainly around Iran), and for irrigation techniques like drip irrigation that conserve water and with which it is easy to control the amount of fertilizers. The latter in combination with water-absorbing polymers is also considered. And, as technology for preventing sand movement, combining plants with sand walls, and "grass lattices" braided from rice and wheat straw and then buried in the sand are some applications that have been thought of.

2) As applications of modern techniques there are methods for preventing drifting sand by fixing the surface of the sand in place with chemical substances such as asphalt emulsions (called mulching); various techniques for preventing salt damage, where salinity in the earth accumulates in the ground (e.g., lowering the water level by means of wells and so forth, removing salinity by means of elution, etc.); using water-absorbent polymers, inorganic pearlite and vermiculite, and so forth as water-retaining agents; building underground dams (Figure 2.3.7-1[4]), etc.

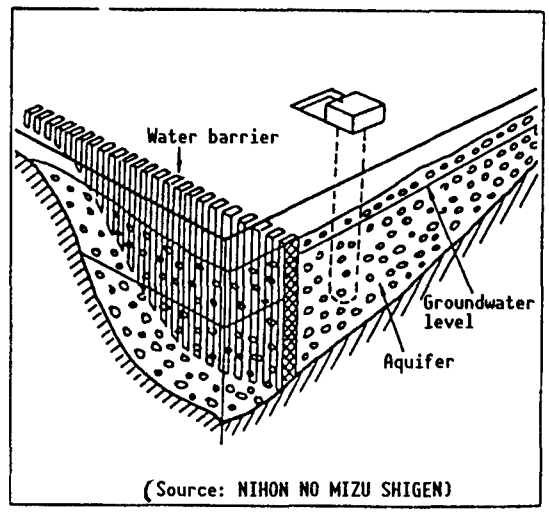


Figure 2.3.7-1 Conceptual Diagram of Underground Dam

3) Future techniques that are anticipated include the use of salt-resistant plants (there are ways to improve the salt resistance of rice and other crops, and methods that use the intrinsically salt-resistant Akaza plant as fodder), and the use of new energies such as solar energy and wind energy for irrigation power and for desalinating seawater (Figure 2.3.7-2[4]). In addition to these, research is also being conducted on artificial rainfall.[4]

(3) Acid Rain Countermeasures

Oxides of sulfur, oxides of nitrogen, and hydrocarbons are some of the substances that cause acid rain. They come mainly from industrial facilities, such as power plants, and from transportation machines that use petrochemical

fuels, such as automobiles. The acid-rain-causing substances emitted remain in the air in the form of gas and particles. In addition to directly harming the plants and so on to which they adhere, these substances are taken up into cloud droplets and raindrops, fall down to the ground as acidic rain and fog, and cause damage to forests and buildings. The term acid rain is sometimes used as the general name for these phenomena.

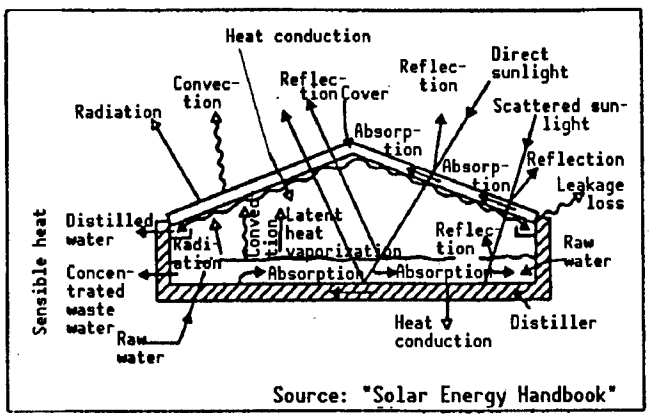


Figure 2.3.7-2 Distillation Apparatus That Uses Solar Energy

Acid rain countermeasures include technology for eliminating the substances that cause it, and technology using energy that either generates very little or none of those acid-rain-causing substances.

(a) Desulfurization

Techniques for eliminating sulfur oxides from the smoke of power plants and other such industrial facilities include the use of petroleum fuels that contain little sulfur, and technology for chemically removing sulfur oxides from the smoke (smoke desulfurization). The mainstream has shifted away from desulfurized petroleum energy over to smoke desulfurization. The subject in smoke desulfurization is a method called wet absorption, which uses limestone, caustic soda, and other such alkaline substances as absorbents; the absorption rate with this method is over 95%. Thus, desulfurization is said to be in a technologically mature stage, and topics in new technology development include simplification of the process, labor-saving operations by means of new control systems, and reducing the amounts of chemicals used.[5]

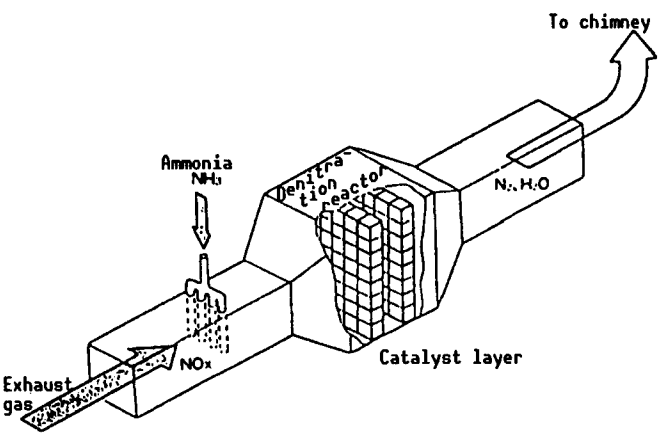


Figure 2.3.7-3 Abbreviated Configurational Model of Denitration Apparatus

(b) Denitration

Because oxides of nitrogen inevitably result from high- temperature combustion processes, technology for removing them from smoke is the subject, and a method called ammonia catalytic reduction is the mainstream (Figure 2.3.7-3[6]). Denitration equipment based on this method has already achieved plenty of good results. Efforts from now on include measures so that denitration equipment is

used under conditions where the temperature of the emitted gas is low, and improvements upon the catalysts so that the equipment can be adapted to garbage incinerators that emit harmful gases.

As an example of technology for holding down the amounts of nitrogen oxides formed as a result of combustion, research is being done to introduce a two-stage combustion method into sludge incineration.[7]

(c) Automotive Catalysts

The catalyst that purifies exhaust gases from automobiles is also called catalytic converter rhodium. When the theoretical combustion fuel-air ratio [is one to one], the components of the exhaust gas that will be oxidized (hydrocarbons, carbon monoxide, hydrogen, etc.) and the oxidizing components (oxygen, nitrogen oxides, etc.) are exactly balanced. Using this, the oxidation of hydrocarbons and carbon monoxide, and the reduction of nitrogen oxides take place at the same time. Therefore, when the catalytic converter must be used in a state where the fuel-air ratio is low (lean) for the purpose of eliminating carbon dioxide emissions in the future, it is predicted that with present-day catalysts, not enough nitrogen oxides will be removed, and the development of new catalytic technology is seen as necessary.[8]

(d) Electric Cars

Uses for various types of secondary batteries, which will become the key point of electric car development, are being considered, as shown in Table 2.3.7-2.[9] Of these the nickel-hydrogen battery, which has excellent electric discharge characteristics, has high energy density, and does not contain harmful cadmium, is getting attention, and progress is being made in making it practical.[10]

(4) Measures Against Destruction of the Ozone Layer

The stratosphere extends from 12~50 km above the earth; ozone exists in high concentrations around 20 km above the earth. Ozone is a very good absorber of the sun's ultraviolet rays, in particular the short-wavelength ultraviolet rays that are harmful to living organisms. Consequently, an increase or decrease in the concentrations of ozone has a great effect on the ecological systems on earth. The danger that the ozone layer is being destroyed by CFCs (chlorofluorocarbons: fluorine-substitution products of methane and ethane) was first pointed out by Molina and Rowland.[11]

After that the ozone hole above the South Pole was observed, and the state of destruction of the stratosphere's ozone layer was made clear. As a counter-measure against this, a proposal to intensify the regulation of ozone-destroying substances, including the total abolition of CFCs by 2000, was adopted at the second meeting of the Montreal Protocol signatories.

CFCs, or freons, have low toxicity; are non-combustible, chemically stable, and noncorrosive; and are used in large volumes. R&D efforts to replace CFCs with other substances are being promoted. Table 2.3.7-3[12] shows the specific

Table 2.3.7-2 Performance and Characteristics of Batteries for Electric Cars

	Energy density (Wh/kg)	Output density (W/kg)	Cycle lifetime	Characteristics
Lead battery	35/45	120/200	400/800	Sealed, inexpensive
Nickel-cadmium battery	50/60	160/180	500/1000<	Sealed, expensive
Nickel-iron battery	50/60	90/120	800/1000<	Nonsealed
Nickel-zinc battery	70/80	160/190	200/500	High-energy and -density, short-life
Nickel-hydrogen battery	50/60	160/180	500/1000<	High-energy and -density, expensive
Bromine-zinc battery	70/80	90/100	700/1000<	High-energy and -density, needs auxiliary equipment
Sodium-sulfur battery	100/100	150/150	350/1000<	Inexpensive, high-temperature (350°C) operation
Room-temperature lithium battery	65/120	100/100	100/500<	High-voltage, short-life

CFCs that are to be totally abolished by the Montreal Protocol, and their substitutes, according to their uses. (Note: CFCs are classified according to their affixed numbers, which show the hydrogen and chlorine they contain. The number on the right shows the fluorine; the number in the 10's position, the number of hydrogens plus one; the number in the 100's position, the number of carbons minus one. Then the number of chlorines is automatically determined from these numbers.)

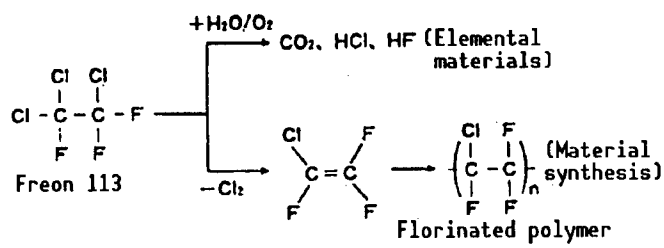


Figure 2.3.7-4 Two Ways To Decompose CFCs

As techniques for holding down the emission of CFCs that are already in existence, methods of breaking them down and changing them into elemental materials, and methods that use the synthesis of fluorinated polymers are being considered (Figure 2.3.7-4[13]). In particular, the kind of methods shown in Table 2.3.7-4[13] are being proposed as a technique for changing CFCs into elemental materials.

Table 2.3.7-3 Substitutes for Specific CFCs, by Use

Uses Major class Subclass	Specific freon	Freon substitutes		Nonfreon substitutes
		New freons	Existing freons	
Coolants				
Car air-conditioners	Freon 12	Freon 134a Freon 22/ Freon 152a/ Freon 124	Freon 22 Freon 22/ Freon 152a/ Freon 114	
Electrical refrigerators	Freon 12	Freon 134a Freon 22/ Freon 152a/ Freon 124	Freon 22, Freon 502 Freon 152a Freon 22/ Freon 142b	Ammonia
Centrifugal coolers	Freon 11	Freon 123, Freon 141b		(Adsorbent bromine lithium)
Industrial-use coolers	Freon 12	Freon 134a	Freon 22, Freon 502	Ammonia
Aerosols				
Body-use products	Freon 12/ Freon 11	Freon 143a/ Freon 123	Freon 22/ Freon 142b	LPG, DME, CO_2, N_2
Medical products	Freon 12/ Freon 11	Freon 143a/ Freon 123	Freon 22/ Freon 142b	
Foaming				
Soft polyurethane	Freon 11	Freon 123, Freon 141b		Methylene chloride, water, air
Hard polyurethane	Freon 11	Freon 123, Freon 141b Freon 123/ Freon 141b		
	Freon 12	Freon 34a	Freon 22, Freon 142b	
Polystyrene	Freon 12	Freon 124, Freon 134a	Freon 22, Freon 142b	Propane, butane
Cleaning				
Precision cleaning	Freon 113	Freon 225 ca,cb Freon 123/ Freon 141b/ methanol Freon 123/ Freon 141b/ Stabilizer Fluropropanol		Water (steam), water/surfactive agent, IPA, ethanol, methylene chloride, terpene, hydrocarbons, higher alcohols, no cleaning

Table 2.3.7-4 Comparison of CFC-Decomposition Methods

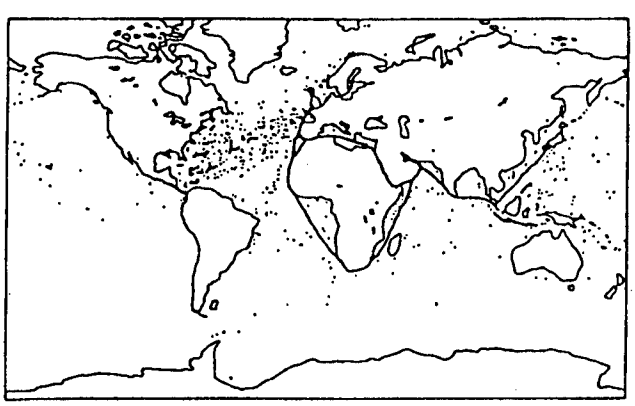
	Decomposition temperature	Decomposition pressure	Reactants
Combustion, heat decomposition	800~1000°C	1 atm.	Hydrocarbon (CH_1)/O_2
Plasma decomposition	about 10,000°C	1 atm.	H_2O, O_2 (hot plasma)
	RT	1 atm.	H_2O, O_2 (corona discharge)
Catalytic decomposition	400~500°C	1 atm.	H_2O
Reagent decomposition	RT~150°C	1 atm.	Sodium phtalenide
	RT~100°C	1 atm.	Superoxide (KIO_4 + H_2O_2)
Supercritical seawater decomposition	about 400°C	300 atm.	H_2O

(5) Measures Against Marine Pollution

Although there are many different substances that pollute the oceans, here we will discuss measures against oil spills, eutrophication, and harmful chemical substances.

(a) Oil Spill Countermeasures

Due to the expanding volumes of petroleum consumed throughout the world, tanker transport from oil-producing countries to consuming countries has suddenly increased. With that there has been an extraordinary increase in oil pollution of the oceans. Figure 2.3.7-5[14] shows the distribution, based on visual records of general commercial ships, of places where oil films in the world's oceans were discovered; it is apparent that oil films are observed in concentrations along major tanker routes. Oil that is discharged from ships during normal navigation can only be limited by means of legal regulation. But in order to minimize the amount of oil spilled when an accident occurs, such as running aground, measures are being taken in the aspect of ship structure, as in the double-hull tanker with a horizontal bulkhead that is shown in Figure 2.3.7-6.[15]



Source : IOC, *Global Oil Pollution*, 1981.

Figure 2.3.7-5 Distribution of Places Where Oil Films Were Discovered

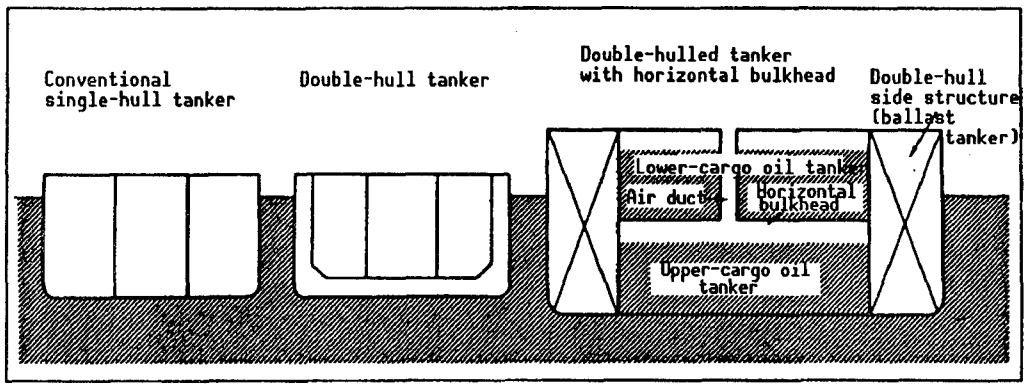


Figure 2.3.7-6 Double-Hull Ship Structure

To recover oil that was spilled into the ocean in large amounts, absorbing mats and processing agents are used. But it is known that there are some microbes (bacteria and molds) that can break down petroleum into harmless substances such as water, so technology is being developed to utilize those microbes.[16]

(b) Eutrophication Countermeasures

Occurrences of red tides, which are caused by marine eutrophication, were thought to be localized phenomena in inland harbors of highly industrialized and heavily populated areas and other such temperate areas of Japan and the United States. After the 1980s, however, occurrences were seen to have increased in scale, and a worldwide expansion was observed in the ocean areas where red tides occurred (International Red Tide Symposium, November 1987, Takamatsu City).[14]

Organic substances, phosphorus, and nitrogen are some of the substances that cause eutrophication. Phosphorus is being dealt with by reducing the amounts in mainly human waste water (detergents without phosphorus). Ways to deal with the phosphorus in water for industrial use, however, are being considered, e.g., reducing the phosphorus contained in the water used in boilers. As for the water used in boilers, if it contains soil components such as calcium and chlorides, it can lead to operational problems, such as scales occurring, so before the water is used, phosphates are poured in as processing agents (boiler compounds). Substances to replace the phosphates, such as poly-acrylates and polymetaacrylates, are being put to practical use. From now on improvements in safety, such as putting food additive materials to work, and further advances in energy and resource conservation, such as the reuse of water, are desired.

Because sewage has spread to only about 40% of Japan, sewage facilities lag behind those of Europe and the United States, but Japan's processing technology is advancing. Technologies where Japan is ahead in practical applications include 1) advanced processing technology for reusing as intermediate water the water processed from sewage; 2) technology for using microbes to remove the odorous gases that arise from the putrification of

sulfurous compounds during processing; 3) sludge-fusion technology, which melts the sludge that remains after processing, and provides a way to reuse the sludge.[18]

(c) Measures Against Harmful Chemical Compounds

As for the pollution due to heavy metals such as organic mercury, localized pollution in advanced countries and damage through the concentrations of those chemicals in fish and shellfish (Minamata disease, etc.) have been known up until now, but the state of worldwide pollution is not clear. Organochlorine compounds such as PCB, which take a very long time to decompose and die away in the environment, are also being detected in broad extents of the oceans, and are bringing about the wide-scale death of seals and other animals. Thus marine pollution by harmful chemical compounds is spreading on a global scale, and effective countermeasures are desired. Here we will discuss one example of technology for preventing the pollution of the ocean that is due to organic tin compounds.

Organic tin compounds are used as antifouling paints for preventing barnacles from adhering to the bottoms of ships. But, in addition to the poor growth, death, and malformation that occurs in shellfish as a result of the heavy metals contained in the paints, there is also the fear of ill effects on humans as well, so in recent years these paints are regulated by laws throughout the world. Because a constant amount of the effective components of organic tin paints always dissolves into the water as a result of hydrolysis, they last a long time (five years) and it is easy to control their lifetime. On the other hand, the cuprous oxide bottom paints now being used as substitutes, which are called self-disintegrating paints, are the type of paint that physically disintegrates as a result of the ship's movement through water, so they have short lifetimes (at most two years) and controlling them is difficult. Consequently there is a rush to make practical hydrolyzing paints that do not contain organic tin. Research is also being carried out on antifouling techniques that do not use paint: methods that involve coating the bottoms of ships and fish nets with copper alloys to utilize the antifouling effects of copper ions; techniques for preventing living organisms from adhering to the bottom by running electrical current through conductive paint that was painted on the ship's bottom and thereby electrolyzing the seawater (ClO ions form); etc.[19])

(6) Observation Technology

To get an accurate grasp on the state of global-scale environmental problems, the following are thought to be necessary: the long-term gathering of observational data, the automation of observations for that purpose, an increase in the number of places from which observations are made, diversification of observational methods, a higher degree of precision, and a broader range of chemical species that are observed.

In Japan, development of the ADEOS (earth observational platform satellite) is being conducted, with the goal of a 1995 launch. Various kinds of sensors for observing carbon dioxide, methane, CFC gases, and other such substances in the

atmosphere are also being developed for the purpose of loading them onto this satellite.[20]

In order to get a good grasp on the state of the stratospheric ozone layer, observations by satellite must be augmented, and earth-based observations must be replete. Plans are being made to set up in the Environmental Agency's NDSC (Network for the Detection of Stratospheric Change) remote measurement equipment, such as laser radar[21] and microwave radiometers, at five or six spots at the South Pole and other places.[22]

References

1. N. Washida, Chikyu Kibo no Kankyo Mondai I (Global-Scale Environmental Problems I), Chuo Horistu Shuppan, 1990, pp 102- 111.

2. NIHON KEIZAI SHIMBUN, 5 January 1991.

3. I. Kobori, DOBOKU SHIKO, Vol 31 No 11, 1990, p 11.

4. M. Maekakiuchi, Ibid., p 29.

5. M. Torii, TRIGGER, October 1990, p 80.

6. H. Aoki, Ibid., p 82.

7. S. Kato, KOGAI TO TAISAKU, 24, 1545, 1988.

8. A. Ichihara, TRIGGER, October 1990, p 88.

9. M. Yamaji, Ibid., p 90.

10. O. Furukawa, NIKKEI MECHANICAL, 7 January 1991, p 80.

11. M.J. Molina and F.S. Rowland, NATURE, Vol 239, 1974, p 810.

12. T. Takaichi, TRIGGER, October 1990 (Supplemental issue), p 96.

13. A. Mizuno, Ibid., p 100.

14. K. Watanabe, Chikyu Kibo no Kankyo Mondai I (Global-Scale Environmental Problems I), Chuo Horistu Shuppan, 1990, pp 352- 365.

15. TRIGGER, October 1990 (Supplemental issue), p 124.

16. NIHON KEIZAI SHIMBUN, 23 August 1990.

17. TRIGGER, October 1990 (Supplemental issue), p 126.

18. H. Iwabe, Ibid., p 128.

19. NIKKEI NEW MATERIAL, 5 March 1990.

20. K. Tsuchiya, TRIGGER, October 1990 (Supplemental issue), p 146.

21. The Environmental Agency's Investigative Meeting on Protection of the Ozone Layer, Ozonso no Mamoru (Protecting the Ozone Layer), Nihon Hoso Shuppan Kyokai.

22. S. Hayashida, Chikyu Kibo no Kankyo Mondai I (Global-Scale Environmental Problems I), Chuo Hoki Shuppan, 1990, pp 44-80.

2.3.8 Recycling S&T

From now on the science and technology for effectively utilizing resources and for recycling resources from wastes will be seen as increasingly important. We will discuss several examples of this kind of S&T, which we define as recycling S&T.

(1) CO_2 Recycling Technology

As mentioned in Section 2.3.7, "New Global Environmental S&T," there are various forms of ongoing research that are aimed at suppressing the emissions of carbon dioxide, which is thought to be the main culprit in global warming. Here we will discuss research that is aimed at recovering and reprocessing carbon dioxide that was emitted, without spreading it in the atmosphere, and then reusing it again.

1) A physical processing technique that is being considered involves hydrating recovered carbon dioxide by injecting the gas 3,000 m deep (300 atm) into the sea, and then just letting the hydrated carbon dioxide sink on its own. Because the relative weight of hydrated carbon dioxide is heavier than water, it will not float to the surface of the water. But it is thought that the hydrated carbon dioxide will gradually dissolve into seawater, so its effects on the environment must be adequately studied. Furthermore, the facilities for injecting carbon dioxide deep into the ocean, the problem of cost, and so forth remain as future research topics.[1]

2) As chemical techniques, artificial photosynthesis that uses catalysts to fix carbon dioxide into methane, methanol, formic acid, or other such substances is being considered (Figure 2.3.8-1).[2] Research using titanium dioxide, or a semiconductor such as silicon carbide, as the catalyst has been carried out, and it was confirmed that methane could be formed. However, because the yield and the efficiency of light utilization are still low, more basic research is thought to be necessary.

3) As biological techniques, the utilization of biomass is being considered, in addition to techniques for cultivating large volumes of plants that can fix large amounts of carbon dioxide (C4 plants); techniques that make plant-like plankton fix carbon dioxide that merged into seawater[3]; and bioreactors[4] that utilize the photosynthesis of blue-green algae; etc.

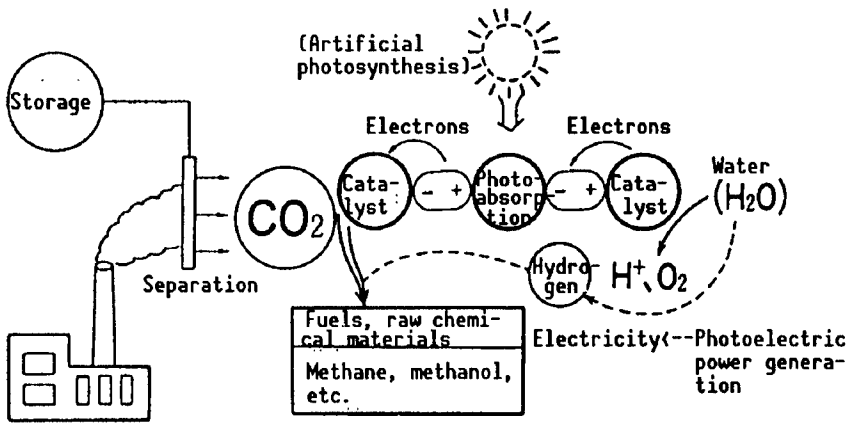


Figure 2.3.8-1 CO_2 Fixation (Separation and Purification, Storage, and Chemical Utilization of CO_2

(2) Recovery and Processing of Harmful Chemicals

We can think of harmful chemicals as being divided into intentionally produced substances and unintentionally produced substances, as shown in Figure 2.3.8-2,[5] depending on how they originated.

- Intentionally produced substances (Industrial chemicals, agricultural chemicals...)
- Unintentionally produced
  - Impurities of the production process (during normal production, during accidents)
  - Processing byproducts (water purification, waste processing...)
  - Products from reactions in the environment (photochemical reactions, microbial decomposition...)

Figure 2.3.8-2 Origins of Harmful Chemicals

In the case of intentionally produced harmful substances, and particularly in the case where substitution with a safer substance is not possible, effective recovery and processing technology is needed for reducing the amounts of those substances that are produced and used.

Because organochlorine solvents, which are used as degreasing and cleaning agents for electronic parts, have been shown to cause cancer in human beings, techniques for removing and recovering them from waste gases, waste water, sludge, etc., are being thought of and used. For example, techniques for removing organochlorine solvents from waste gases include 1) cooling and compression methods that recover the solvents by liquefying the vapors of the solvents, and 2) adsorption-desorption methods that recover the solvents by letting them desorb after they were adsorbed by activated carbon. Techniques for removing and recovering organochlorine solvents from waste water include

1) aeration, which involves feeding air into the water and then expelling the solvents out while they are in a gaseous phase; and 2) adsorption by means of activated carbon. For all of these methods, however, there is not enough basic data about the equipment itself and the conditions under which the methods are to be used. Because it is hard to say that these methods have been optimized, hope is being placed on future research.[6]

Unintentionally produced substances that are getting a great deal of attention lately are the waste gases from urban garbage incineration facilities, and the dioxins that are contained in the waste water from paper mills. Hanai[7] reports that the dioxins generated in urban garbage incineration facilities form in the electrical precipitators, not the incinerators, and that quickly cooling the waste gases of the furnace and then precipitating them at low temperatures can greatly curb the generation of dioxins. Yamazaki, et al.,[8] shed light on the fact that dioxins contained in waste water can be almost completely broken down by heating the waste water to a high temperature between 200 and 300°C. In addition to dioxins, it is known that various other harmful chemicals are discharged from places of waste incineration, as shown in Figure 2.3.8-3.[9] Effective ways to recover mercuric chlorides, in particular, which are generated by the incineration of the mercury, cadmium, and plastic contained in discarded dry-cell batteries, are not being adopted, and counter-measures are thought to be necessary.

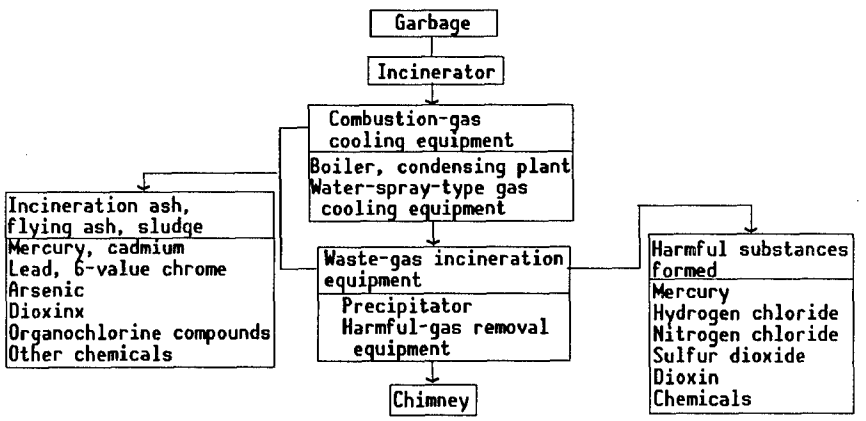


Figure 2.3.8-3 Garbage Incineration Process, and Where Harmful Substances Are Generated

(3) Radioactive-Waste Processing

Nuclear power has been developed as a powerful method for ensuring energy resources, but the processing of radioactive wastes that are generated along with the use of nuclear energy was late in getting started. Figure 2.3.8-4[10] shows the nuclear fuel cycle, from the enrichment of uranium ore to the reprocessing of nuclear fuels after they have been used to generate electrical power. Japan not only imports uranium ore, but also relies on other countries for much of the important processes such as enrichment and reprocessing. For this reason, the construction of nuclear fuel recycling facilities, including facilities for reprocessing radioactive wastes, is being planned.

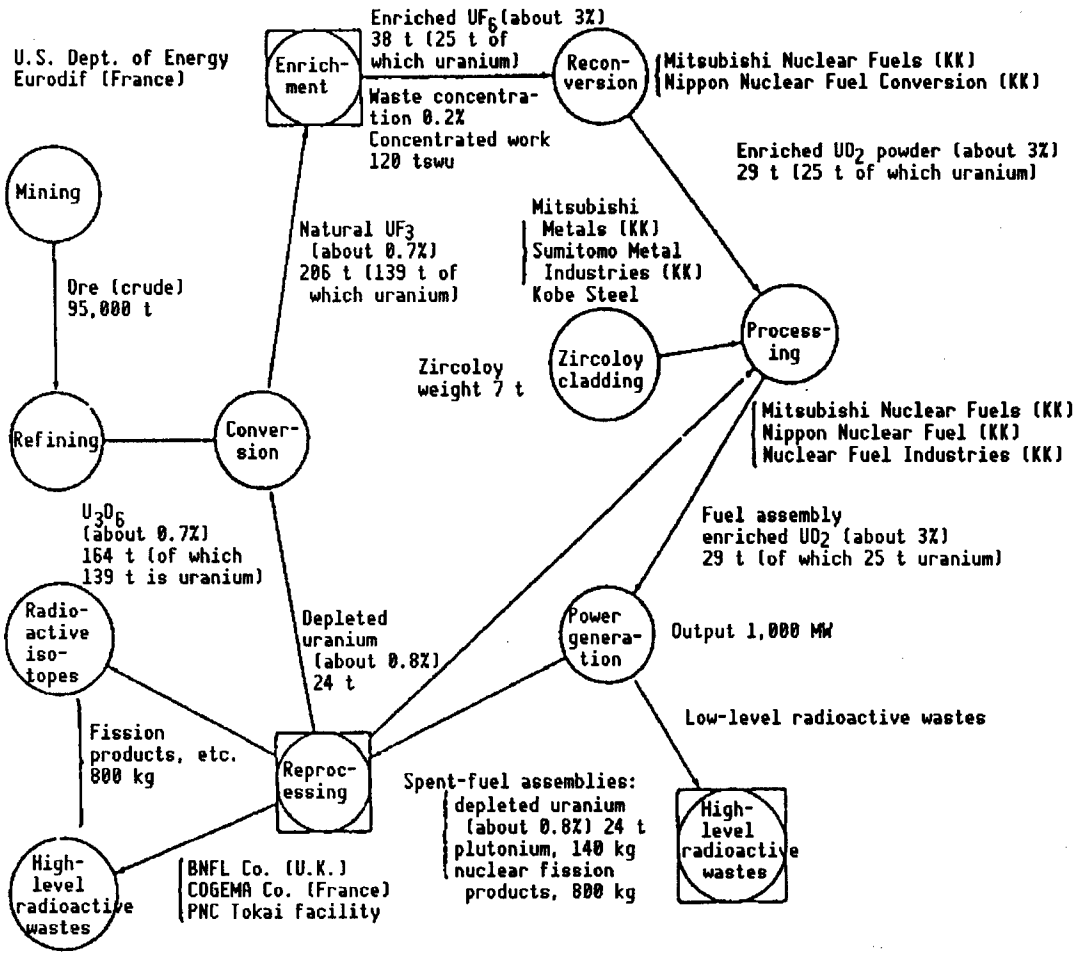


Figure 2.3.8-4 Nuclear Fuel Cycle

Note 1) The numbers for each process are the amounts needed to run a 1,000-MW light water reactor for one year.

Note 2) The squares are facilities construction projects that are currently being promoted for Rokkasho village in Aomori Prefecture.

Radioactive wastes are divided into low-level radioactive waste (filters used for purifying the gaseous or liquid waste, enriched solids of liquid wastes, replaced parts, etc.) and high-level radioactive waste (fission products contained in the spent fuels from nuclear reactors). Low-level radioactive waste is now sealed in drum cans and stored in concrete buildings, but future plans are to dispose of it by burying it in the ground. On the other hand, disposing of high-level radioactive waste by solidifying it with a method such as glass vitrification, then burying it in the ground is being considered. As for the safety of glass vitrification, it was recently confirmed that the speed of corrosion in a natural state is on the order of 1 micron in 2,000 years.[11]

(4) Recycled Paper

Figure 2.3.8-5 shows the changes in the percentage of old paper that is recovered and used in Japan. Most of the used paper that is recovered is old newspapers for which recovery routes are established. As for the recovery of used office paper, the amount of which is increasing, measures are just beginning to be implemented.

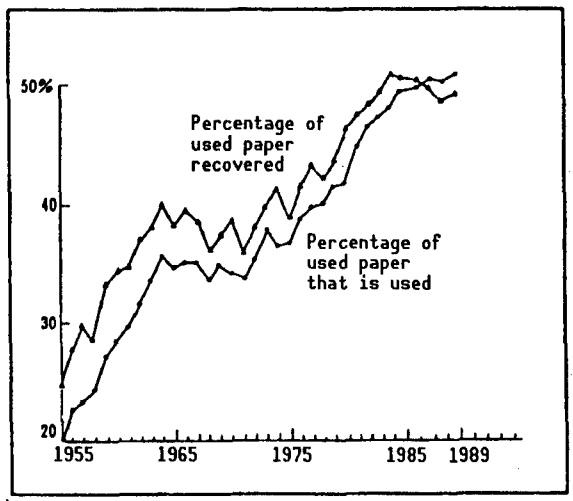


Figure 2.3.8-5 Change in Utilization of Used Paper

There are four major processing techniques for recycling old paper into pulp: 1) loosening the old paper into fibers by means of mechanical power and surface-active agents, or by means of alkaline chemicals, along with "disaggregation," which peels the ink off from the fibers; 2) "dust removal" that removes foreign materials; 3) "de-inking," which expels from the system the ink that was peeled off; and 4) "bleaching." Present-day copy paper that uses recycled paper is required to have a greater degree of whiteness than that used in the past. To meet that requirement, not only bleaching but an appropriate combination of bleaching, disaggregation, and de-inking is seen as necessary, and various techniques are being developed.

(5) Degradable Plastics

In the past, improvements in the durability of many materials were thought to be essential. Consequently, because of their chemical stability, plastic materials were produced in mass volumes and used in all the different fields. This chemical stability is due to the fact that the structures of many polymers (plastics) are formed from stable covalent bonds between carbon atoms. Because of their stability, however, plastics are now considered to be one of the main culprits in environmental pollution: thrown-away plastics do not break down in the environment; they are becoming a source of marine pollution; because of their high heat of combustion, they do damage to waste incinerators. Owing to this kind of background, biodegradable plastics and photodegradable plastics are gaining attention as plastics that are gentle to the environment.

(a) Biodegradable Plastics

Plastics that are broken down by microorganisms, like natural polymers such as starch, are called biodegradable plastics. They are classified as in Table 2.3.8-1[13,14] by Tokiwa.[13,14]

An example of a unique biodegradable plastic that is produced by microorganisms is Biopol, a product of the British ICI Co. However, Doi[15] succeeded in forming a polymer with better characteristics than Biopol by applying a

Table 2.3.8-1 Varieties of Biodegradable Plastics

Type	Variety	Ring	Features	Uses	Problems	Development topics
A (Completely biodegradable)	① Produced by micro-organisms	·Polyhydroxin butyrate (PHB) and derivatives ·Pluran	·High biodegradability ·Biocompatibility	·Fishing nets, fishing line ·Drug-release regulating base materials	·High cost (productivity of culture media, strains and product refining) ·Heat-resistance, mechanical strength narrow in width	·Breeding of strains ·Improvements in culturing methods ·Search for other polymer-producing microorganisms
	② Utilization of natural polymers	·Cellulose-chitosan mixture ·Esterification of cellulose or amylose, & wood flour	·High biodegradability ·Some are gas permeable	·Agricultural use films ·Flowerpots, rope	·Not thermoplastic ·Weak in water ·Conservation of resources	·Development of processing methods ·Giving the materials water-resistance
	③ Biodegradable synthetic polymers from petroleum materials	·Copolymers of polyester and nylon ·Polyester Copolymers	·Plastics with various physical, chemical properties can be made ·Relatively inexpensive	·Various packaging materials ·Plates for refrigerated food products ·Containers for instant food and drink prod.	·Must control copolymerization to make plastic completely biodegradable	·Development of copolymerization control methods ·Elucidation of relationship between physical and chemical properties and biodegrad.
B (Biodisintegratable)	④ Starch blends (composites)	·Starch and polyethylene blends	·Low cost	·Shopping bags ·Grass clipping bags ·Multifilms	·Mechanical strength is reduced ·The plastics are opaque	·Improving distegratability ·Development of advanced starch-mixing techniques
	⑤ Aliphatic polyester blends	·Blends of aliphatic polyesters and general-purpose plastics	·Mechanical strength can be improved ·Transparent films can be made ·Various plastics can be made	·Shopping bags ·Various kinds foam containers ·Bottles	·High cost ·Biodegradability differs depending on the state of the blending	·Development of intersoluble agents ·Elucidation of relationship between physica and chemical properties and biodegrad.

different starting substance to the same bacteria used to produce Biopol (Alcaligenes eutophus).

Chitin and chitosan, which were mentioned in 2.3.5, are getting attention as biodegradable plastics that are derived from natural polymers. Nishikawa, et al.,[16] are succeeding in developing low-cost, easily-moldable biodegradable plastics by compounding chitosan and cellulose.

As biodegradable synthetic polymers, polyvinyl alcohol (PVA), polyether, polyurethane, copolymers of aromatic polyester and aliphatic polyester, and copolymers of polyamide and aliphatic polyamide are reported.[17]

(b) Photodegradable Plastics

A photodegradable plastic called ECO, which is a copolymer of ethylene and carbon monoxide, has already been made into products; it has over ten years of good grades. There is also the example of a photodegradable plastic material for water and temperature retention in arid-land farming that breaks down in time with the harvest season. However, unlike biodegradable plastics, it takes time for photodegradable plastics to completely decompose into water and carbon dioxide. Furthermore, because they do not break down in soil, there are even some who have voiced their doubts about the effectiveness of photodegradable plastics.

(6) Biomass

Biomass, a concept that was originally called "biological mass" in ecology, expresses the weight or amount of energy in plants and animals and other such organic entities on the earth. Biomass often generally means the organic substances that living organisms use solar energy to produce. Uses of biomass that make the most of it as a "resource that is reproduced" are, of course, its use as an energy source, and then its uses as food, fodder, and as raw materials for industry, and its use in maintaining and improving the environment. Biomass is categorized as a product from agriculture, forestry, or fisheries, or as an under-utilized resource (Figure 2.3.8-6[19]).

Biomass is solar energy stored as organic chemical energy; the energy can be taken out in the form of hydrocarbons. The use of enzymes and microorganisms is getting attention as technology for efficiently and selectively taking the effective components from biomass resources that have complex high-order structures, i.e., cellulose and other such polysaccharides, proteins, lignins, fats, etc. As examples of this, we will discuss the research trends in ethanol fermentation and methane fermentation.

(a) Ethanol Fermentation

Fermenting ethanol from sugar cane or blackstrap molasses, which are polysaccharides, is both efficient and technically easy. Techniques for fermenting ethanol from starch and cellulose, however, involve complicated processes and necessitate the development of advanced technology. For example, research is being carried out on 1) techniques using genetic recombination to breed yeasts that synthesize enzymes that break down starches, and then directly forming ethanol without going through the process where the starches turn into sugars[20]; 2) techniques for decomposing lignin, a ligneous material that is difficult to break down, by means of microorganisms[21]; and 3) isolating microorganisms that activate powerfully in response to cellulase, which is an enzyme that decomposes cellulose.[22]

(b) Methane Fermentation

Methane fermentation is a phenomenon that occurs naturally in offensive places such as paddies and swamps where there are a lot of organic substances. Since long ago there have been techniques of using as fuel the methane that is

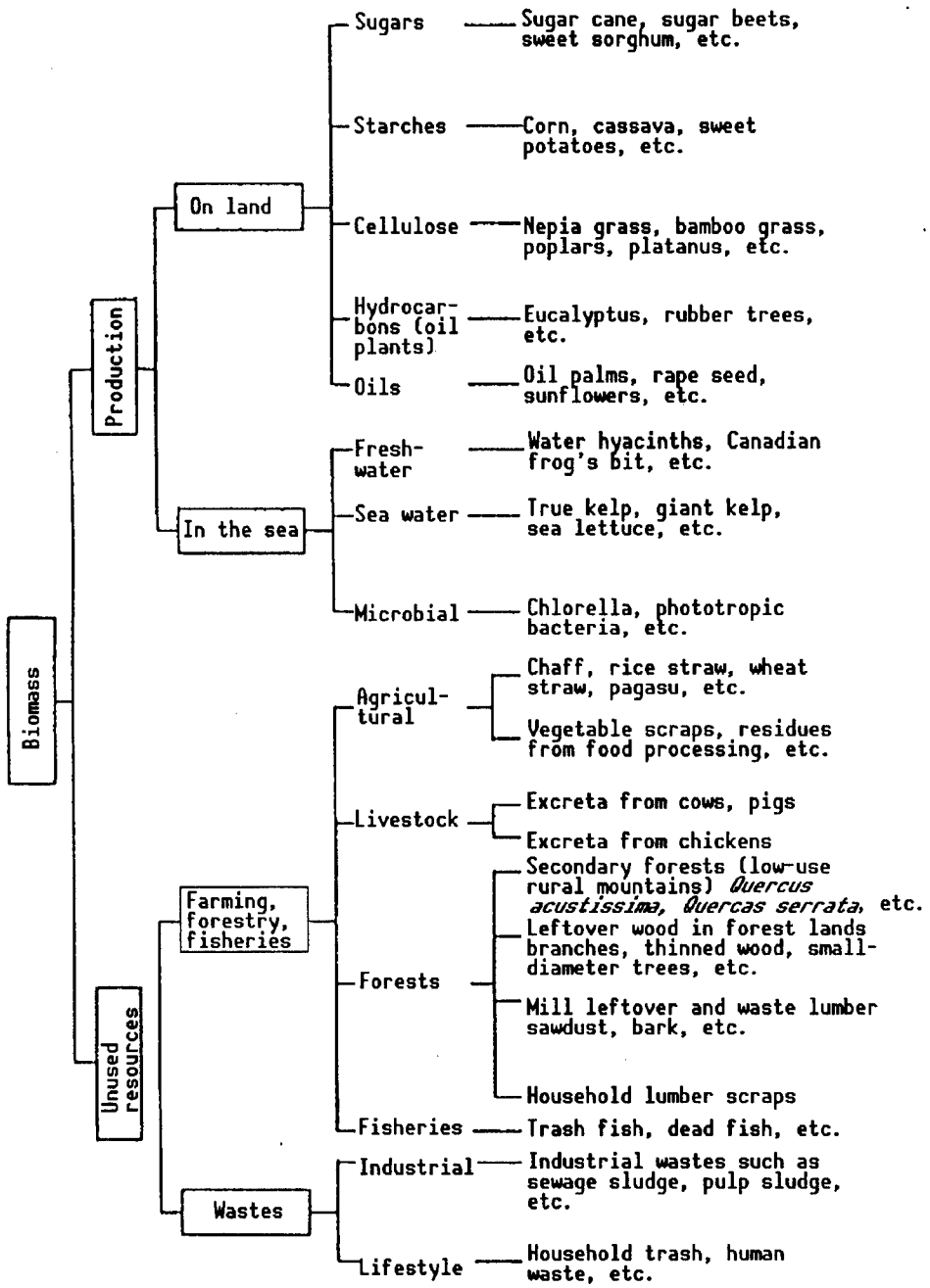


Figure 2.3.8-6 Classification of Biomass Resources

produced when livestock wastes and other such substances are put into a fermentation tank. With methane fermentation, oxygen need not be supplied and aeration energy is not necessary; it also produces little sludge. However, the decomposition is slow, so efforts are being made to develop reactors with high methane-formation efficiency.[23]

The microorganisms in the methane fermentation sludge consist of numerous microorganisms such as hydrolysis bacteria, which break down cellulose and

other such ligneous materials, and methane- producing bacteria. It is thought that advances in research on these symbiotic bacteria will enable more efficient methane fermentation. Practical applications of enzymes that convert sludge into methanol, which is a liquid fuel (suitable for transportation) are also anticipated.[24]

(7) Bacteria Leaching

The bacteria that are called autotrophic bacteria and live in underground mines are very tough creatures that grow in acidic environments where there are a lot of heavy metals. These bacteria get their energy by oxidizing inorganic compounds of metals and sulfur, and they use carbon dioxide to synthesize cellular components. In particular, the ferroxydation bacteria (*Thiobacillus ferroxydans*) changes the iron in many different compounds into trivalent iron, which has an extremely powerful capacity for oxidation; trivalent iron has the effect of dissolving out many metals from natural ores, e.g., copper, uranium, zinc, nickel, tin, etc. Thus, the name bacterial leaching is given to the technique of using bacteria to dissolve out various kinds of metals. Bacteria leaching is primarily used as a technique for dissolving out copper from open-pit mines; in the United States, more than 10% of the total amount of copper produced is produced by means of bacteria leaching. In Japan not much bacteria leaching is done because, with our rainy and humid climate, the leach liquor used for dissolving ends up getting diluted. However, bacteria leaching is gaining attention as a means of solving current problems that surround the mining industry, such as 1) the exhaustion of high-quality mining resources; 2) the movement of mining spots to deeper places underground; 3) environmental pollution problems that are concomitant with the refining of sulfide minerals; and 4) higher energy costs needed for fire refining (refining methods that use blast furnaces).

The problem with bacteria leaching is that dissolving out the metals takes time. To make the dissolution speed higher and improve the efficiency, heavy-metal- and acid-resistant thermophilic microorganisms will have to be bred, and there will have to be continuous, more efficient leaching inside the reactor. For example, because *E. coli* in which the protein that detoxifies heavy metals (metallothionein) was cloned remarkably improved their resistance against heavy metals, they are thought to hold promise as leaching microorganisms.

In addition to mining-related applications, such as in low-grade ores and scrap ores (debris), bacteria leaching is also expected to have applications in the processing of waste water that contains heavy metals, desulfurization, and so on. That will necessitate molecular breeding (breeding that involves the direct manipulation of DNA) of microorganisms that corresponds to the particular objective.

References

1. KAGAKU ASAHI, December 1990, p 132.
2. T. Yubisuku, TRIGGER, October 1990 special edition, p 120.
3. NIKKAN KOGYO SHIMBUN, 14 January 1991.
4. NIKKEI SANGYO SHIMBUN, 14 November 1991.
5. O. Nakasugi, KANKYO JOHO KAGAKU, Vol 18, 1989, p 2.
6. H. Urano, KOGAI TO TAISAKU, Vol 26, 1990, p 1155.
7. Y. Hanai, ANZEN KOGAKU, Vol 27, 1988, 336.
8. NIKKAN KOGYO SHIMBUN, 26 January 1990.
9. T. Murata, KOGAI TO TAISAKU, Vol 25, 1989, p 1178.
10. H. Nagakubo, Ibid., p 1002.
11. NIKKAN KOGYO SHIMBUN, 25 January 1990.
12. M. Iwasaki, TRIGGER, October 1990 special edition, p 134.
13. Y. Tokiwa, KOGYO ZAIRYO, Vol 38, 1990, p 29.
14. Y. Tokiwa, KAGAKU ASAHI, March 1990, p 30.
15. Y. Doi, KAGAKU, Vol 45, 1990, p 104.
16. M. Nishiyama and J. Hosokawa, KOGAKU ZAIRYO, Vol 38, 1990, p 47.
17. Y. Tokiwa, Microbial Decomposition of Synthetic Polymers and the Biodegradability of Polymer Blends (Joint Symposium of BIDEC and the Kinki Bioindustry Promotion Council, 13 October 1989, Osaka).
18. D. Gilead and G. Scott, Time-Controlled Stabilization of Polymers, Developments in Polymer Stabilization-5, Chapter 4, Applied Science Publisher, 1982.
19. A. Hayami, Baiomasu, Seibutsu Shigen no Kodo Riyo (Advanced Utilization of Biological Resources), (edited by Nippon Noei Kagaku Kai), Asakura Shoten, pp 1-26.
20. H. Yoshizumi, HAKKO TO KOGYO, Vol 45, 1987, p 579.
21. M. Kuwahara, BAIOSAIENSU TO INDASUTORI, Vol 46, 1988, p 3374.

22. T. Yamanobe, Y. Mitsuishi and Y. Takasaki, AGRIC. BIOL. CHEM., Vol 51, 1987, p 65.

23. K. Kida and K. Nakata, BAIOSAIENSU TO INDASUTORI, Vol 45, 1987, p 107.

24. K. Takeda; Baiotekunoroji, Raifusaiensu, Baiomasu Riyo Gijutsu (Biotechnology, Bioscience, and Biomass Utilization Techniques), Nippon Bijinesu Repoto, 1990, p 178.

25. T. Karube, Y. Katsuki and I. Endo, Baio no Chosen (The Biochallenge), Kodansha, 1985.

2.3.9 Computing S&T

In recent years computers have come to play an increasingly important role in the advance of science and technology. The field of "computing S&T" that we will take up here involves modeling natural and artificial structures on a computer to re-express natural phenomena and the phenomena in artificial structures; altering conditions in various ways in order to predict changes in phenomena; and investigating the suitability of those models. It also involves discerning the true nature of phenomena and designing new substances that have new functions.

While computing S&T is a field of its own, at the same time it is important in propelling the evolution of all S&T, given that it is neither "theoretical" nor "experimental" scientific and technological methodology, but a third new category of methodology. The remarkable advances in recent years in the capabilities of supercomputers tremendously heightens the possibilities and importance of computing S&T. Furthermore, it is predicted that computer simulation and computer graphics will become more necessary in not only S&T but in all fields of human activity. In this sense, too, computing S&T will become increasingly important in the future.

The ways of using computing S&T in research are broadly divided into two methods. One method involves computing simplified models, in terms of primary principles and without including experiential parameters, to predict the structure of substances, simulate the movement of complex systems, and so forth. The other method is to select optimal materials, design new materials, and so forth, starting from a database in which vast amounts of experimental data is accumulated over the years. The "creation of the universe" computer experiment described later in subsection (1), and predicting the structure of substances by means of molecular dynamics, described in subsection (2), are examples of the first method. Drug design using computers, described in subsection (3), is an example of the second method. In order to bring about further advances in computing S&T research, the computational power of supercomputers will have to be improved, and supercomputers will have to be such that any researcher can use them. In order to promote research that uses the second method of computing S&T, in addition to improved capabilities and user-friendliness in supercomputers, various kinds of databases will have to be set up as property that is common to mankind, and those databases will have to be such that anybody, anywhere can use them.

Below we will give an overview of several examples of computing S&T research.

(1) "Creation of the Universe" and "Formation of the Planets" Computer Experiments

In the natural sciences, which are generally based on experiments, theory and experiment have evolved together. In a field such as cosmology, however, even if observations can be made, experiments are, in principle, not possible. In an experiment, various conditions and environments can be freely controlled to a certain degree, and relative studies can be made of the results obtained under different conditions. In contrast, an observation is just looking passively at the appearance of reality; observation has a completely different nature than actively experimentation. Thus, in cosmology there are constraints on the research methods, i.e., in principle, experiments cannot be done. However, advances in computers have made possible "computer experiments," even in fields like cosmology where experiments are in principle impossible. In other words, with the vast memory and super-high speed of supercomputers, simulation of the entire universe can now be done with a sufficient degree of accuracy.[1,2]

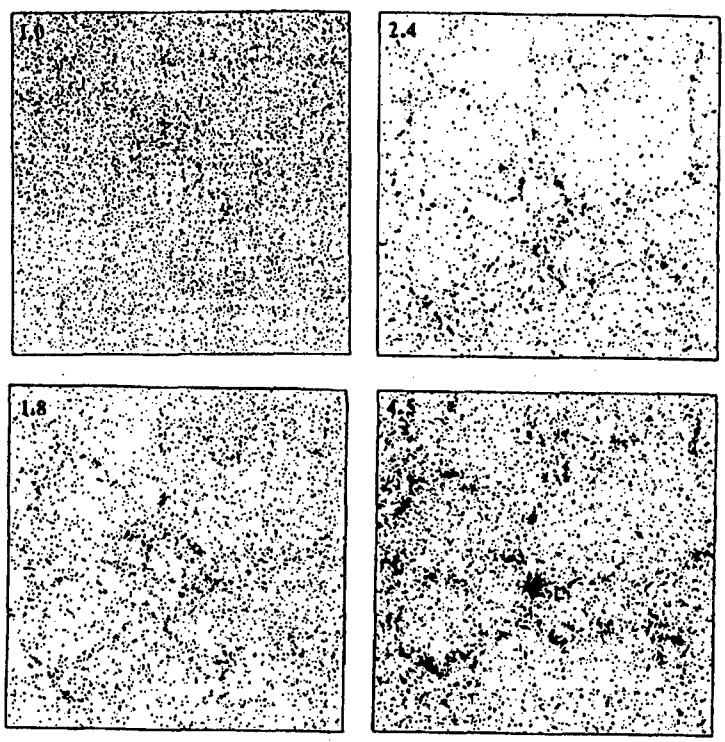


Figure 2.3.9-1 Large-Area Structural Evolution of the Universe in the 'Cold Dark Matter' Scenario
Numbers in the left-hand corners show the sizes of the scale factors. The spatial mesh is 64 x 64 x 64; the number of particles is 32,768; the computational time was about 30 minutes on a VAX 11/750.

There are now several theoretical models that attempt to explain the structural formation of the universe, starting with the scenario of "Cold Dark Matter"; simulation of the structural formation of the universe based on these theoretical models is widely carried out.[1,2] Figure 2.3.9-1 is an example of the simulation of the large-scale structure of the universe according to the Cold Dark Matter scenario.[3] In order to choose the "true universe" from the various theoretical models of the formation of the universe, observing the universe in a deeper, broader, and more precise fashion is essential. Along with that, however, direct comparison of observational results with the results of simulations based on the theoretical models is becoming an increasingly powerful method.[2]

In the field of astrophysics, in addition to the structural formation of the universe described above, computer experiments on the formation of planets from gas-fluid bodies are also being done.[4]

(2) Predicting the Structures of Crystals and Amorphous Substances, and Simulation of Electronic Materials and Electronic Devices

Using computations to explain and predict the natures of substances known to have crystalline structures is a central topic in the theory of physical properties. In contrast, while explaining and predicting the structures of substances is another important topic, little research has been done up until now in this area. The reason for that is, even to just compute the cohesion energies for a specific substance, or for several highly possible crystalline structures, with enough accuracy to compare large and small relationships, an enormous amount of numerical calculations were needed with computers of the past. With the recent advances in computers, however, molecular dynamics,[5] which follows from the classical dynamics of atomic motion, can now be used to predict not only ideal crystalline structures, i.e., those with minimal cohesion energy, but also the actual structures of solids that are created under various sample-producing conditions.[6]

Actually, molecular dynamics is being used in simulations of amorphous silicon structures,[6,7] molecular beam epitaxy (MBE),[8,9] metallic organic chemical vapor deposition (MOCVD),[10] and reconfiguration of silicon (001) surfaces.[11] Figures 2.3.9-2 and -3 show typical examples of reconfigurations obtained on (4 x 2) silicon (001) surfaces.[11] Starting from ideal surfaces, even with relaxation at the same set temperature of 300 K, there will be several structures that satisfy the energy minimum, and depending on the initial speed, any of those will be realized. In Figure 2.3.9-2, c(2 x 2) was obtained; in Figure 2.3.9-3, c(4 x 2).

Because of the importance of its applications, a good deal of research is being done on the simulation of silicon materials and devices.[12]

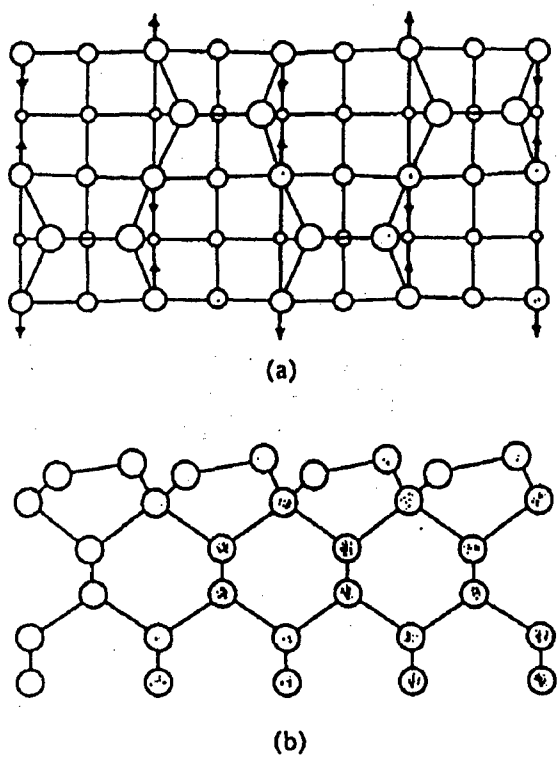


Figure 2.3.9–2 Example of Reconfigurations Obtained by Means of Molecular Dynamics: c(2 x 2)
In surface diagram (a), smaller circles indicate atoms that are deeper from the surface. The arrows show the changes in position of the second layer atoms. In the diagram of the lateral face, (b), the dimers are at an angle of about 10 degrees with respect to the surface.

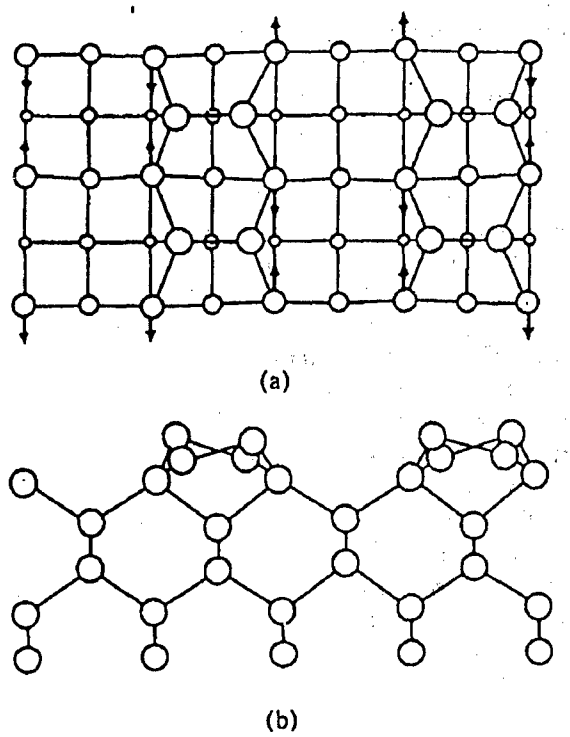


Figure 2.3.9–3 Example of Reconfigurations Obtained by Means of Molecular Dynamics: c(4 x 2)
(a) surface diagram; (b) diagram of the lateral face.

(3) Computational Chemistry, and Pharmaceutical Design Using Computers

In the field of chemistry as well, the evolution of computational science is remarkable. The electron states of substances, which are described by quantum mechanics, can be determined by using a computer to solve the Schroedinger equation. It is now possible to compute the structures of molecules that are not too large (molecules having up to 10 atoms) with a precision where the average inter-nuclear distance is 0.01 Å, and to predict the characteristics of the molecules by means of computation.[13,14] Furthermore, with the help of experimental data, the solid structures of macromolecules such as proteins are being simulated; in order to understand the manifestation of functions, computer simulations are used to investigate the dynamics of atoms inside proteins and other such macromolecules[15,16]; and light is being shed on the interrelationships among molecules' three-dimensional, electronic, and hydrophobic characteristics and the characteristics that the molecules display.

Computer simulations are being done not only for the purpose of elucidating the functions of molecules that currently exist, but also for the purpose of creating molecules that have new functions. One of those important areas is drug design, where researchers employ database information that was accumulated in the past, and then make free use of computer simulation and computer graphics.[17,18] With conventional methods that rely on the experience and intuition of researchers, the probability of finding a new drug is one in a thousand or less. Of these kinds of methods, expectations are growing for drug design by means of computers as a technique for the rational design of drug candidates.[18] The important thing in drug design is simulating the structure of the drug when it is binding to a receptor (B in Figure 2.3.9-4[18]) and then finding out the structures that have functions for obstructing and activating the action of the receptor.

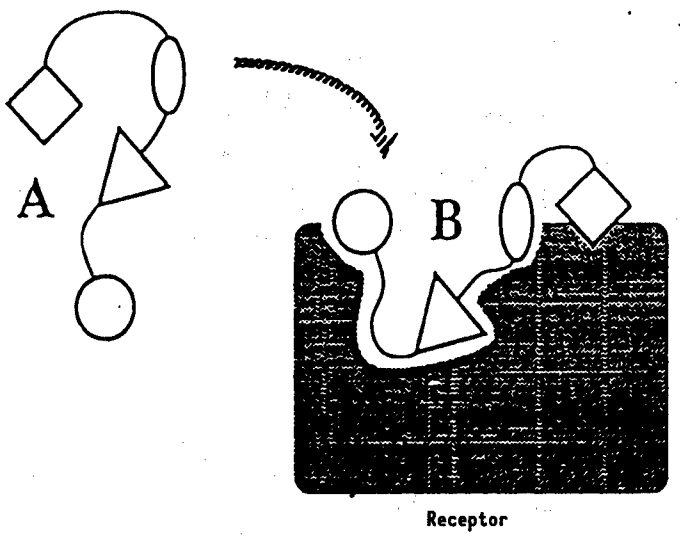


Figure 2.3.9-4 Type Diagram of Structural Changes of a Drug
Shows the activity when a drug changes its Structure A in a crystal or solution to Structure B when it binds to receptor.

(4) Modern Meteorology By Means of Computer Simulation

The connection between meteorology and electronic computers goes back to the birth of the electronic computer. When von Neumann organized the project to produce an electronic computer at Princeton's high-class research lab in 1946, he took up weather forecasting, which requires numerical solutions to nonlinear differential equations, as a problem that computers should be used to solve. He set up a meteorology group, and then in 1950 made public his thesis on the first numerical weather forecast.[19]

A summary of the world's weather is understood from simulations that are based on the "general atmospheric circulation model."[19,20] Extratropical cyclones, which are born out of the temperature differences between the equator and the poles, act in such a way as to eliminate the temperature differences by carrying heat to the poles. On the other hand, however, the intensity of sunlight falling on the earth is the greatest at the equator, and this always creates a temperature difference with the poles. The "general atmospheric circulation model" is based on this kind of idea. Figure 2.3.9-5[19] shows the average monthly pressure distribution for January that was obtained with an atmospheric circulation model of the Meteorological Agency's Meteorological Research Institute (upper diagram) and the actual distribution corresponding to that (lower diagram).

In the simulation of Figure 2.3.9-5, climatic fluctuations due to increases in CO_2 concentrations are also being estimated by using a method that involves computing seawater temperature, sea-ice thickness, snow depths on land, and even the amount of moisture retention in the ground, as variables. Although the distributions of seawater temperatures and sea and land ice apply observed values as external conditions, effects from the outside are restricted to the distribution of sunshine over land and water and the distribution over mountain ranges. According to the results computed from this simulation, a doubling of the CO_2 concentration will cause the overall average atmospheric temperature of the earth to rise about 3°C, and the temperature of the polar regions to rise about 7°C.[19]

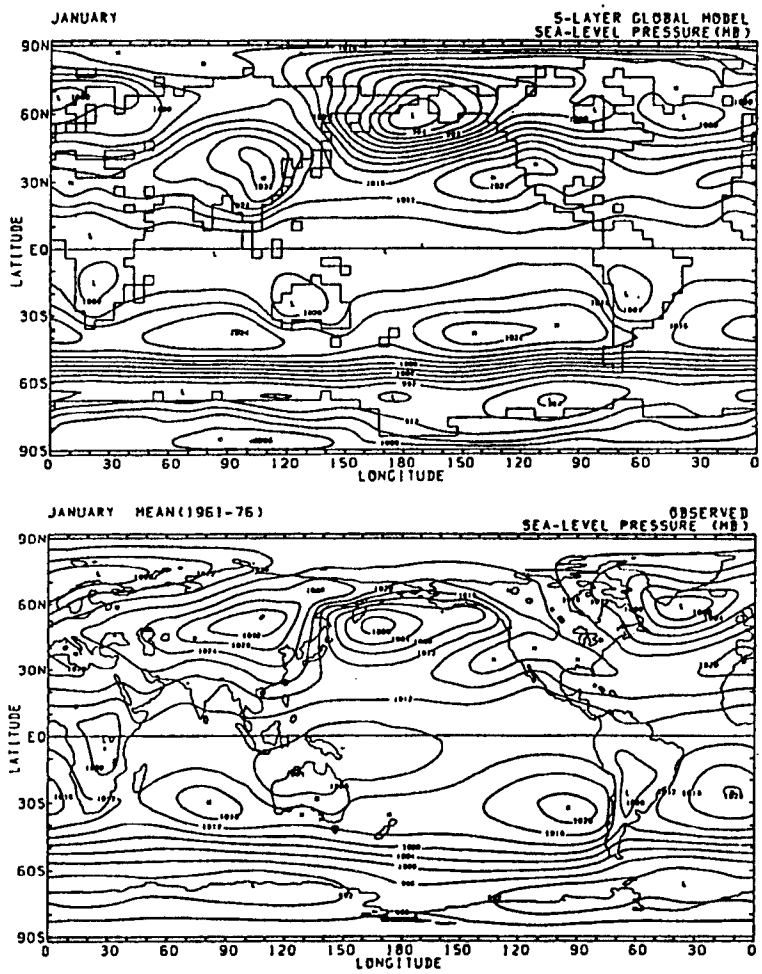


Figure 2.3.9-5 Average Monthly Pressure Distribution for January That Was Obtained With the Meteorological Research Institute's Atmospheric Circulation Model (upper) and the Corresponding Distribution That Was Actually Observed (lower) By Tokioka et al, 1985.

In earth science fields that include meteorology, as in astrophysics, experiments in the originally intended sense are not possible, but because "computational experiments" have become possible, advances are anticipated in research that is based on the new idea (but a rather common idea in other fields) of experimenting under artificial conditions.[19,20]

References

1. K. Sato and Y. Sudo, SURIKAGAKU, October 1985, p 7.

2. T. Suginohara, KAGAKU ASAHI, February 1991, p 22.

3. M. Davis, G. Efstathithiou, C.S. Frenk and S.D.M. White, ASTROPHYS. J., Vol 292, 1985, 371.

4. M. Miyama, Keisan Butsurigaku (Computational Physics), edited by the Nippon Butsuri Gakkai, Baifukan, 1991, p 74.

5. For example, M. Tanaka, Keisan Butsurigaku to Keisan Kagaku (Computational Physics and Computational Chemistry), edited by R. Yamamoto, Kaibundo, 1988, p 1.

6. T. Uda, Ibid., p 80.

7. T. Uda, Konpyuta ni yoru Shirikon Tekunoroji I (Silicon Technology Using Computers I), edited by R. Yamamoto, Kaibundo, 1990, p 61.

8. K. Hara, M. Ikeda, O. Ohtsuki, K. Terakura, M. Mikami, Y. Taga and T. Oguchi, PHYS. REV., Vol B39, 1989, 9476.

9. K. Ota, Konpyuta ni yoru Shirikon Tekunoroji I (Silicon Technology Using Computers I), edited by R. Yamamoto, Kaibundo, 1990, p 115.

10. M. Menon and R.E. Allen, Vol B38, 1989, 6196.

11. T. Uda and S. Ihara, NIPPON BUTSURI GAKKAISHI, Vol 46, 1991, 314.

12. For example, Konpyuta ni yoru Shirikon Tekunoroji I, II (Silicon Technology Using Computers I, II), edited by R. Yamamoto, Kaibundo, 1990; Nihon Kogyo Shinkokai, Zairyo Kaihatsu CAD Chosa Hokoku II (Materials Development CAD Survey II), report of the Electronic Materials Technology Subcommittee, February 1990.

13. H. Hosoya, Keisan Zairyo Kagaku (Computational Materials Science), edited by A. Doyama and R. Yamamoto, Kaibundo, 1987, p 122.

14. H. Kashiwagi, SURI KAGAKU, October 1985, p 61.

15. H. Waizumi, N. Go, Keisan Butsurigaku to Keisan Kagaku (Computational Physics and Computational Chemistry), edited by M. Tanaka and R. Yamamoto, Kaibundo, 1988, p 196.

16. A. Wada, H. Nakamura, and A. Toyama, SURI KAGAKU, October 1985, p 50.

17. G. Yoshida, Keisan Zairyo Kagaku (Computational Materials Science), edited by A. Doyama and R. Yamamoto, Kaibundo, 1987, p 197.

18. M. Ishiguro, KAGAKU TO KOGYO, Vol 44, 1991, 780.

19. T. Matsuno, SURI KAGAKU, October 1985, p 31.

20. A. Sumi, Ibid., August 1989, p 50.

2.4 Directory of Researchers

Table 2.4-1 is a directory of researchers who are involved in the nine representative advanced areas of multidisciplinary research. The names shown in the table are mainly those that came up during interviews, more so than names taken from reference documents. It is a list of representative researchers, but of course is not all-inclusive.

Table 2.4-1 Researcher Directory (1)

(1) Intelligent Materials

No	Researcher	Research field	Affiliated research organization
1	M. Aizawa		Tokyo Institute of Technology Bioscience and Engineering Department, Bioengineering Section
2	T. Oda		Tokyo Institute of Technology Engineering Department, Electronic Physics and Engineering Section
3	A. Okano		Tokyo Women's Medical College Medical Engineering Research Facility
4	J. Tanaka		Science and Technology Agency, National Research Institute for Inorganic Materials, 10th research group
5	H. Sasano		Science and Technology Agency, National Research Institute for Metals, Functional Characteristics Research Department
6	K. Miyata		Tokyo Institute of Technology Engineering Department, Materials Systems Engineering Section
7	H. Katsumata	Magnetism	RIKEN, Magnetism Lab
8	Y. Sakaki	Ultrasmall devices	Tokyo University, Advanced S&T Research Center
9	Y. Sakurai	Medical engineering	Tokyo Women's Medical College
10	T. Shinjo	Artificial lattice magnetism	Kyoto University, Chemistry Lab

Table 2.4-1 Researcher Directory (2)

(2) Frontier Measurement and Control Technology

No	Researcher	Research field	Affiliated research organization
1	M. Aono	Atom craft	RIKEN, Surface Engineering Lab
2	Y. Aoyagi		RIKEN, Laser Science Lab
3	K. Ikuta	Micromechanics	Kyushu Institute of Technology
4	Y. Ishida	Material interconnections	Tokyo University, Production Technology Lab
5	T. Endo	Human genome analysis	RIKEN, Chemical Engineering Lab
6	N. Ogata	Biopolymers	Sophia University, Physics and Engineering Department, Chemistry Section
7	H. Kuroda	SOR chemistry	Tokyo University, Physical Science Department, Chemistry Section
8	Y. Sakurai	Medical engineering (micromachines)	Tokyo Women's Medical College, Medical engineering research facility
9	A. Sawaoka	Elucidation of shock wave phenomena	Tokyo Institute of Technology, Ceramics Center
10	Y. Shiraki	Photonic materials	Tokyo University, Advanced S&T Research Center
11	M. Takami	Atomic manipulation using lasers	RIKEN, Inorganic Chemistry and Physics Lab
12	K. Takeuchi	Cluster evaluation	RIKEN, Separation Engineering Lab
13	H. Tanihata	Research based on unstable nuclear beams	RIKEN, Linear Accelerator Lab
14	H. Toyota	Laser processing technology	RIKEN, Semiconductor Engineering Lab
15	H. Yanagida	Chemical recognition materials	Tokyo University, Advanced S&T Research Center
16	Y. Yamaguchi	Living organisms, ultrafine structures	RIKEN, Microbiological Control Lab
17	I. Yamaguchi		RIKEN, Optical Engineering Lab

Table 2.4-1 Researcher Directory (3)

(3) New Genetic Manipulation Technology

No	Researcher	Research field	Affiliated research organization
1	H. Ikeda	Genetic recombination	Tokyo University, Medical Science Lab
2	T. Ishii	Mechanisms that control genetic expression	RIKEN, Life Sciences Tsukuba Research Center
3	M. Inuzuka	Eucaryotic cell DNA	Fukui Medical School, Medical Dept.
4	E. Ohtsubo	Genetic recombination	Tokyo University, Applied Microbiology Lab
5	T. Okazaki	Eucaryotic cell DNA	Nagoya University, Physical Sciences Dept., Molecular Biology Section
6	E. Ogawa	Genetic recombination	Osaka University, Physical Sciences Dept., Biological Sciences Section
7	A. Sakakura	Eucaryotic cells	RIKEN, Life Sciences Tsukuba Research Center
8	K. Shino	Molecular biology of plants	RIKEN, Life Sciences Tsukuba Research Center
9	T. Shibata	Genetic recombination	RIKEN, Microbiology Lab
10	T. Nishimoto	Chromosome construction	Kyushu University, Medical Dept., Molecular Life Sciences
11	F. Hanaoka	Eucaryotic cells	RIKEN, Radiobiology Lab
12	M. Yanagida	Chromosome construction	Kyoto University
13	H. Yoshikawa	Eucaryotic cell DNA	Osaka University, Medical Dept.

Table 2.4-1 Researcher Directory (4)

(4) New Neuroscience and Technology

No	Researcher	Research field	Affiliated research organization
1	Y. Aoyagi	Neurodevices	RIKEN, Laser Science Lab
2	S. Shiono		Mitsubishi Electric (KK) Central Research Lab, Biotechnology Research Group
3	I. Yamaguchi	Neuroscience in connection with image processing and image recognition	RIKEN, Optical Engineering Lab
4	K. Nakano	Associative memory models	Tokyo University, Engineering Dept. Digital Engineering Section
5	K. Fukushima	Pattern recognition with self-organization functions	Osaka University, Basic Engineering Dept., Bioengineering Section
6	S. Amari	Neurocomputers	Tokyo University, Engineering Dept., Digital Engineering Section
7	M. Ito	Learning mechanisms in the brain	Tokyo University, Medical Dept.
8	Y. Miyashita	Memory mechanisms the brain	Tokyo University, Medical Dept.

Table 2.4-1 Researcher Directory (5)

(5) Biomolecular S&T

No	Researcher	Research field	Affiliated research organization
1	S. Aizawa	Soft polymer structures	New Technology Enterprises Group, Creative S&T Promotion Enterprise (within Stanley Electric)
2	T. Iizuka	Role of Fe, O in the bodies of living organisms	RIKEN, Biophysical Chemistry Lab
3	T. Ishimura	Role of Fe, O in the bodies of living organisms	Keio University, Medical Dept.
4	T. Uno	Mechanisms of cell cycle regulation	Tokyo University, Applied Microbiology Lab
5	S. Ogawa	Sugar chain engineering	RIKEN, Cell Control Chemistry Lab
6	H. Katsumata	Biomagnetism	RIKEN, Magnetism Lab
7	T. Kanegasaki	Role of Fe, O in the bodies of living organisms	Tokyo University, Medical Sciences Lab
8	T. Kira	Science of large molecular aggregate systems	RIKEN, Reaction Physics and Chemistry
9	H. Kuzuhara	Enzyme models	RIKEN, Organic Biochemistry Lab
10	T. Sakakura	Eucaryotic cells	RIKEN, Life Sciences Tsukuba Research Center
11	H. Sasagibe	Interactions between living organisms and inorganic substances	RIKEN, Biopolymer Physics Lab
12	K. Seno	Mechanisms of cell cycle regulation	National Genetics Lab
13	Y. Nagai	Elucidating principles of living organisms	Tokyo University, Medical Dept.
14	I. Morishima	Role of Fe, O in the bodies of living organisms	Kyoto University, Engineering Dept., special study in Molecular Engineering
15	T. Yamakawa	Sugar chains, polymer films	Tokyo Prefecture Clinical Medicine Research Institute
16	I. Yamaguchi	Interactions among living organisms	RIKEN, Microbiological Control Lab
17	I. Yamaguchi	Recognition mechanisms of the eye	RIKEN, Optical Engineering Lab

Table 2.4-1 Researcher Directory (6)

(6) Temporal Bioscience and Technology

No	Researcher	Research field	Affiliated research organization
1	K. Abe	Clinical temporal biology	University of Occupational and Environmental Health, Neuromedicine Lab
2	K. Eto	Clinical temporal biology	University of Occupational and Environmental Health, Neuromedicine Lab
3	A. Kawasaki	Clinical temporal biology	Kyushu University, Health Science Center
4	K. Takahashi	Clinical temporal biology	National Mind and Nerve Center, Mental Health Maintenance Lab
5	S. Takahashi	Clinical temporal biology	Shiga University of Medical Science, courses in neuromedicine
6	K. Honma	Clinical temporal biology	Hokkaido University, Medical Dept., first course in physiology

Table 2.4-1 Researcher Directory (7)

(7) New Global Environmental S&T

No	Researcher	Research field	Affiliated research organization
1	A. Ichihara	Automotive catalysts	Japan Catalytic Chemical Industry (KK) Catalyst Lab
2	S. Ogawa	Sugar chain engineering	RIKEN, Cell Control Chemistry Lab
3	I. Kobori	Deserts	Meiji University, Politics and Economics Dept.
4	T. Takaichi	Freon substitutes	Showa Denko (KK) Chemical Products Lab
5	K. Tsuchiya	Remote sensing	Chiba University, Video Observation Research Center
6	S. Hayashida		National Institute for Environmental Research
7	O. Furukawa	Secondary batteries	Sanyo Electric (KK) Functional Materials Lab, Electrochemical Research Dept.
8	M. Maekakiuchi		Kiyomizu Construction (KK), Main Technology Dept., Desert Development Office
9	A. Mizuno	Freon gas decomposition techniques	Agency of Industrial Science and Technology, National Research Institute for Pollution and Resources
10	I. Yamaguchi	Control of plant-disease causing insects	RIKEN, Microbiological Control Lab
11	M. Yamaji	Electric car batteries	Japan Storage Battery (KK), R&D headquarters
12	N. Washida		National Institute for Environmental Research, Atmospheric Environment Dept.
13	K. Watanabe		National Institute for Environmental Research, international research cooperation official

Table 2.4-1 Researcher Directory (8)

(8) Recycling S&T

No	Researcher	Research field	Affiliated research organization
1	T. Yubisuki	Artificial photo-synthesis	Agency of Industrial Science and Technology, National Research Institute for Pollution and Resources
2	M. Iwasaki	Recycled paper	Oji Paper (KK) Central Research Lab
3	H. Urano	Technology for removing, recovering organochlorine solvents	Yokohama National University, Engineer-Dept., Substance Engineering Section
4	S. Ogawa	Sugar chain engineering	RIKEN, Cell Control Chemistry Lab
5	K. Takeuchi	Separation, enrichment by means of lasers	RIKEN, Separation Engineering Lab
6	K. Takeda	Biomass utilization technology	Agency of Industrial Science and Technology, Fermentation Research Institute for Pollution and Resources
7	Y. Tokiwa	Degradable plastics	Agency of Industrial Science and Technology, Fermentation Research Institute for Pollution and Resources
8	Y. Doi	Degradable plastics	Tokyo Institute of Technology, Resources Chemistry Lab
9	M. Nishikawa	Chitin, chitosan	Agency of Industrial Science and Technology, Government Industrial Research Institute, Shikoku
10	Y. Hanai		Yokohama National University, Environmental Science Research Center
11	J. Hosokawa	Chitin, chitosan	Agency of Industrial Science and Technology, Government Industrial Research Institute, Shikoku

Table 2.4-1 Researcher Directory (9)

(9) Computational S&T

No	Researcher	Research field	Affiliated research organization
1	M. Ishiguro	Computational chemistry	Suntory Biomedical Research Lab
2	T. Iwata		JAERI, Physics Dept.
3	K. Uda		Kyoto University, Engineering Dept., Mathematical Engineering Section
4	T. Uda	Computational physics	Hitachi Ltd., Basic Research Lab
5	I. Okada		Tokyo Institute of Technology, General Physics and Engineering Lab
6	Y. Kataoka		Kyoto University, Physical Sciences Dept., Chemistry Section
7	N. Go	Biophysics	Kyoto University, Physical Sciences Dept., Chemistry Section
8	M. Suzuki	Statistical dynamics	Tokyo University, Physics Dept.
9	M. Takahashi		Tokyo University, Substances Lab
10	M. Tanaka		Tohoku University, Engineering Dept., Basic engineering chemistry classroom
11	K. Nakanishi		Kyoto University, Engineering Dept., Engineering chemistry classroom
12	K. Nishihara		Osaka University, Laser Fusion Research Center
13	S. Nose		Keio University, Physics and Engineering Dept., Physics Section
14	H. Hiwatari		Kanazawa University, Physics and Engineering Dept., Physics Section
15	R. Yamamoto	Environment-resistant materials	Tokyo University, Advanced S&T Research Center

2.5 Summary of Theme Names

2.5.1 Summary of Theme Names, From Interviews

Although Table 2.1.2-1 already showed examples of research themes that were obtained from interviews of knowledgeable people, Table 2.5.1-1 shows examples of research themes that correspond to the nine representative areas of multidisciplinary research.

Table 2.5.1-1 Summary of Theme Names, From Interviews (1)

(1) Intelligent Materials

Research theme	Keyperson	Contents
1 Artificial lattice magnetism	T. Shinjo (Kyoto University, Chemistry Lab)	New physical properties are expected from the combination of insulators and metals
2 Organic ferromagnets	H. Katsumata (RIKEN)	Now magnetism is detected at temperatures on the order of that of liquid nitrogen
3 Relationship between magnetism and high Tc	H. Katsumata (RIKEN)	Theoretical elucidation of high-temperature superconductivity
4 Neurocomputers	Y. Aoyagi (RIKEN)	Development of neurodevices on chips (intelligent materials)

Table 2.5.1-1 Summary of Theme Names, From Interviews (2)

(2) Frontier Measurement and Control Technology

Research theme	Keyperson	Contents
1 Control of molecular arrangement that applies chemical reaction mechanisms of living organisms	N. Ogata (Sophia University, Physics and Engineering Dept.	Elucidating chemical reactions that occur under normal temperatures and pressures in living organisms (why almost 100% are achieved). Aiming for molecular arrangement control in future.
2 Processing technology that uses lasers	H. Toyota (RIKEN)	Fine processing technology. Applications in opto-related devices.
3 Short-wavelength laser technology	" "	Short-wavelength lasers and optical devices. X-ray microscopes, X-ray lithography, etc.
4 Mesoscopic science	M. Takami(RIKEN) K. Kutsu (Technological Univ. of Nagaoka)	Elucidating mechanisms of Freon manifestation. Techniques that utilize selective reactions by means of solid structures similar to enzymes.
5 Atomic manipulation	M. Takami (RIKEN)	Super-low-temperature atomic gas deposition using lasers.
6 Development of ppt-level analysis methods	" "	Laser-resonance ionization, radioactive analysis.
7 Atomic control (Atom Craft)	M. Aono (RIKEN)	Manipulating atoms one by one. Applications in memory, genetic manipulation, etc.
8 Extremely high vacuum generating technology	" "	Aiming for $1/10^{10}$~10^{11} Torr and lower vacuums.
9 Completely new surface measurement technology	" "	Development and evaluation of completely new apparatuses.
10 Micromechanics (micromachines)	K. Ikuta (Kyushu Inst. of Technology	Micropumps, microvalves, etc.
11 Cluster evaluation	K. Takeuchi (RIKEN)	Chemical elucidation of cluster reactions, which cause obstacles in uranium refining, and refining.

Table 2.5.1-1 Summary of Theme Names, From Interviews (3)

(3) New Genetic Manipulation Technology

Research theme	Keyperson	Contents
1 Elucidation of aging genes	F. Hanaoka (RIKEN)	Basic mechanisms of cancer gene occurrence. Predicting what will become important in 10 or so years.
2 Eucaryotic cell DNA synthesis	M. Inuzuka (Fukui Medical School, Medical Dept.) T. Okazaki (Nagoya Univ., Physical Sciences Dept.) M. Yoshikawa (Osaka Univ., Medical Dept.)	Research on DNA replication, division. (Much is unclear about eucaryotic cells.)
3 Chromosome construction	F. Hanaoka (RIKEN) M. Yanagida (Kyoto Univ.) T. Nishimoto (Kyushu Univ.) T. Shibata (RIKEN)	Research on structure and functions of chromosomes. (Dynamics of chromatin in eucaryotic cells).
4 Genetic recombination	E. Ogawa (Osaka Univ., Physical Sciences Dept.) H. Ikeda (Tokyo Univ., Medical Science Lab) E. Ohtsubo (Tokyo Univ., Applied Microbiology Lab) T. Shibata (RIKEN)	Elucidating mechanisms genetic recombination of chromosomes, and the relationship with proteins.
5 Genetic manifestation control mechanisms	T. Ishii (RIKEN)	Elucidating the mechanisms of manifestation of genes that are the basis of high-order life phenomena.
6 Molecular biology of plants	K. Shino (RIKEN)	Elucidation of photosynthesis (substance metabolism), totipotency of differentiation, and environmental responses

Table 2.5.1-1 Summary of Theme Names, From Interviews (4)

(4) New Neuroscience and Technology

Research theme	Keyperson	Contents
1 Neurocomputers	Y. Aoyagi (RIKEN)	Development of neurodevices on chips (intelligent materials).
2 Neuroscience in connection with image processing and image recognition	I. Yamaguchi (RIKEN)	Research that ties together neurocomputers and image processing. Moving-image processing, etc.
3 Biosensors	M. Karube (Tokyo Institute of Technology, Resources Chemistry Lab)	

Table 2.5.1-1 Summary of Theme Names, From Interviews (5)

(5) Biomolecular S&T

	Research theme	Keyperson	Contents
1	Mechanisms of cell cycle regulation	T.Uno (Tokyo Univ., Applied Microbiology Lab) K.Seno (National Genetics Lab)	Elucidating the mechanisms that control the cell cycle.
2	The roles of iron and oxygen in the bodies of living organisms	T. Iizuka (RIKEN) T. Ishimura (Keio Univ., Medical Dept.) I. Morishima (Kyoto Univ., Engineering Dept.) T. Kanegasaki (Tokyo Univ., Medical Dept.)	Elucidating the roles that iron plays in enzymes (cytochrome oxidase, detoxication enzyme, etc.) that use oxygen and hemoglobin (a macromolecular complex containing iron)
3	Interactions among plants and other living organisms	Y. Yamaguchi (RIKEN)	Elucidating subtances that play a part in interactions among living organisms (substitutes for harmful agricultural chemicals, etc.
4	Basic research on enzyme models	H. Kuzuhara (RIKEN)	Basic research on biomimetics. Research on interactions between proteins and between proteins and sugars (molecular binding).
5	Mechanisms of biofunctional stability	T.Sakakura (RIKEN)	Multifunctional cells in the form of unit aggregates, e.g., genes, monoclonal antibodies, etc., are stable only in limited functions within tissue (many other functions are wasted). Elucidating the mechanisms of what is called cell sociology, i.e., the interactions among cells, information transmission among cells, etc.
6	Sugar chain engineering	S. Ogawa (RIKEN)	Elucidating the mechanisms of protein and sugar chain interaction relating to the social characteristics of cells in living organisms, and the recognition mechanisms of fellow cells.
7	Connection between biomaterials and sugar chain engineering	〃	Research on development of new materials including not just functional and structural analyses but substance production as well.
8	Fusion of sugar chain engineering and protein engineering	〃	Research on biological information other than genetic information (in connection with protein and sugar chain interactions in the information that regulates cell societies).
9	Elucidating the physics of living organisms	S. Aizawa (New Technology Enterprises Group)	Elucidating the mechanisms of ATP energy exchange, differentiation (what determines the form of a living organism), protein interactions, and photosynthesis; genetic-level analysis of muscles.

Table 2.5.1-1 Summary of Theme Names, From Interviews (6)

(5) Biomolecular S&T (continued)

	Research theme	Keyperson	Contents
1	Interactions between living organisms and inorganic substances (Biomimelization)	H. Sasagibe (RIKEN)	Elemental technology of biodevices.
2	Science of large molecular aggregate systems (mesoscopic science)	T. Kira (RIKEN)	The middle of the road between chemistry and biology. Elucidation of intermolecular electron transitions (energy exchange), multi-electron-process oxidation/reduction, and chemical feedback control mechanisms.
3	Chemical reaction mechanisms	N. Ogata (Sophia Univ., Physics and Engineering Dept.)	Elucidation of chemical reactions that occur in organisms at normal temperatures and pressures (why almost 100% are achieved). Aimed at future molecular configuration control.
4	Chemistry of molecular recognition	〃	To study molecular recognition and molecular configuration control during cell differentiation; separation of optical isomers.
5	Biomagnetism	H. Katsumata (RIKEN)	Magnetism of hemoproteins, its role.
6	Recognition mechanisms of the eye	I. Yamaguchi (RIKEN)	Research that links the structure of the eye with its function (observations of psychological phenomenalism, characteristics of the eye, etc.)
7	Mechanisms of biofunctional stability	T. Sakakura (RIKEN)	Multifunctional cells in the form of unit aggregates, e.g., genes, monoclonal antibodies, etc., are stable only in limited functions within tissue (many other functions are wasted). Elucidating the mechanisms of what is called cell sociology, i.e., the interactions among cells, information transmission among cells, etc.)
8	Living organisms and fine structure	Y. Yamaguchi (RIKEN) Y. Aoyagi (RIKEN)	Elucidation of the relationship between growth of a living organism and cell structure (why does growth stop? why is there directionality? etc.) Applications in devices (sensors).

Table 2.5.1-1 Summary of Theme Names, From Interviews (7)

(6) Temporal Bioscience and Technology

	Research theme	Keyperson	Contents
1	Clinical temporal biology	S. Takahashi (Shiga Univ. of Medicine, Medical Dept.) K. Takahashi (National Mind and Nerve Center) K. Honma (Hokkaido Univ.)	Basic theory of biorhythms: elucidation of causes of diseases, applications in medical treatment.

(7) New Global Environmental S&T

	Research theme	Keyperson	Contents
1	Interactions among plants and other living organisms	I. Yamaguchi (RIKEN)	Elucidating the subtances that play a part in interactions among living organisms (substitutes for harmful agricultural chemicals)
2	Plant biotechnology	"	Control of plant-disease-causing insects without using chemicals (environmental preservation, etc.)
3	Relationship between biomaterials and sugar chain engineering	S. Ogawa (RIKEN)	Not only functional and structural analysis but research on development of new materials that also includes substance production.
4	Research on deserts	I. Kobori (Meiji Univ., Politics and Economics Dept.)	•Desert formation mechanisms •Lifestyles in the desert •Desert engineering •Dry-land farming

(8) Recycling S&T

	Research theme	Keyperson	Contents
1	Relationship between biomaterials and sugar chain engineering	S. Ogawa (RIKEN)	Not only functional and structural analysis, but research on development of new materials that also includes substance production.
2	Cluster evaluation	K. Takeuchi (RIKEN)	Chemical elucidation of cluster reactions, which cause obstacles in uranium refining, and refining.

(9) Computational S&T

	Research theme	Keyperson	Contents
1	Drug design	M. Ishiguro (Suntory Biomedical Research Lab)	Applications of computational chemistry in the creation of drugs.

2.5.2 Summary of Theme Names, From Questionnaires

Of the research themes in Japan that were obtained from a questionnaire survey of general researchers, we extracted those themes that correspond to the advanced multidisciplinary research areas of Section 2.3. Table 2.5.2-1 is a summary of those themes, classified under the respective research area.

Of the research themes and researchers outside of Japan that were obtained from a questionnaire survey of general researchers, we extracted those themes that correspond to the advanced multidisciplinary research areas of Section 2.3, classified them, and summarized them in Table 2.5.2-2.

Table 2.5.2-1 Summary of Themes, From Questionnaire Surveys (1)

(1) Intelligent Materials (no special order)

Name of research theme	Core fields (starting point)/ Deeply related fields	I/G /U
1 Dynamics of microclusters	Particle, nuclear physics/ Electronic properties	U
2 Developmental research on higher-function fiber technology using compound plasmas	Fluid theory, plasmas, electric discharge/Structure of substances, radiophysics	G
3 Properties of semiconductor crystal defects	Mechanical properties and thermal characteristics/ Electronic properties	U
4 Catalytic characteristics of inorganic thin films	Physical chemistry/ Metrology, instrumentation	G
5 Molecular recognition, molecular devices	Chemistry of complexes/ Space and earth sciences	U
6 Organic optical materials	Organic chemistry/Physical chemistry	G
7 Nonlinear optical materials	Organic chemistry/Physical chemistry	I
8 Structure and properties of nonequilibrium alloys	Metals engineering/Magnetism	U
9 Development of gradient functional materials	Metals engineering/Mechanical engineering	I
10 Ceramics for bodily use	Chemical engineering/Medicine	U

I/G/U = Industry/Government/Universities

Table 2.5.2-1 Summary of Themes, From Questionnaire Surveys (2)

(2) Frontier Measurement and Control Technology (no special order)

Name of research theme	Core fields (starting point)/ Deeply related fields	I/G /U
1 Research of systems that use accelerators in an engineering-type manner	Elementary particles, nuclear physics/ Quantum mechanics, general relativity, etc.	G
2 General accelerator science	Particle physics, nuclear physics/ Fluid theory, plasmas, electric discharge	U
3 Development, research of large radiation facilities	Particle physics, nuclear physics/Mechanical properties and thermal characteristics	G
4 Techniques of using soft X-rays	Atoms, molecules/Metrology, instrumentation	G
5 Plasma measurement by means of lasers	Fluid theory, plasmas, electric discharge/Metrology, instrumentation	U
6 Materials research using radiation	Structure of substances, radiation physics/Quantum mechanics, general relativity, etc.	I
7 X-ray optics	Structure of substances, radiophysics/Mechanical engineering	I
8 Controlling friction characteristics of materials by means of surface processing	Mechanical properties and thermal characteristics/Electronic properties	G
9 Research on use of synchrotron radiation spectra	Mechanical properties and thermal characteristics/Metrology, instrumentation	G
10 Laser processing technology	Electronic properties/ Metals engineering	G
11 Development of laser ion-beam machining processes for assisting lasers	Electronic properties/ Electrical engineering	G
12 Nonlinear Organic chemistry materials	Optical properties/ Electronic properties	G
13 Research related to development of wideband gap optoelectronics engineering materials	Optical properties/ Electronic properties	G

Table 2.5.2-1 Summary of Themes, From Questionnaire Surveys (3)
(2) Frontier Measurement and Control Technology (continued)

Name of research theme	Core fields (starting point)/ Deeply related fields	I/G /U
14 Evaluation of semiconductor properties by means of electrical and optical methods	Optical properties/ Electronic properties	U
15 Applications of beam technology in analytical sciences	Physical chemistry/Quantum mechanics, general relativity, etc.	I
16 Radiation utilization, nonlinear optical materials, nanochemistry	Physical chemistry/Analytical chemistry, separation techniques	G
17 Research of microbeam analysis	Analytical chemistry, separation techniques/Inorganic chemistry	G
18 Dynamic-volume microsensors (semiconductors)	Biochemistry, molecular biology/ Electronic properties	I
19 Applied measurements, mechatronics	Metrology, instrumentation/ Magnetism	I
20 Development of optical actuators	Systems and control engineering/ Mechanical engineering	U
21 X-ray microscopes	Information engineering/ Bioengineering	I
22 Ultrafine processes	Electrical engineering/ Electronic properties	U
23 Free-electron lasers and technology that utilizes them	Electrical engineering/ Nuclear engineering	I
24 Research on micromachines	Mechanical engineering/Systems and control engineering	G
25 1) Very-high vacuum development research; 2) Surface analysis quantization research	Metals engineering/Quantum mechanics, general relativity, etc.	U
26 Crystal growth on intermetallic compound surfaces	Metals engineering/Structure of substances, radiophysics	G
27 Relationships between mechanical properties and material organization, and dynamic characteristics	Metals engineering/ Structure of substance radiophysics	U
28 Research on improving properties of surfaces by ion injection	Metals engineering/Mechanical properties and thermal characteristics	G

Table 2.5.2-1 Summary of Themes, From Questionnaire Surveys (4)

(3) New Genetic Manipulation Technology

Name of research theme	Core fields (starting point)/ Deeply related fields	I/G /U
1 New organic reactions utilizing protein engineering	Organic chemistry/ Biochemistry, molecular biology	I
2 Protein engineering	Macromolecular chemistry/ Physical chemistry	I
3 Mechanisms of mutation and carcinogenesis	Biochemistry, molecular biology/ Quantum mechanics, general relativity, etc.	U
4 Human genome project	Biochemistry, molecular biology/ Genetics, evolution	G
5 Alteration of genetic information in eucaryotes	Biochemistry, molecular biology/ Genetics, evolution	G
6 Activation of inositol lipid-metabolizing enzymes through T-cell receptors	Biochemistry, molecular biology/ Immunology	U
7 Research on endoseline receptors	Biochemistry, molecular biology/ Cytology	I
8 Protease unique in acidic amino acids and its inhibitor	Biochemistry, molecular biology/ Microbiology, virology	U
9 Biochemical research of micro-biologically produced proteins, genetically engineered microbes, and alteration of proteins	Biochemistry, molecular biology/ Microbiology, virology	I
10 Molecular biology; in particular, plant DNA	Biochemistry, molecular biology/ Botany	I
11 Biological evolution from amino acid and base sequences	Biochemistry, molecular biology/ Zoology	U
12 Elucidating carcinogens and mechanisms of carcinogenesis	Biochemistry, molecular biology/ Medicine	U
13 Cancer research	Biochemistry, molecular biology/ Medicine	G
14 Molecular immunology, chromosome engineering	Genetics, evolution/ Biochemistry, molecular biology	G
15 Molecular mechanisms that cause mutations	Genetics, evolution/ Biochemistry, molecular biology	U

Table 2.5.2-1 Summary of Themes, From Questionnaire Surveys (5)
(3) New Genetic Manipulation Technology (continued)

Name of research theme	Core fields (starting point)/ Deeply related fields	I/G /U
16 Bioengineering	Genetics, evolution/ Biochemistry, molecular biology	I
17 Behavior of environment-resistant genes	Genetics, evolution/ Ecology, environmental biology	G
18 Embryological genetics, genetic cell biology, cancer cell biology	Genetics, evolution/ Cytology	U
19 Murobiology	Immunology/ Ecology, environmental biology	G
20 Immune suppression	Immunology/ Ecology, environmental biology	G
21 Occurrence of immune mechanisms	Cytology/Immunology	U
22 Aging mechanisms in animals	Cytology/Zoology	G
23 Quick diagnoses (systems using antibody DNA)	Microbiology, virology/Medicine	I
24 Production of useful substances using enzyme methods	Botany/Microbiology, virology	I
25 DNA repair and radiation-generated cancer	Radiobiology/ Biochemistry, molecular biology	G
27 Mechanisms of DNA correction in higher animals	Radiobiology/Genetics, evolution	U
27 Radiobiology, analysis of mechanisms of human cells' susceptibility to radiation	Radiobiology/Genetics, evolution	U
28 In vitro splicing reaction apparatus	Bioengineering/ Macromolecular chemistry	G

Table 2.5.2-1 Summary of Themes, From Questionnaire Surveys (6)

(4) New Neuroscience and Technology (no special order)

Name of research theme	Core fields (starting point)/ Deeply related fields	I/G /U
1 Applications of neural networks	Biochemistry, molecular biology/Molecules, atoms	I
2 Information transmission in biofunctions	Biochemistry, molecular biology/Cytology	G
3 Search for neuro-nutritive factors	Cytology/ Biochemistry, molecular biology	I
4 Applications in air traffic control of information processing functions of living organisms	Bioengineering/ Information engineering	G
5 Basic research on human interfaces	Metrology, instrumentation/ Bioengineering	G
6 Theories of learning as information engineering (including neural networks)	Systems and control engineering/Information engineering	U
7 Mathematical engineering; neural network research	Systems and control engineering/Information engineering	I
8 Development of decision support systems that use fuzzy logic	Systems and control engineering/Environmental engineering	G
9 Voice generation systems using neural networks	Information engineering/ Theoretical biology, biophysics	I
10 Combining symbol manipulation and pattern processing; knowledge science, AI	Information engineering/ Biochemistry, molecular biology	I
11 Self-organization of information processing systems	Information engineering/ Genetics, evolution	U
12 Object models of intelligent structures	Information engineering/Systems and control engineering	U
13 Research on sound perception, intelligence	Information engineering/Systems and control engineering	U

Table 2.5.2-1 Summary of Themes, From Questionnaire Surveys (7)

(5) Biomolecular S&T (no special order)

Name of research theme	Core fields (starting point)/ Deeply related fields	I/G /U
1 Principles of biological macromolecular construction; molecular evolution	Atoms, molecules/ Organic chemistry	I
2 Bioelectro-chemistry; bioelectrical analytical chemistry	Physical chemistry/Analytical chemistry, separation techniques	U
3 Correlation between three-dimensional structure of molecules and molecular interactions; quantitative research on molecular identification	Physical chemistry/ Organic chemistry	U
4 Roles of cell growth factors in development	Physical chemistry/ Biochemistry, molecular biology	G
5 Living organisms and water	Physical chemistry/ Biochemistry, molecular biology	U
6 Bio-geo-chemistry of stable isotopes	Analytical chemistry, separation techniques/Atoms, molecules	I
7 Bio, separation	Analytical chemistry, separation techniques/Optical properties	I
8 Development of methods for analyzing biosubstances using fixation enzymes	Analytical chemistry, separation techniques/ Biochemistry, molecular biology	U
9 Chemical research on activated structure of zinc-containing enzymes	Chemistry of complexes/ Organic chemistry	U
10 Bio-inorganic chemistry	Chemistry of complexes/ Biochemistry, molecular biology	U
11 Peptide chemistry	Organic chemistry/ Physical chemistry	G
12 Design and synthesis of compounds with pharmacological activation	Organic chemistry/ Biochemistry, molecular biology	I
13 Development of new physiological activation substances	Organic chemistry/ Microbiology, virology	U

Table 2.5.2-1 Summary of Themes, From Questionnaire Surveys (8)
(5) Biomolecular S&T (continued)

Name of research theme	Core fields (starting point)/ Deeply related fields	I/G /U
14 Elucidating action manifestation mechanisms of chemical substances that play parts in living organisms	Organic chemistry/ Medicine	G
15 Properties of biomembranes and how they relate to illness	Polymer chemistry/ Theoretical biology, biophysics	I
16 NMR-based analysis of mutual recognition of EGF and receptors	Biochemistry, molecular biology/ Physical chemistry	G
17 Research on membrane-fusion-causing mechanisms attributable to proteins, and cytokinin's tumor-cell-inhibiting mechanisms	Biochemistry, molecular biology/ Physical chemistry	U
18 Molecular mechanisms of active transport in living organisms	Biochemistry, molecular biology/ Physical chemistry	I
19 Biochemistry and bioorganic chemistry of isopreid	Biochemistry, molecular biology/ Organic chemistry	U
20 Self-configuration control of molecules	Biochemistry, molecular biology/ Organic chemistry	I
21 Roles and mechanisms of sugar chains in various diseases	Biochemistry, molecular biology/ Immunology	I
22 Production of useful plant substances for use in (cell) transformation drugs	Biochemistry, molecular biology/ Cytology	G
23 Radical structure of mono-oxygenase in mutation-conducive metabolism	Biochemistry, molecular biology/ Botany	U
24 Effects of magnetism on living organisms	Genetics, evolution/ Ecology, environmental biology	G
25 Research on tissue diversity using immunological techniques	Immunology/Cytology	U
26 Research related to measurement of bio-information (in plants and animals)	Ecology, environmental biology/ Bioengineering	I

Table 2.5.2-1 Summary of Themes, From Questionnaire Surveys (9)

(5) Biomolecular S&T (continued)

Name of research theme	Core fields (starting point)/ Deeply related fields	I/G /U
27 Cell biology	Cytology/Theoretical biology, biophysics	U
28 Molecular mechanisms of protein transport in yeast secretory routes	Cytology/Biochemistry, molecular biology	U
29 Functional analysis of bacterial flagella motors	Bioengineering/ Microbiology, virology	G
30 Medical measurements of body by means of light	Bioengineering/Medicine	U
31 Research on technology to measure distribution of responses to infrared, far-infrared beams in an organism's environment	Metrology, instrumentation/ Optical properties	G
32 Elucidating action of physiological activation substances on insects	Agriculture, forestry, fisheries/Organic chemistry	G
33 Plant breeding using cell- and tissue-culture techniques	Agriculture, forestry, fisheries/Genetics, evolution	I
34 Suppression of ultra-low-temperature systems of plants, and development of ultra-low-temperature methods of preservation	Agriculture, forestry, fisheries/Bioengineering	G
35 Creating polymer films, and elucidating relationship between film structure, and electrical characteristics	Electrical engineering/ Polymer chemistry	U

Table 2.5.2-1 Summary of Themes, From Questionnaire Surveys (10)

(6) Temporal Bioscience and Technology (no special order)

Name of research theme	Core fields (starting point)/ Deeply related fields	I/G /U
1 Research related to measurement of bio-information (in plants and animals)	Ecology, environmental biology/ Bioengineering	I
2 Biomeasurements for medical use by means of light	Bioengineering/Medicine	U
3 Research on technology to measure distribution of responses to infrared, far-infrared beams in organism's environment	Metrology, instrumentation/ Optical properties	G

(7) New Global Environmental S&T (no special order)

Name of research theme	Core fields (starting point)/ Deeply related fields	I/G /U
1 Research on mechanisms by which very small aerosol particles form	Atoms, molecules/ Environmental engineering	U
2 Geophysical-scale fluid-dynamical phenomena	Fluid theory, plasmas, electric discharge/Mathematics	U
3 Hydrogen production by using solar energy to thermally break down water	Electronic properties/ Energy engineering	U
4 Elucidating mechanisms of nucleic acid damage by environmental chemicals	Organic chemistry/ Biochemistry, molecular biology	G
5 Research on environment, structure, regeneration, and recovery of tropical forests	Ecology, environmental biology/ Theoretical biology, biophysics	G
6 Effects of environmental pollutants on ecological systems	Ecology, environmental biology/ Microbiology, virology	G
7 Biocenosic movement in natural environments and effects of disruptive substances	Ecology, environmental biology/ Metrology, instrumentation	G
8 Aerospace medicine	Ecology, environmental biology/ Space and earth sciences	G

Table 2.5.2-1 Summary of Themes, From Questionnaire Surveys (11)
(7) New Global Environmental S&T (continued) (no special order)

Name of research theme	Core fields (starting point)/ Deeply related fields	I/G /U
9 Characteristics of coastal swampland soil in Southeast Asia and utilization possibilities	Ecology, environmental biology/ Agriculture, forestry, fisheries	U
10 River basin environments	Ecology, environmental biology/ Environmental engineering	I
11 Research related to space environment forecasting	Space and earth sciences/Fluid theory, plasmas, electric discharge	G
12 Effect of human activities on material environments	Space and earth sciences/ Analytical chemistry, separation techniques	U
13 Geo-environmental studies (optimum scale theory)	Space and earth sciences/ Ecology, environmental biology	I
14 Research on distribution, migration of heavy metals and harmful elements in environment (environmental science)	Space and earth sciences/ Ecology, environmental biology	G
15 Measurement of earth's atmosphere using space Litthrow reflectors	Space and earth sciences/ Metrology, instrumentation	G
16 Development of space, space-time measurement technology; building a standard coordinate system	Space and earth sciences/ Systems and control engineering	G
17 Soil microorganisms	Agriculture, forestry, fisheries/Environmental engineering	G
18 Closed-cycle MHD (magneto-hydrodynamics)	Energy engineering/Fluid theory, plasmas, electric discharge	G
19 Electrochemical energy technology	Energy engineering/ Physical chemistry	G
20 Research on safety assessment of underground disposal of solidified high-level radioactive waste liquids	Nuclear engineering/ Physical chemistry	U

Table 2.5.2-1 Summary of Themes, From Questionnaire Surveys (12)
(7) New Global Environmental S&T (continued)

Name of research theme	Core fields (starting point)/ Deeply related fields	I/G /U
21 Tritium adsorption, desorption behavior in various materials	Nuclear engineering/ Metrology, instrumentation	U
22 Superconducting power generation system development	Electrical engineering/ Electronic properties	I
23 Remote sensing from space	Electrical engineering/ Space and earth sciences	G
24 Research on wind power conversion systems; development of large wind power generation systems	Mechanical engineering/ Energy engineering	G
25 Technology for increasing amount of manipulatable geothermal energy	Mechanical engineering/ Energy engineering	G
26 Developmental research on chemical heat accumulation and chemical heat pumps	Mechanical engineering/ Energy engineering	U
27 Research based on international cooperation to elucidate physical, chemical and biological phenomena	Mechanical engineering/ Energy engineering	I
28 Assessment of anti-global-warming technology; development of electric cars	Mechanical engineering/ Electrical engineering	G
29 Afforestation of arid lands and environmental impact assessments	Environmental engineering/ Ecology, environment "	U
30 Air pollution	Environmental engineering/ Space and earth sciences	G
31 Environmental information	Environmental engineering/ Information engineering	G
32 Active noise control; effects of low frequency noise on human body	Environmental engineering/ Information engineering	U
33 Analysis of atmospheric aerosol particle shapes, deterioration, and sources	Environmental engineering/ Energy engineering	G

Table 2.5.2-1 Summary of Themes, From Questionnaire Surveys (13)

(8) Recycling S&T (no special order)

Name of research theme	Core fields (starting point)/ Deeply related fields	I/G /U
1 Very-high-purity metals	Electronic properties/Analytical chemistry, separation techniques	U
2 Correlation between microbial decomposition of chemicals (activated sludge) and structural activation	Physical chemistry/ Quantum mechanics, general relativity, etc.	G
3 Energy conversion: artificial photosynthesis	Physical chemistry/ Optical properties	U
4 Research on advanced utilization of synthetic crude oil	Organic chemistry/ Physical chemistry	g
5 Microbial decomposition of synthetic polymer compounds	Polymer chemistry/ Organic chemistry	U
6 Research on microbe-degradable plastics	Polymer chemistry/ Ecology, environmental biology	G
7 Bio-decomposition of decomposition-resistant substances in wastewaters	Microbiology, virology/ Ecology, environmental biology	I
8 Development of microorganism functions (now, mainly radiation bacteria)	Microbiology, virology/ Ecology, environmental biology	U
9 Selection of highly capable root nodule bacteria; development of inoculation technology	Microbiology, virology/ Botany	G
10 Dynamic regulation of photosynthetic energy conversion functions	Botany/ Biochemistry, molecular biology	G
11 Soil processing of polluted water	Environmental environment/ Analytical chemistry, separation techniques	G
12 R&D of comprehensive water recycling systems	Environmental engineering/ Analytical chemistry, separation techniques	G
13 High-temperature-action bioreactors that use heat-resistant enzymes	Chemical engineering/ Biochemistry, molecular biology	G

Table 2.5.2-1 Summary of Themes, From Questionnaire Surveys (14)

(9) Computational S&T (no special order)

Name of research theme	Core fields (starting point)/ Deeply related fields	I/G /U
1 Computational engineering (computational physics)	Atoms, molecules/Fluid theory, plasmas, electric discharge	I
2 Simulation of thin film growth	Fluid theory, plasmas, electric discharge/Atoms, molecules	U
3 Research on modeling of quasi-crystalline structures	Structure of substances, radio-physics/Mathematics	G
4 Using dislocation theory, metal deformation and dynamic configuration equations that derive from thermodynamics	Mechanical properties, thermal characteristics/Mechanical engineering	G
5 Thin-film growth processes	Physical chemistry/ Optical properties	U
6 Molecular design, materials design using computers	Physical chemistry/ Optical properties	I
7 Computer chemistry (theoretical chemistry computing), biophysical chemistry, pharmacology, organic synthesis chemistry, etc.	Physical chemistry/ Information engineering	I
8 Numerical analysis, numerical fluid dynamics, differential geometry, quantum field theory, relativity	Nuclear engineering/Mathematics	I
9 Turbulence processing models and direct numerical simulation	Mechanical engineering/ Metrology, instrumentation	U

Table 2.5.2-2 Summary of Foreign Researchers and Themes, From Questionnaire Surveys (1)

(1) Intelligent Materials---Not applicable

(2) Frontier Measurement and Control Technology (no special order)

Name of research theme	Country	Researcher	Affiliation, position
1 Intensity standards for vacuum UV rays, soft X- rays	Germany	M. Kuhne	Chief, Synchrotron Radiation, Metrology Section
2 X-ray projection lithography	U.S.	Jeff Bokor	AT&T Bell Labs
3 New neutron spectroscopy	US, UK	J.L. Finney	Britain's Rutherford Aberton Labs
4 Technology that uses emitted light	US, EC		
5 Nanochemistry	US, EC		
6 Creation of new catalysts	EC		
7 X-ray crystal analysis	US		
8 Isotope distribution within molecules	US	E. Bengsh	GBM-CNRS, professor
9 SI sensors	Holland	Middelhoek	Telftoe University, prof.
10 SI microturbines	US	R.S. Muller	Univ. of California, Berkeley, prof.
11 Medical sensors	US	W.H.K.O.	CWRU, professor
12 Free-electron lasers	US	C.A. Brau	Vanderbilt Univ., prof.
13 Scanning X-ray microscopes	US	J. Kirtz	New York Univ., prof.
14 X-ray microscopes	Germany	S. Schmahl	Guchingen Univ., prof.
15 X-ray microscopes	UK		
16 Semiconductor processes	US	Armold, Reisman	Microelectronics Center of N. Carolina, prof.
17 " "	US	Jim Gibbons	Stanford Elec. Lab., prof.
18 " "	Germany	Anton Heuberget	Fraunhofer Inst. for microstructure Technology, prof.

Table 2.5.2-2 Summary of Foreign Researchers and Themes, From Questionnaire Surveys (2)

(3) New Genetic Manipulation Technology (no special order)

Name of research theme	Country	Researcher	Affiliation, position
1 Human Genome Project	US	Watson	
2 NO production by macrophages	US	J.B. Hibbs	Utah Univ., prof.
3 Metallic ion nucleotide interactions	Switzerland	H. Sigel	Basel Univ., Inorganic Sciences Research Institute, prof.
4 Biochemistry and molecular biology of Bt insecticide proteins	UK	D. Ellar	Cambridge University
5 Research on Bt insecticide proteins	Belgium		Plant Gemtio System Co.
6 Molecular mechanisms of radiation carcinogenesis	US	G. Tim Bonden	Arizona University, prof.
7 Molecular mechanisms of radiation carcinogenesis	UK	R. Cox	MRC
8 American Association for Cancer Research	US	I. Bernard Weinstein	Professor
9 Human Genome Project	US NIH	J.D. Watson	Cold Spring Harbor, director
10 Human Genome Initiative	US DDE	C. Cantor	Lawrence Berkeley Lab
11 Human Genome Project	UK ICRF	R. Bodoper	
12 Research using ribosomes	US	D. Papahadjoponlos	
13 Mutagen susceptibility of human cells	UK	H.I. Evans	
14 Radiation susceptibility of human cells	UK	D. Scott	
15 Mechanisms of chromosome abnormality formation	Holland	A.T. Natarajan	
16 Environmental mutagens	several countries	F.H. Sobels	

Table 2.5.2-2 Summary of Foreign Researchers and Themes, From Questionnaire Surveys (3)

(3) New Genetic Manipulation Technology (continued) (no special order)

Name of research theme	Country	Researcher	Affiliation, position
17 Molecular mechanisms of protein transport in yeast secretory routes	US	Randy Schekman	
18 Genetic manifestation control with steroids	US		
19 Detecting manifested proteins with steroids	US	D.A. Young	University of Rochester

(4) New Neuroscience and Technology (no special order)

Name of research theme	Country	Researcher	Affiliation, position
1 Neurocomputers	France	G. Saucier	INPG, Prof.
2 Superparallel computers	US	H.T. King	GMU, Prof.

Table 2.5.2-2 Summary of Foreign Researchers and Themes, From Questionnaire Surveys (4)

(5) Biomolecular S&T (no special order)

Name of research theme	Country	Researcher	Affiliation, position
1 SI distribution in ecological systems	US	K.B.K. Fry	Ecosystem Center
2 SI distribution	USSR	E.M. Galimov	Vernadsky Inst., Prof.
3 Action of blood-vessel-expansion factor NO	UK	S. Moncada	Wellcome Labs
4 Structure and functions of metallic proteins	Italy	I. Bertsisi	Florence Univ., Chemistry Prof.
5 Electron transmission in ecological systems	US	H.B. Gray	Caltech, Prof.
6 Synthesis of fluorine-containing inositol	US	A.P. Kozikewski	Univ. of Pittsburgh, Prof.
7 Sugar's interactions with water	Italy	Barone	Napoli University, Prof.
8 Molecular recognition	several countries		
9 Calorimetric measurements of molecular inclusion	Sweden	Wadso	Lund University, Prof.
10 Effects of magnetic fields on ecological systems	US	T.S. Tenforde	University of California, Prof.
11 Electromagnetics in Biology and Medicine	Intl. Union of Radio Science	New Commission	Commission K

(6) Temporal Bioscience and Technology

Not applicable

Table 2.5.2-2 Summary of Foreign Researchers and Themes, From Questionnaire Surveys (5)

(7) New Global Environmental S&T (no special order)

Name of research theme	Country	Researcher	Affiliation, position
1 Geostrophic turbulence, turbulence of rotational elements	France	M. Lesieur	Institute de Mecanique de Grenoble, Prof.
2 Isolated eddies (modon)	US	G.R. Flieul	Dept. of Earth Science, MIT
3 Geostrophic turbulence, isolated turbulence	US	J. McWilliams	NCAR Boulder Co.
4 Environmental preservation of pristine areas	US	T.A. Cahill	Univ. of California, Prof.
5 Space-drunkenness countermeasures	US	M. Reschke	NASA
6 Deconditioning of circulatory systems	US	John Charles	NASA
7 Bones, calcium metabolism	US	V. Schneider	NASA
8 Integrated Screening Program	UK	J.P. Grime	UCPE, Prof.
9 Effects of heavy metals on ecological systems	US	G. Stotzky	New York Univ., Life Sciences
10 Pollutants and microcosms	US	P.H. Pritchard	
11 International global rotation	France, US (alliance)	R.E. Schutz	Texas University, Prof.
12 Global warming and climatic fluctuations	Sweden	T. Rosswal	
13 Global warming and climatic fluctuations	Kore	K.H. Kim	
14 Superconducting power generator development	Germany	Riese	Siemens/KMV, Department manager
15 Superconducting power generator development	France	Sabrie	Alstom, Department manager
16 Closed-cycle MHD (magnetohydrodynamics)	Holland	Rietjens L. Hlh	Eindhoven University, Prof.

Table 2.5.2-2 Summary of Foreign Researchers and Themes, From Questionnaire Surveys (6)

(7) New Global Environmental S&T (continued) (no special order)

Name of research theme	Country	Researcher	Affiliation, position
17 Characteristics of atmospheric aerosols, analysis of generation sources	US	S.K. Kfriedlauder	Univ. of California, LA, Prof.
18 Global-scale transport of aerosols	US	J. Winchester	Florida State Univ., Prof.
19 Physics of aerosols	Austria	O. Preining	Univ. of Vienna, Prof.

(8) Recycling S&T (no special order)

Name of research theme	Country	Researcher	Affiliation, position
1 Photoadaptation of photosynthesis	US	A. Meris	University of Calif., Berkeley, Prof.
2 Environmental biology of seaweeds	US	E. Gantt	Univ. of Maryland, Prof.
3 Regulation of chloroplast formation	Australia	Jan Anderson	Head researcher
4 Bacterial decomposition of wood components	US	K.F. Eriksson	Georgia University, Prof.

(9) Computational S&T (no special order)

Name of research theme	Country	Researcher	Affiliation, position
1 Structure and properties of quasi-crystals	China	Si Xin Guo	China Institute of Sciences, Electron Microscope Lab
2 Theoretical chemistry computing	US	Kollman, Kirplus	UCSF, Harvard
3 Verification and development of turbulence models	US	P. Bradshaw	Stanford Univ., Prof.
4 Verification and development of turbulence models	UK	M. Savill	Cambridge Univ.

Chapter 3. Current State of Researchers in Multidisciplinary Areas as Seen in Questionnaire Surveys

We conducted a questionnaire survey of general researchers with the objective of broadly investigating the current state of research themes in multi-disciplinary research areas, and the research promotion policies in those areas. Below we will summarize the implementation of the questionnaire survey and describe the results of that survey. A part of the survey results, however, were already reported in Section 2.5.2 of Chapter 2.

3.1 Summary of Questionnaire Implementation

3.1.1 Questions

Table 3.1.1-1 gives a summary of the question items.

3.1.2 Questionnaire Form

Attached Figure 1 shows the major parts of the questionnaire request, and Attached Figure 2 shows the "questionnaire survey form."

3.1.3 Subjects of Questionnaires

From the registers of the 32 academic societies listed in Table 1.2-1, we randomly extracted a total of 1,524 names of the researchers to be surveyed; the numbers of researchers were equally divided among industry, government, and universities (508 names for each sector).

As for the allotment of survey subjects among the academic societies listed in Table 1.2-1, we decided to make the number of survey subjects from each nearly proportional to the number of members in the respective academic society. However, in the smallest academic societies we made sure of having 15 survey subjects; conversely, we reduced the number of survey subjects from the Electronic Information and Communications Society, Electricity Society, and Japan Machinery Society, which have many members, to 75% of the number of members in the respective academic society.

Table 3.1.1-1 Questionnaire Survey Items Part

Part/Question contents	Main areas
I About the person being surveyed —Post of duty —Field of specialty —Attributes	—Character of the person responding —Correlative analysis of attributes and contents of responses —Discerning whether or not the person is doing research in a multi-disciplinary area
II About researchers working in multidisciplinary areas —Name of the research theme —Contents of the research —Research environment —Trends in Japan and overseas	—Getting a grasp of research themes in multidisciplinary areas, classification by related academic fields —Getting a grasp of study societies in multidisciplinary areas
III For researchers working in multidisciplinary areas, with regard to the main theme research: —Name of the research theme —Contents of the research —Research environment —Trends in Japan and overseas	—For research themes where the researcher himself is not aware of the theme being a multidisciplinary area, grasping the contents of that research —Where possible, classification by related academic fields

Attached Figure 1

"Survey of Status and Development Directions of Advanced Multidisciplinary Research Areas in Japan"

Requesting your cooperation in this survey

15 November 1990
Science and Technology Agency,
Science and Technology Promotion Bureau

Greetings. At this time we wish you good spirits.

In this bureau we are conducting a "Survey of Status and Development Directions of Advanced Multidisciplinary Research Areas in Japan." As a part of that, we decided to ask the opinions of researchers by means of a questionnaire.

We apologize about bothering you when you are so busy, but would you please fill in the attached survey form and mail it back to us in the envelope provided.

Respectfully

Summary of Survey

1. Gist of Survey

Advanced science and technology of late is developing in the direction towards multidisciplinary research areas.* In the background behind this are the various study societies that cross over the boundaries of existing academic societies, and the activation of research exchange at the level of individual researchers.

From now on it is essential that Japan efficiently and effectively promotes research in such multidisciplinary areas so that it can promote creative basic research as the duty it has as a scientifically and technologically advanced nation.

This survey is an attempt to get a grasp on the state and development directions of multidisciplinary research areas, and to clarify the directions in which these areas will be driven in the future.

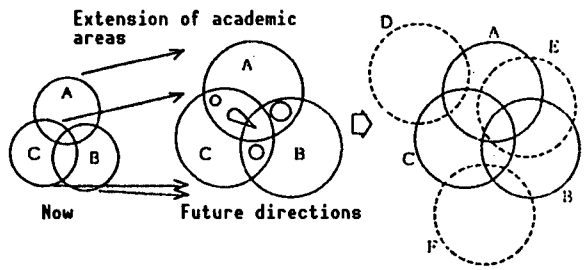


Figure 1. Multidisciplinary Research Areas and Their Development
A, B, and C indicate "specialized fields"

* In this survey multidisciplinary research areas are the so-called border research areas, or interdisciplinary research areas. Concretely, for example, they are the areas that straddle several of the "specialized fields" shown in Table 1; they correspond to the diagonal lines in Figure 1.

Attached Figure 2

Survey Questionnaire Form

Page 1

1. Questions about yourself.

1) Fill in your name, where you can be contacted, etc., below.

Name:_____
Where you can be contacted:_____Tel._____
Name of place where you work:_____
Name of your department, section:_____Your title:_____

Affix your business card here:

2) What is your age? Circle the number that applies.

1. under 26 years	2. 26–30 years	3. 31–35 years
4. 36–40 years	5. 41–45 years	6. 46–50 years
7. 51–55 years	8. 56–60 years	9. over 61 years

3) Which of the following describes where you are employed? Circle the number that applies.

1. University or an affiliated research institute
2. National laboratory (including special corporations and incorporated foundations)
3. Private firm
4. Other (please specify:_____)

4) We will send a copy of the aggregate results of this survey to those who would like to receive it. Indicate below whether or not you would like a copy of the results.

1. Would like to see results. 2. Do not care to see results.

5) Which of the following is closest to your duties? Circle the number that applies.

1. Management
2. Specialized research

6) State in concrete terms the place(s) where your research is carried out (or will be carried out):

_____

That place is which of the following? Circle the number that applies.

1. University or an affiliated research institute
2. National laboratory (including special corporations and incorporated foundations)
3. Private firm
4. Other (please specify:_____)

7) Select from Table 1 on Page 11 (the last page) the number(s) that corresponds to your field of specialization. If possible select only one, but if your work straddles more than one field, select up to five fields in order of importance. Write the corresponding number(s) below.

Order	1	2	3	4	5
Number	___	___	___	___	___

If none of the fields in Table 1 correspond to your field of work, please specify the name of your field, then select from Table 1 the fields of study that you think are strongly related to your field, and write those numbers below in order of their degree of relevance to your field.

Name of field:_____

(Select from fields listed in Table 1)

Order	1	2	3	4	5
Number	___	___	___	___	___

[Page 2]

8) Select from Table 2 on Page 11 (the last page) the number(s) that corresponds to the academic society with which you are affiliated, and write the number(s) below. (Multiple answers possible.)

Number(s):_____

Those who enter 34 ("Other"), please write the name(s) of the academic society with which you are affiliated below. (Multiple answers possible.)

_____

9) Is your current research work, or the research work that you plan to carry out in the future, in a multidisciplinary research area (refer to the note in the page at the beginning of the survey form, "Summary of Survey")? Circle the number that applies.

1. Currently doing research in a multidisciplinary area.
2. Not currently doing research in a multidisciplinary area, but plan to in the future.
3. Not currently doing research in a multidisciplinary area, and do not plan to.

Those who answered 1. or 2. in 9), go on to II of Page 3.
Those who answered 3. in 9), go on to III of Page 7. Page 3

[Page 3]

II. Questions about research in "multidisciplinary areas" that you are carrying out or plan to carry out.

1) Please write the name of your research theme. For those who cannot write the name of their research theme, please write the name of your research field.

_____

2) Is this the main research theme for you, or is it research that you carry out separately from another theme that is the main research theme (i.e., is this a sub-theme)? Circle the number that applies.

1. Main theme 2. Sub-theme

3) Answer the following questions about the contents of your research.

(1) When was this research started, or when will it be started?

(year) _____

(2) How long will the research be carried out?

_____ years

(3) Please write down the goals and objectives of the research:

_____

(4) This research corresponds to which of the following? Circle the number that applies.

1. Pure scientific research
2. Basic research with applications in mind
3. Product development research

(5) Please write down your methods of research and your ways of approaching the research objectives:

---

(6) Which of the three items below generally describes the motivation for starting your research? Circle the number that applies.

1. To search for breakthroughs
2. To develop completely new technology
3. Because of purely scientific interest
4. Other (please specify:_____)

(7) What about utilization of research promotion systems (e.g., Scientific Research Grants, Coordination Funds for Promoting S&T, Public Welfare Scientific Research Grants, private-sector and foreign grants-in-aid, etc.)? Circle the number that applies.

1. Currently utilizing such system(s). (State concretely the name of the system being used:
_____)
2. Would like to use, but cannot use because we were left out of the selection.
3. If there is an appropriate system, will use it.
4. No need whatsoever.

(8) If you have any opinions about the directions of development of your research environment (research facilities, personnel, economic aspects, etc.), state in concrete terms:

---

(9) State in concrete terms anything that becomes a bottleneck in progressing with your research; distinguish between the bottlenecks that are topics of the research theme itself (barriers), and those that are problems with the research environment.

(i) Topics of the research theme itself (barriers)

(ii) Problems with the research environment (research facilities, personnel, economic aspects, etc.)

[Page 4]

(10) The Science and Technology Agency drives the following basic research promotion systems:

—Creative S&T Promotion System (1981 ~)
—Frontier Research System (1986 ~)
—Priority Basic Research System (1985 ~)
—Inter-Agency Basic Research System (1988 ~)
—Basic Science Special Researcher System (1989 ~)
—S&T Special Researcher System (1990 ~)
—Creative Individual Research Cultivation Project—Pioneer Research 21—(requests for FY 1991 pending)

If you have any wishes with respect to these governmental measures, state in concrete terms:

_____

(11) If you think that exchange with researchers from other fields is needed in order to solve the research bottlenecks mentioned in (i) of Question (9), select from Table 1 on Page 11 (the last page) the numbers that correspond to the names of those fields. (Multiple answers possible.)

Numbers _____

For those who cannot select a field from Table 1, specify the name of the field, then select from Table 1 up to five fields of study that are related to this field, and write them below in order of their importance.

Name of field:_____

(Write the numbers of the fields considered relevant to the field that you named above.)

Order	1	2	3	4	5
Number	___	___	___	___	___

(12) Of the fields of study that are related to your research, select from Table 1 on Page 11 (the last page) the one field that either will be at the center or has become the starting point of your research, and write the corresponding number below.

Number _____

(13) Excluding the field of study that you gave in Question (12), select from Table 1 on Page 11 (the last page) up to five fields of study that are related to your research, and write them below in order of their importance.

Order 1 2 3 4 5
Number ___ ___ ___ ___ ___

(14) If there are any fields of study that you think will become newly relevant to your research as it progresses in the future, which fields would those be? Select from Table 1 on Page 11 (the last page) and write the number(s) of the field(s) below. (Multiple answers possible.)

Numbers _____

(15) As research progresses, which field of study, if any, do you think will become the center of research and will become more important than at present? Select from Table 1 on Page 11 (the last page) and write the number of only one field below.

Number _____

For those who cannot select a field from Table 1, specify the name of the field, then select from Table 1 up to five fields of study that are related to this field, and write them below in order of their importance.

Name of field: _____

(Write the numbers of the fields that you think are related the field you named above.)

Order 1 2 3 4 5
Number ___ ___ ___ ___ ___

4) Questions about the contents of research-related activities.

(1) Does your multidisciplinary research that you are now working on (or plan to work on in the future) involve any activities of study societies? Circle the number that applies

1. Does involve study society activities
2. Does not involve study society activities

Those who selected 1., go on to Question (2) of Page 5.
Those who selected 2., go on to Question (3) of Page 5.

[Page 5]

(2) For researchers involved in activities of study societies

(i) Write the name of the study society:_____

(ii) Concretely, what were the motives behind setting up this study society?

_____

(iii) Write the name, affiliation, title, and field of specialization of the keyperson (representative).

Name:_____
Affiliation and Title:_____
Field of Specialization:_____

(iv) Write the specialization fields of the members, the number of people in each field, and the total number of members.

Field of specialization	Number of people	Field of specialization	Number of people
_____	_____	_____	_____
_____	_____	_____	_____
_____	_____	_____	_____
_____	_____	_____	_____
_____	_____	Total	_____

(v) When did the activities of this study society begin, or when will they begin? (Year) _____

(vi) How often does the study society meet?
_____ times per year

(vii) State in concrete terms the directions along which research activities in the form of study meetings will develop:

_____

Now go on to Question 5) of Page 6.

(3) For researchers who are not involved in activities of study societies

(i) Do you plan to become involved in the activities of a study society in the future? Circle the number that applies.

1. Plan to 2. Do not plan to

For those who answered 1., when do you plan to become involved in the activities of a study society?
(Year) _____
For those who answered 2., state your reasons for not becoming involved:

Now go on to Question 5) of Page 6.

[Page 6]

5) If you know of any other multidisciplinary research in Japan, give the research theme and then answer questions (2) to (4) below.

Question	Answer Column
(1) Name of research theme	
(2) Main researcher	
Name	
Affiliation, title	
Address of affiliated organization	
Tel., Fax	
Field of specialization	
(3) Name of study society that is carrying out this research	
(4) Summary of contents of research	

6) Questions about trends in similar research overseas.

Give the name(s) of the research theme(s) (multiple answers possible) and then answer questions (2) to (6) about each theme below.

Question	Answer Column (1)	Answer Column (2)	Answer Column (3)
(1) Name of research theme			
(2) Country			
(3) Main researcher			
Name			
Affiliation, title			
Address of organization			
Tel., Fax			
Field of specialization			
(4) Name of study society that is carrying out this research			
(5) Summary of contents of research (Points where this research is similar to and different from research in Japan.)			

(6) Degree of progress in comparison with research in Japan. (Circle the number that applies and indicate in the parentheses the extent of difference.)	1. Ahead ( ) years 2. Same 3. Behind ( ) years	1. Ahead ( ) years 2. Same 3. Behind ( ) years	1. Ahead ( ) years 2. Same 3. Behind ( ) years

That completes the survey for those researchers who are currently working in, or who plan to work in, multidisciplinary areas. Thank you for your cooperation.

[Page 7]

The remaining sections are for those researchers who currently do not do research in, or who do not plan to do research in, multidisciplinary areas.

III. Questions about the main theme of the research you are carrying out.

1) Write the name of your research theme. For those who cannot write the name of their research theme, please write the name of your research field.

_____

2) Answer the following questions about the contents of your research.

(1) When was this research started, or when will it be started? (year) _____

(2) How long will the research be carried out? _____ years

(3) Please write down the goals and objectives of the research:

_____

(4) This research corresponds to which of the following? Circle the number that applies.

1. Pure scientific research
2. Basic research with applications in mind
3. Product development research

(5) Please write down your methods of research and your ways of approaching the research objectives:

_____

6) Which of the three items below generally describe the motivation for starting your research? Circle the number that applies.

1. To search for breakthroughs
2. To develop completely new technology
3. Because of purely scientific interest
4. Other (please specify:_____)

(7) What about utilization of research promotion systems (e.g., Scientific Research Grants, Coordination Funds for Promoting S&T, Public Welfare Scientific Research Grants, private-sector and foreign grants-in-aid, etc.)? Circle the number that applies

1. Currently utilizing such system(s). (Please specify the name of the system being used:

_____)

2. Would like to use, but cannot use because we were left out of the selection.
3. If there is an appropriate system, will use it.
4. No need whatsoever.

(8) If you have any opinions about the directions of development of your research environment (research facilities, personnel, economic aspects, etc.), state in concrete terms:

_____

(9) State in concrete terms anything that becomes a bottleneck in accomplishing your research; distinguish between the bottlenecks that are topics of the research theme itself (barriers), and problems with the research environment.

(i) Topics of the research theme itself (barriers)

_____

(ii) Problems with the research environment (research facilities, personnel, economic aspects, etc.)

_____

[Page 8]

(10) The Science and Technology Agency drives the following basic research promotion systems:

—Creative S&T Promotion System (1981 ~)
—Frontier Research System (1986 ~)
—Priority Basic Research System (1985 ~)
—Inter-Agency Basic Research System (1988 ~)
—Basic Science Special Researcher System (1989 ~)
—S&T Special Researcher System (1990 ~)
—Creative Individual Research Cultivation Project—Pioneer Research 21—(requests for FY 1991 pending)

If you have any wishes with respect to these governmental measures, state in concrete terms:

_____

(11) If you think that exchange with researchers from other fields is needed in order to solve the research bottlenecks mentioned in (i) of Question (9), select from Table 1 on Page 11 (the last page) the numbers that correspond to the names of those fields. (Multiple answers possible.)

Numbers _____

For those who cannot select a field from Table 1, specify the name of the field, then select from Table 1 up to five fields of study that are related to this field, and write them below in order of their importance.

Name of
field:_____

(Write the numbers of the fields considered relevant to the field that you named above.)

Order	1	2	3	4	5
Number	___	___	___	___	___

(12) Which fields are deeply related to your research? Choose only one field from Table 1 on Page 11 (the last page) and write that number below.

Number _____

(13) If there are any fields of study that you think will become newly relevant to your research as it progresses in the future, which fields would those be? Select from Table 1 on Page 11 (the last page) and write the number(s) of the field(s) below. (Multiple answers possible.)

Numbers _____

(14) As research progresses, which field of study, if any, do you think will become the center of research and will become more important than at present? Select from Table 1 on Page 11 (the last page) and write the number of only one field below.

Number _____

For those who cannot select a field from Table 1, specify the name of the field, then select from Table 1 up to five fields of study that, if seriously taken up, will be relevant to this field, and write them below in order of their importance.

Name of field: _____

(Write the numbers of the fields that you think are related the field you named above.)

Order	1	2	3	4	5
Number	___	___	___	___	___

(15) If there are any fields of study other that those named in questions (12) to (14), that if seriously taken up would be relevant to your research now, choose the field(s) from Table 1 on Page 11 (the last page) and write that number below. If there are more than one field, write the numbers in the order of importance of the fields.

Order	1	2	3	4	5
Number	___	___	___	___	___

3) Questions about the contents of research-related activities.

(1) Does the multidisciplinary research that you are working on, or plan to work on in the future, involve any activities of study societies? Circle the number that applies.

1. Does involve study society activities
2. Does not involve study society activities

Those who selected 1., go on to Question (2) of Page 9.
Those who selected 2., go on to Question (3) of Page 9.

[Page 9]

(2) For researchers involved in activities of study societies

(i) Write the name of the study society:_____

(ii) Concretely, what were the motives behind setting up this study society?

_____

(iii) Write the name, affiliation, title, and field of specialization of the keyperson (representative).

Name:_____
Affiliation and Title:_____
Field of Specialization:_____

(iv) Write the specialization fields of the members, the number of people in each field, and the total number of members.

Field of specialization	Number of people	Field of specialization	Number of people
_____	_____	_____	_____
_____	_____	_____	_____
_____	_____	_____	_____
_____	_____	_____	_____
_____	_____	Total	_____

(v) When did the activities of this study society begin, or when will they begin? (Year) _____

(vi) How often does the study society meet?
_____ times per year

(vii) State in concrete terms the directions along which research activities in the form of study meetings will develop:

_____

Now go on to Question 4) of Page 10.

(3) For researchers who are not involved in activities of study societies

(i) Do you plan to become involved in the activities of a study society in the future? Circle the number that applies.

1. Plan to 2. Do not plan to

For those who answered 1., when do you plan to become involved in the activities of a study society?
(Year) _____
For those who answered 2., state your reasons for not becoming involved:

_____

Now go on to Question 4) of Page 10.

[Page 10]
5) If you know of any other multidisciplinary research in Japan, give the research theme and then answer questions (2) to (4) below.

Question	Answer Column
(1) Name of research theme	
(2) Main researcher	
Name	
Affiliation, title	
Address of affiliated organization	
Tel., Fax	
Field of specialization	
(3) Name of study society that is carrying out this research	
(4) Summary of contents of research	

6) Questions about trends in similar research overseas.

Give the name(s) of the research theme(s) (multiple answers possible) and then answer questions (2) to (6) about each theme below.

Question	Answer Column (1)	Answer Column (2)	Answer Column (3)
(1) Name of research theme			
(2) Country			
(3) Main researcher			
Name			
Affiliation, title			
Address of organization			
Tel., Fax			
Field of specialization			
(4) Name of study society that is carrying out this research			
(5) Summary of contents of research (Points where this research is similar to and different from research in Japan.)			
(6) Degree of progress in comparison with research in Japan. (Circle the number that applies and indicate in the parentheses the extent of difference.)	1. Ahead ( ) years 2. Same 3. Behind ( ) years	1. Ahead ( ) years 2. Same 3. Behind ( ) years	1. Ahead ( ) years 2. Same 3. Behind ( ) years

That completes the entire survey.
Thank you for your cooperation.

Table 1.

No.	Field of study
1	Mathematics
Physics	
2	Quantum mechanics, general relativity, etc.
3	Elementary articles, nuclear physics
4	Atoms, molecules
5	Fluid theory, plasmas, electric discharge
6	Structure of substances, radiation physics
7	Mechanical properties, thermal characteristics
8	Electronic properties
9	Magnetism
10	Optical properties
11	Physical chemistry
12	Analytical chemistry, separation techniques
13	Inorganic chemistry
14	Chemistry of complexes
15	Organic chemistry
16	Polymer chemistry
Biological Sciences	
17	Theoretical biology, biophysics
18	Biochemistry, molecular biology
19	Genetics, evolution
20	Immunology
21	Ecology, environmental biology
22	Cytology
23	Microbiology, virology
24	Botany
25	Zoology
26	Radiobiology
27	Bioengineering
28	Metrology, instrumentation
29	Space and earth sciences
30	Agriculture, forestry, fisheries
31	Medicine
Engineering	
32	Ssytems and control engineering
33	Information processing
34	Energy engineering
35	Nuclear engineering
36	Electrical engineering
37	Mechanical engineering
38	Environmental engineering
39	Metals engineering
40	Chemical engineering

Table 2.

No.	Name of Academic Society
1	Japan Mathematics Society
2	Japan Physics Society
3	Applied Physics Society
4	Japan Chemistry Society
5	Japan Polymer Society
6	Japan Biophysics Society
7	Japan Biochemistry Society
8	Japan Genetics Society
9	Japan Immunology Society
10	Japan Ecology Society
11	Japan Cell Biology Society
12	Japan Microbiological Ecology Society
13	Japan Virology Society
14	Japan Botany Society
15	Japan Zoology Society
16	Japan Radiobiology Society
17	Japan M.I. Society
18	Japan Astronomy Society
19	Japan Geology Society
20	Geo-Electromagnetism, Earth and Planets Society
21	Japan Agricultural Chemistry Society
22	Japan Forestry Society
23	Japan Fisheries Society
24	Japan Medical Society
25	Systems Control and Information
26	Information Processing Society
27	Japan Solar Energy Society
28	Japan Nuclear Power Society
29	Electronic Information and Communications Society
30	Electricity Society
31	Japan Machinery Society
32	Japan Environmental Society
33	Japan Metals Society
34	Other

3.2 Aggregate Subjects

From the responses that were collected We narrowed down the aggregate subjects of the survey, based on the contents of their research and on the state of their implementation of research in multidisciplinary areas.

Incidentally, the number of valid responses shown for each item of the aggregate results is the number of responses collected, or the number of aggregate subjects, minus the number of nonresponses to the corresponding question.

3.2.1 Narrowing Down the Aggregate Subjects

(a) Population

Table 3.2.1-1 shows the population of the questionnaire survey. The overall recovery rate was 44%.

Table 3.2.1-1 Population

	Industry	Govern-ment	Univer-sities	Other	Total
Questionnaires sent	508	508	508	0	1,524
Questionnaires recovered	228	221	214	1*	664
Recovery rate	45%	44%	42%		44%

* The one other name is that of a student.

(b) Classification of Those Responding to the Survey According To the Contents of Their Research (Valid responses: 481, No response: 183)

These are the results of answers to questions about the contents of the research that the survey subjects are engaged in (Questions II.3) and 4) in Attached Figure 2). The choices were:

1. Pure scientific research (abbreviated to "pure science")
2. Basic research with applications in mind (abbreviated to "applied basic science")
3. Product development research (abbreviated to "product development")

Most of the responses were "applied basic research." Next after "applied basic research," industrial researchers replied "product development," and university researchers replied "pure science" (Figure 3.2.1-1 and Table 3.2.1-2). Reflecting the spirit of this investigation, we used those who answered "applied basic research" or "pure science" as the aggregate subjects, and excluded from the aggregate subjects those who replied "product development."

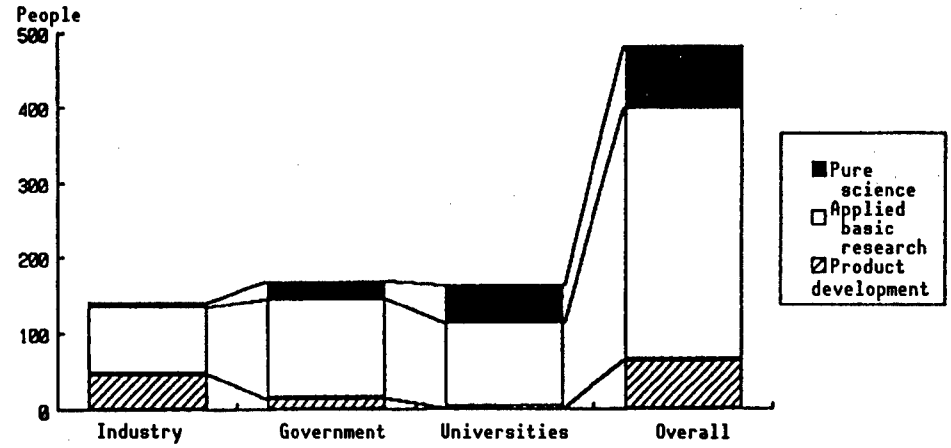


Figure 3.2.1-1 Classification of Those Responding to the Survey According to the Contents of Their Research (Valid responses: 481, No responses: 183)

Table 3.2.1-2 Classification of Those Responding to the Survey According to the Contents of Their Research (Valid responses: 481, No response: 183)
(Upper: number of responses; Lower: %)

	Industry	Government	Universities	Overall
Doing	67	123	133	323
	74%	83%	90%	84%
Plan to do	23	25	16	64
	26%	17%	11%	17%
Not planning to do	0	1	0	1
		1%		0%

(c) State of Implementation of Research in Multidisciplinary Areas (Valid responses: 388, No response: 28)

This is the result of classifying those who responded that they are engaged in research other than product development according to the state of implementation of research in multidisciplinary areas (Question I.9 in Attached Figure 2). The choices were:

1. Currently doing research in a multidisciplinary area (abbreviated to "doing")
2. Not currently doing research in a multidisciplinary area, but plan to in the future (abbreviated to "plan to do")

3. Not currently doing research in a multidisciplinary area, and do not plan to (abbreviated to "not planning to do")

Figure 3.2.1-2 and Table 3.2.1-3 show the results. Overall there was only one case where the person surveyed said that he is"not planning to do" research in a multidisciplinary area.

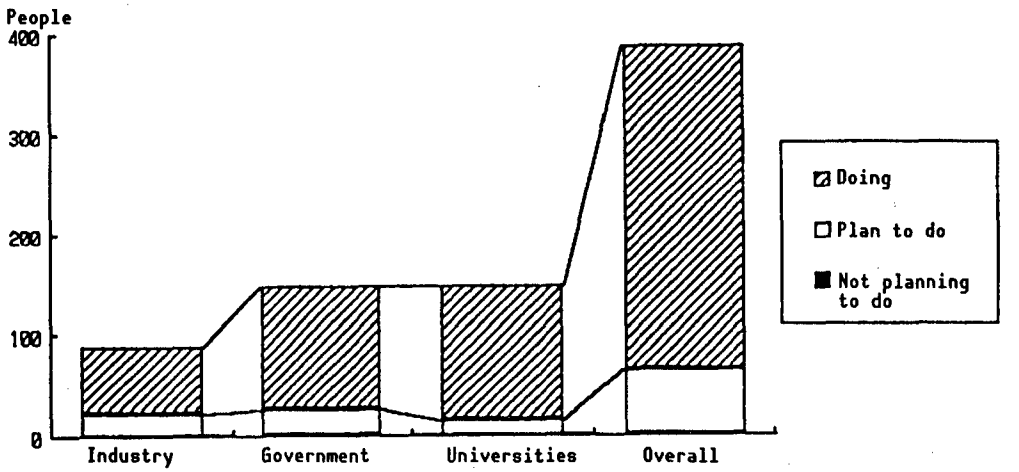


Figure 3.2.1-2 State of Implementation of Research in Multi-disciplinary Areas (Valid responses: 388, No responses: 28)

Reflecting the spirit of this investigation, we used those who answered "doing" or "plan to do" as the aggregate subjects, and excluded from the aggregate subjects those who replied "not planning to do."

Table 3.2.1-3 State of Implementation of Research in Multidisciplinary Areas (Valid responses: 388, No response: 28)

(Upper: Number of responses; Lower: %)

	Industry	Government	Universities	Overall
Doing	67	123	133	323
	74%	83%	90%	84%
Plan to do	23	25	16	64
	26%	17%	11%	17%
Not planning to do	0	1	0	1
		1%		0%

(d) Aggregate Subjects

The result of narrowing down the subjects in (b) and (c) was 387 aggregate subjects (Table 3.2.1-4).

Table 3.2.1-4 Aggregate Subjects

	Industry	Govern-ment	Univer-sities	Other	Total
Questionnaires sent	508	508	508	0	1,524
Questionnaires recovered	228	221	214	1	664
Recovery rate	45%	44%	42%		44%
Aggregate subjects	90	148	149	0	387

3.2.2 Analysis of Aggregate Subjects

(a) Age Distribution of Aggregate Subjects
(Valid responses: 386, No response: 1)

Figure 3.2.2-1 and Table 3.2.2-1 show the age distribution of the aggregate subjects that answered Question I.2) in Attached Figure 2. In "industry," more than half of the researchers are 40 years of age or younger, whereas in "government" and "universities," more than half of the researchers are 41 years of age or older: there was quite a contrast in these results. The tendency for researchers in "government" and "universities" to be older is seen.

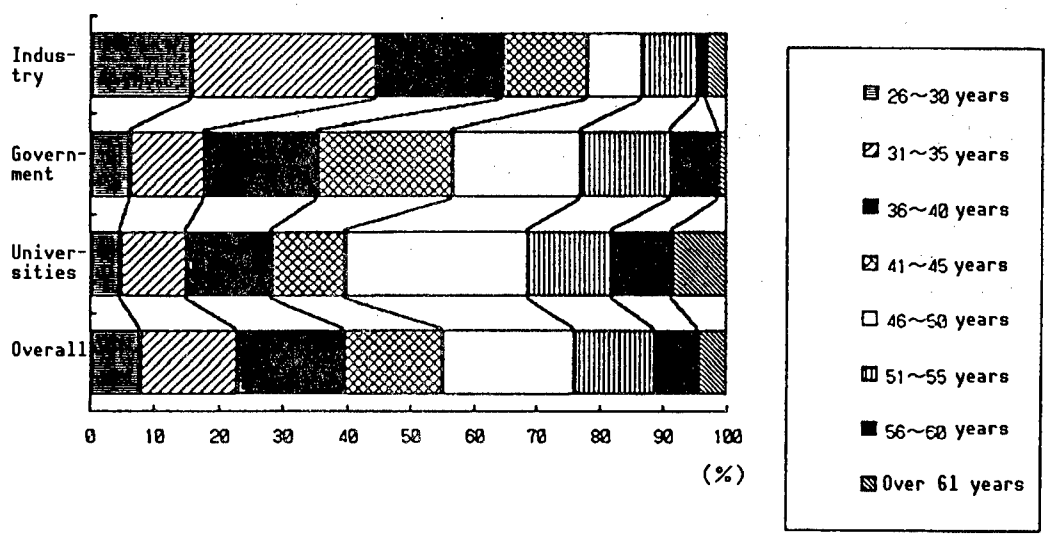


Figure 3.2.2-1 Age Distribution of Aggregate Subjects
(Valid responses: 386, No response: 1)

Table 3.2.2-1 Age Distribution of Aggregate Subjects
(Valid responses: 386, No response: 1)

	Less than 26	26~30	31~35	36~40	41~45	46~50	51~55	56~60	Over 61	Average age
Industry	0	14	26	18	12	8	8	1	3	38.9
		16%	29%	20%	13%	9%	9%	1%	3%	
Government	0	9	17	26	31	30	21	11	2	43.9
		6%	12%	18%	21%	20%	14%	8%	1%	
Universities	0	7	15	20	17	43	20	14	13	46.6
		5%	10%	13%	11%	29%	13%	9%	9%	
Overall	0	30	58	64	0	81	49	26	18	43.8
		8%	15%	17%	16%	21%	13%	7%	5%	

(b) Research Places of Aggregate Subjects (Valid responses: 370, No responses: 17)

Figure 3.2.2-2 and Table 3.2.2-2 show the results of comparing the responses to Question I.6) in Attached Figure 2, "the places where research is carried out," with the organizations that the researchers are affiliated with, and then classifying the places of research according to whether they are the "affiliated organization only" or "somewhere else."

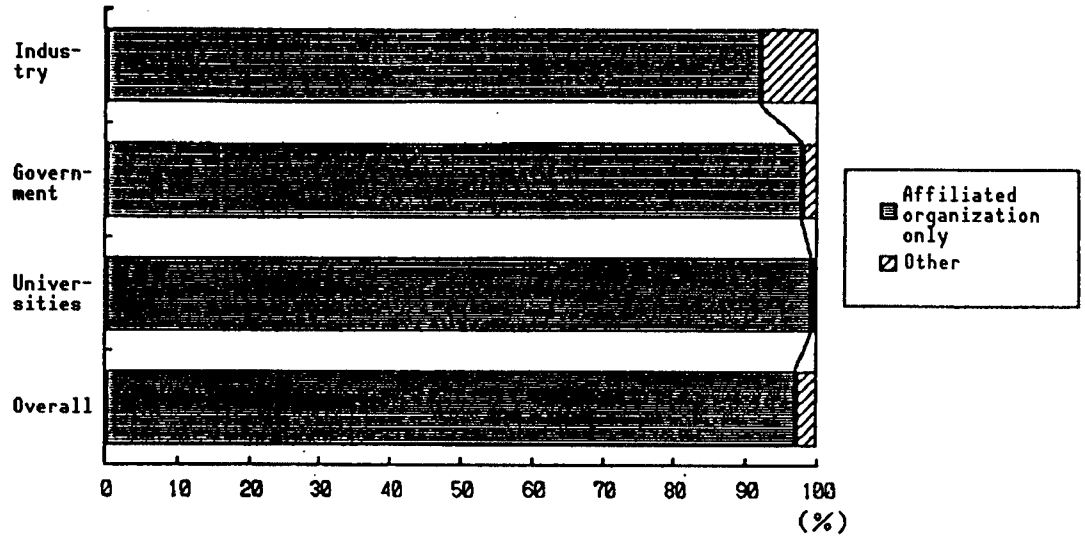


Figure 3.2.2-2 Differences in Places Where Research Is Done
(Valid responses: 370; No responses: 17)

Table 3.2.2-2 Differences in Places Where Research Is Done
(Valid responses: 370; No responses: 17)
(Left side: number of responses; right side: %)

	Affiliated organization only		Other	
Industry	79	92%	7	8%
Government	140	98%	3	2%
Universities	140	99%	1	1%
Overall	359	97%	11	3%

(c) Fields of Specialization (Up to 5 answers possible, total number of responses: 928)

Figure 3.2.2-3 shows the aggregate results of the responses to Question I.7) in Attached Figure 2, "fields of specialization." As for the fields of specialization shown in this figure, when computing the totals we grouped the responses, which were based on the classifications in Table 1 of Attached Figure 2 (JICST-based fields of study), in bunches and resummarized them.

There were hardly any differences attributable to the distinctions of "industry," "government," and "universities." These results are nearly the same as the ratios in Table 1.2-1, "Subjects of Questionnaire Surveys."

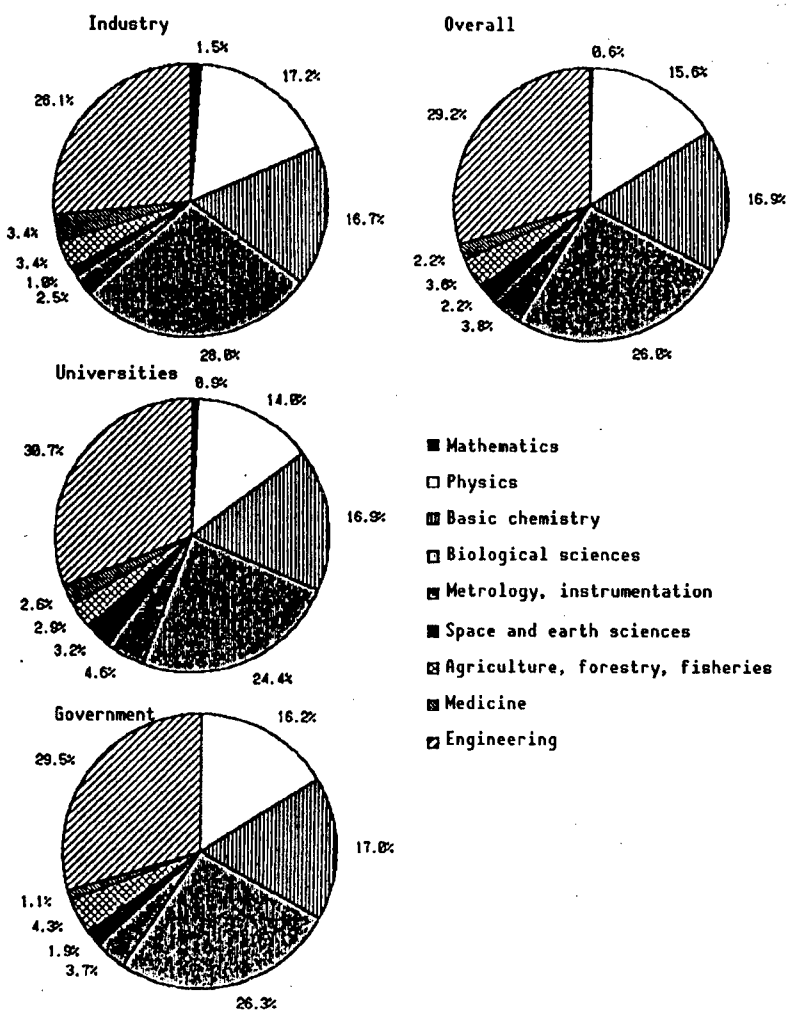


Figure 3.2.2-3 Fields of Specialization (Up to 5 answers possible, total number of responses: 928)

3.3 Questionnaire Survey Results

3.3.1 Classification of Research Themes

These are the aggregate results on the fields of study that are relevant to the aggregate subjects' research themes. Incidentally, in this section the fields "Physics," "Basic Chemistry," "Biological Sciences," and "Engineering" are the large groups under which we summarized the responses when we computed the totals; the responses are based on classifications along the lines of Table 1 in Attached Figure 2 (JICST-based fields of study),

(a) Fields Most Deeply Related to Core Fields (Starting Points)

Each researcher that responded to Question II.3 (12) of Attached Figure 2 named one "core field of study (starting point)" for their research theme; in response to Question II.3 (13), they gave five "related fields of study" in the order of how deeply those fields are related to their research theme. Of these "related fields of study," the "most deeply related fields of study" that were named first are summarized for each "core field of study (starting point)" in Table 3.3.1-1 and Figure 3.3.1-1.

Table 3.3.1-1 Fields Most Deeply Related to Core Fields (Starting Points)

Core field (starting point) \ Most deeply related field	Mathematics	Physics	Basic chemistry	Biological sciences	Metrology, instrumentation	Space and earth sciences	Agriculture, forestry, fisheries	Medicine	Engineering	Other	Total
Mathematics					1						1
					100%						100%
Physics	2	36	4	1	5				11		59
	3%	(61%)	7%	2%	9%				19%		100%
Basic chemistry		20	23	11	2	1		1	4		62
		(32%)	(37%)	(18%)	3%	1%		1%	6%		100%
Biological sciences		5	11	54	1	2	1	6	2		82
		6%	13%	(66%)	1%	2%	1%	7%	2%		100%
Metrology instrumentation		2		1					1		4
		50%		25%					25%		100%
Space and earth sciences		4	1	2	2				5		14
		(29%)	7%	14%	14%				(36%)		100%
Agriculture, forestry, fisheries		2	4	6					2		14
		14%	29%	(43%)					14%		100%
Medicine		1		3					1		5
		20%		60%					20%		100%
Engineering	10	18	10	15	5	3		2	44		107
	9%	17%	9%	14%	5%	3%		2%	(41%)		100%
Other											
Total	12	88	53	93	16	6	1	9	70		348
	4%	25%	15%	27%	5%	2%	0%	3%	20%		100%

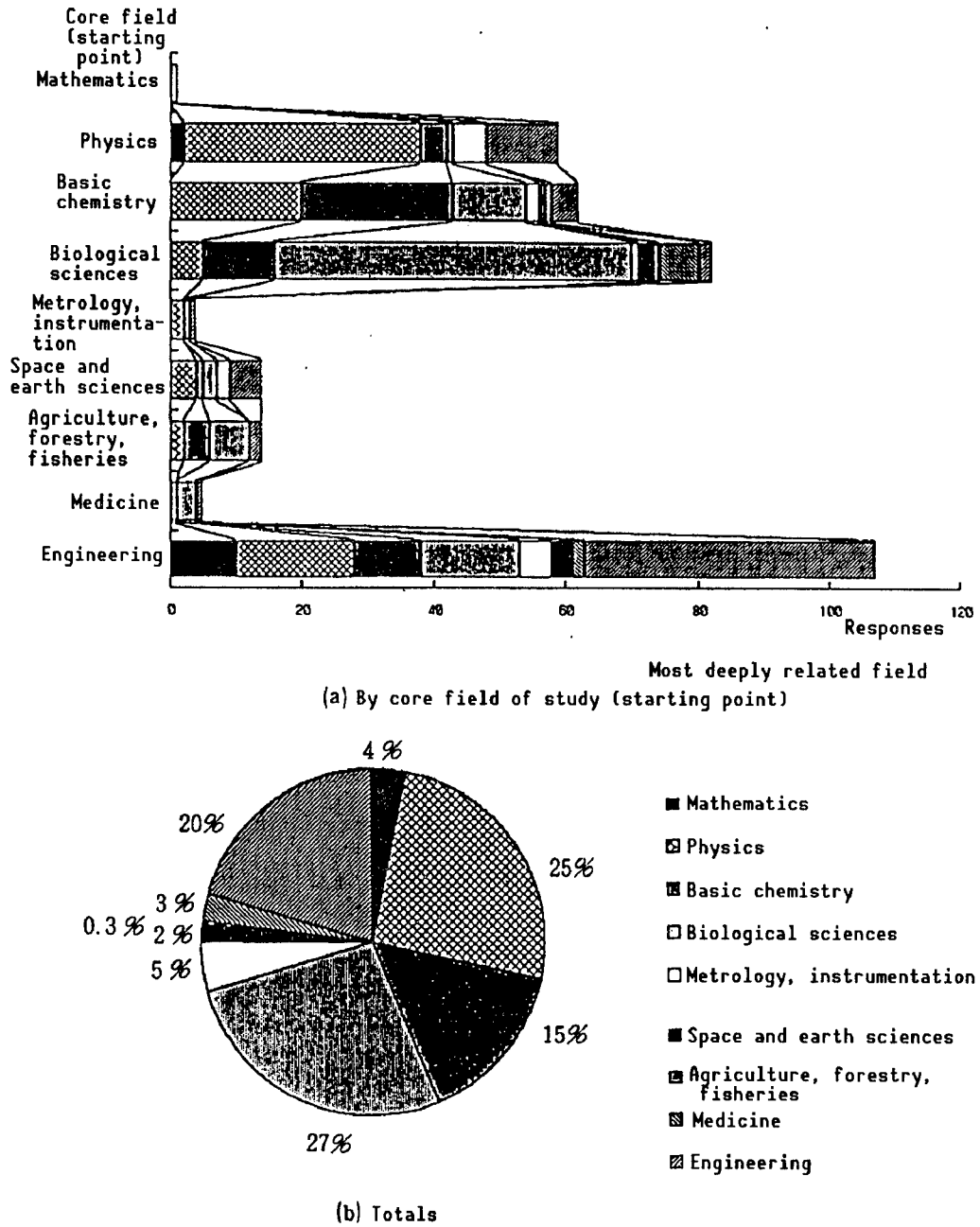
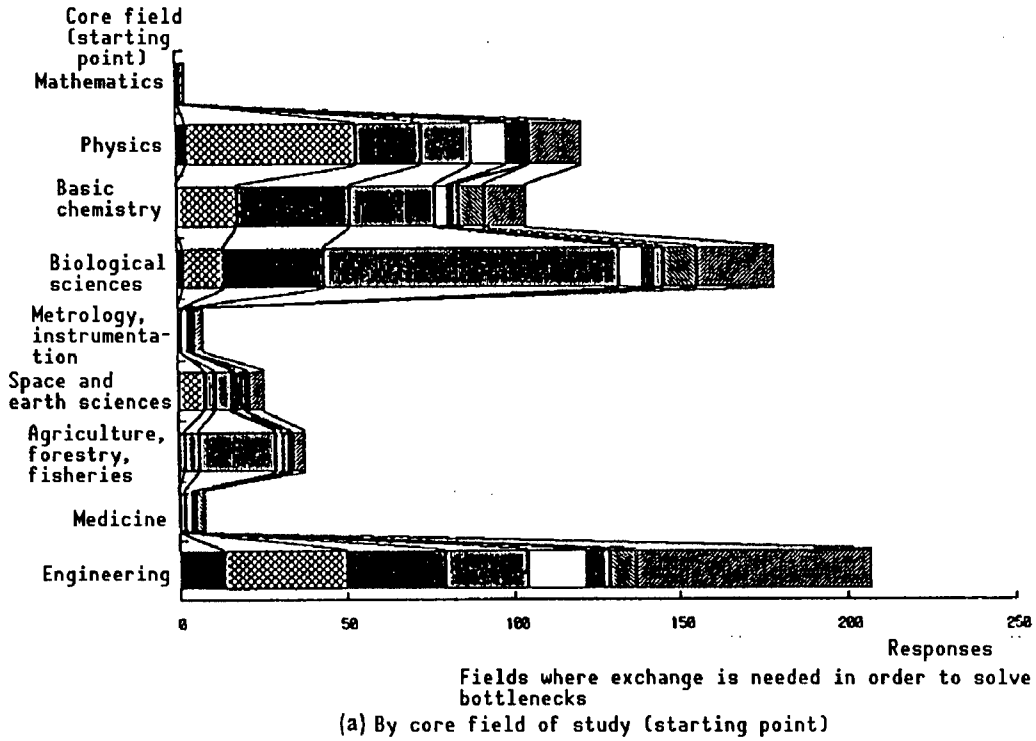


Figure 3.3.1-1 Core Fields (Starting points) and Most Deeply Related Fields of Study

In the cases where the core field of study was "physics" or "biological sciences," more than half of the researchers responded that the most deeply related field of study was the core field itself, i.e., "physics" or "biological sciences." In the case where the core field of study was "basic chemistry," as well, about 30% of the researchers responded that the most deeply related field of study was "basic chemistry," but the other responses were relatively scattered: about the same number, 30%, responded "physics," and 20% responded "biological sciences."

(b) Fields Where Exchange is Needed In Order To Solve Bottlenecks

In Question II.3) (11) of Attached Figure 2, the researchers named the fields of study where, in order to find solutions to bottlenecks, researcher exchange is needed. Figure 3.3.1-2 summarizes these fields of study for each "core field (starting point)."



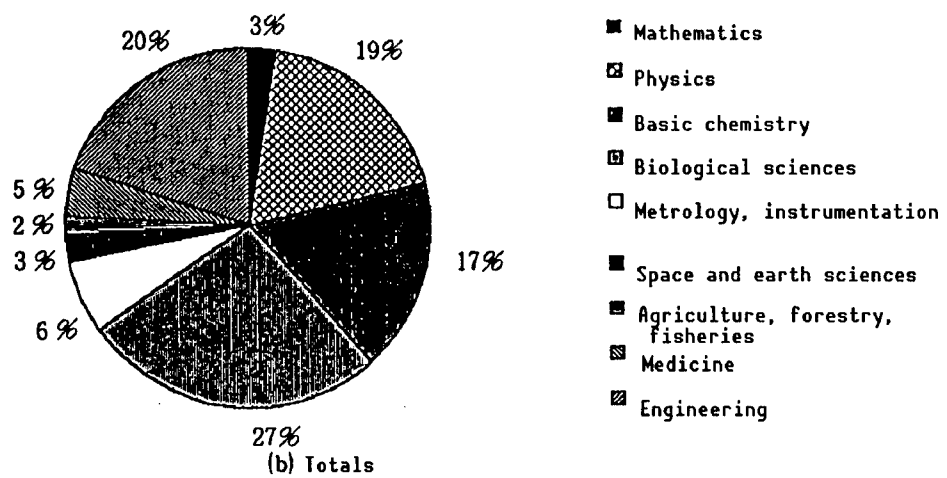
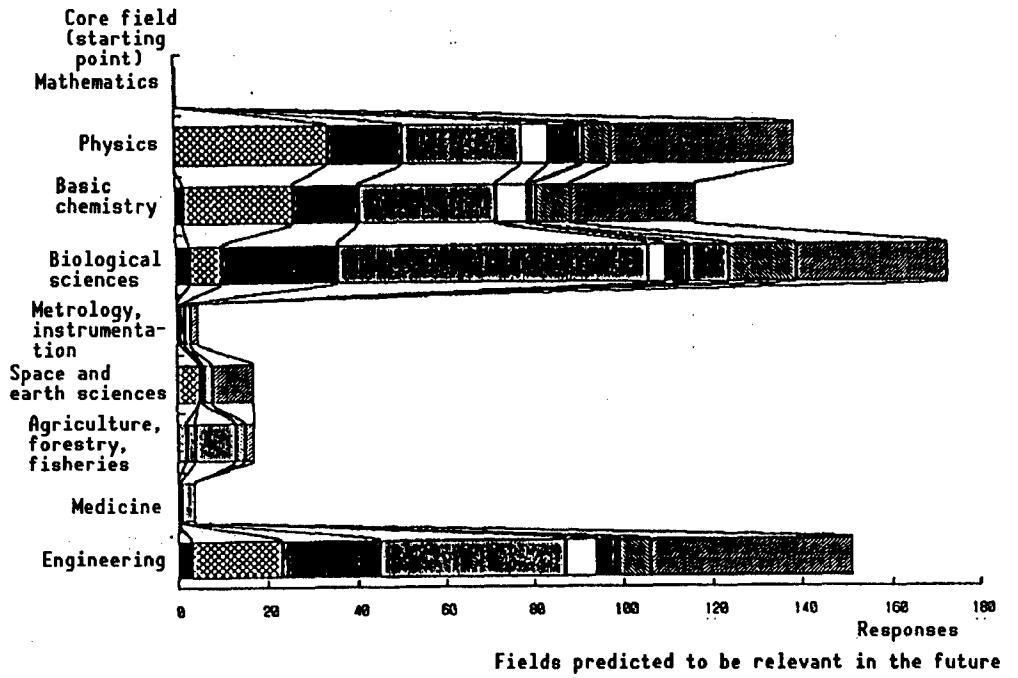


Figure 3.3.1-2 Fields Where Exchange Is Needed in Order To Solve Bottlenecks

In comparison with (a), "most deeply related field of study," there is an overall increase in the percentage of responses that exchange with researchers from other fields is necessary.

(c) Fields Predicted To Be Relevant in the Future

In Question II.3) (14) of Attached Figure 2, the researchers named the "fields of study predicted to be relevant in the future." Figure 3.3.1-3 summarizes these fields of study for each "core field (starting point)."



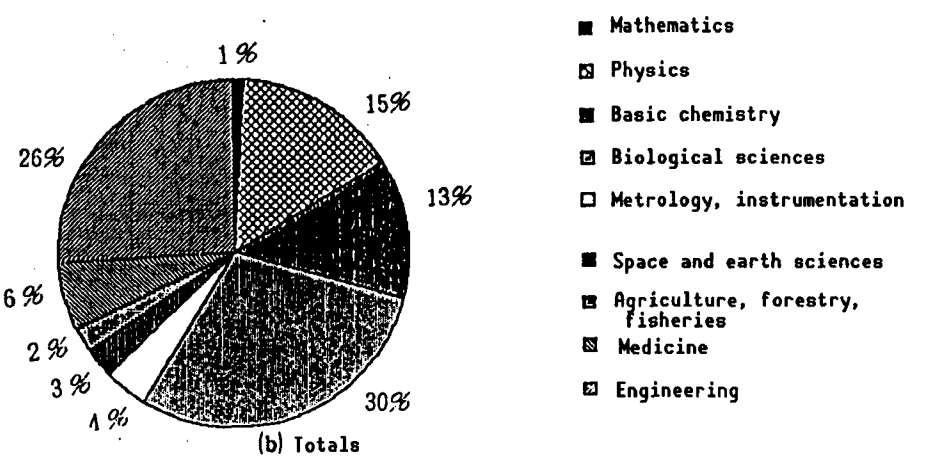
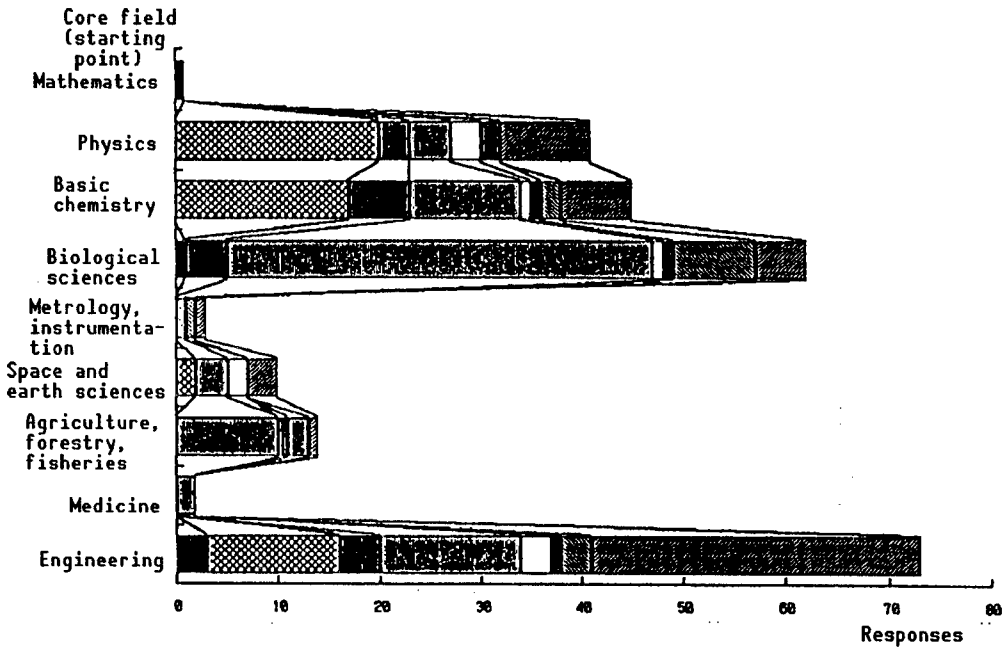


Figure 3.3.1-3 Fields of Study Predicted To Be Relevant in the Future

In comparison with (a), the percentage of those that replied "engineering" or "biological sciences" was higher.

(d) Fields Predicted To Become Central in the Future

In Question II.3) (15) of Attached Figure 2, the researchers named the "fields of study predicted to become central in the future" as research progresses. Figure 3.3.1–4 summarizes these fields of study for each "core field (starting point)."



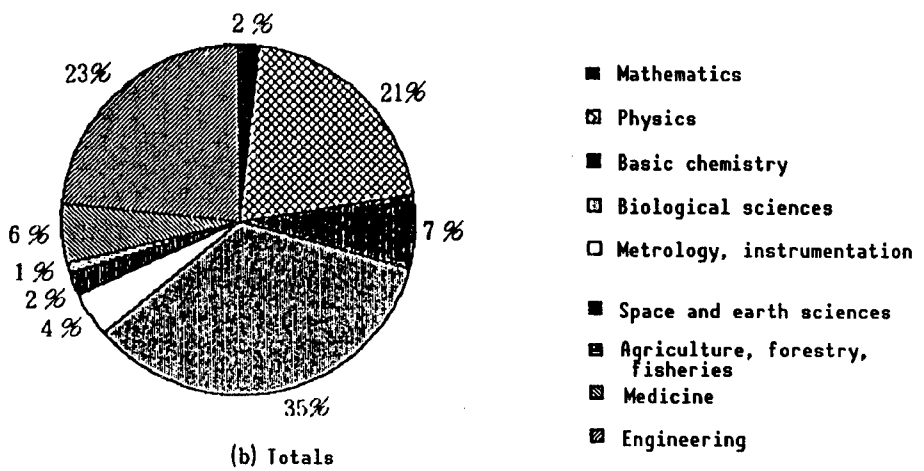


Figure 3.3.1–4 Fields Predicted To Become Central in the Future

The percentage of those that responded "basic chemistry" decreased, and there is an apparent trend that may be called a bipolar differentiation towards "physics" and "biological sciences." In particular, there was a notable increase in the percentage that responded "biological sciences."

3.3.2 Activities of Study Societies (Valid responses: 362, No response: 25)

In Questions II.4) (1) and (3) of Attached Figure 2, researchers answered questions about the state of "study society activities" that are related to their research. In Question II.4) (1) we asked whether their research "1. Does involve study society activities" or "2. Does not involve study society activities." To those that answered "2." in (1) we asked again in (3) whether they "1. Plan to" or "2. Do not plan to" become involved in the activities of a study society in the future. Figure 3.3.2-1 and Table 3.3.2-1 show the results.

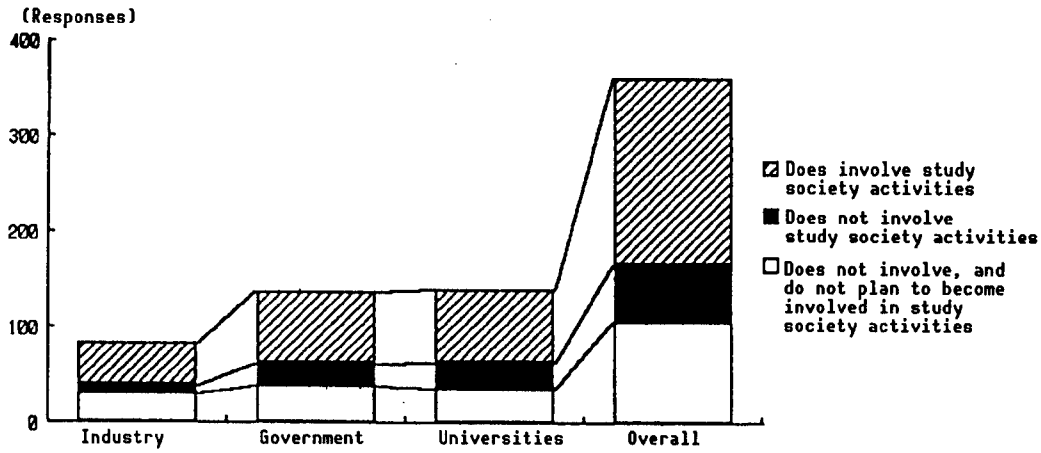


Figure 3.3.2-1 Activities of Study Societies (Valid Responses: 362, No responses: 25)

Table 3.3.2-1 Activities of Study Societies
(Valid responses: 362, No response: 25)
(Upper: Number of responses; Lower: %)

	Industry	Government	Universities	Overall
Not involved	45	75	76	196
	54%	54%	54%	54%
Plan to become involved	8	24	27	59
	10%	17%	19%	16%
Not involved, do not plan to become involved	31	39	37	107
	37%	28%	26%	30%

About 70% of the researchers responded that they are now involved, or they plan to become involved, in study society activities.

The greatest reason cited for not being involved in activities of a study society was that the researcher "would like to become involved after their research progresses more." Other reasons were "to maintain secrecy (industry)," "not enough people or time," "because our theme (information needed for research) is subdivided over many different areas, or because the contents of the research are one-sided, it cannot be consolidated into the form of a study society activity."

3.3.3 Bottlenecks, Directions for Improvements in Accomplishing Research

In Questions II.3) (8) and (9) of the questionnaire form (Attached Figure 2 of Section 3.1.2 in Chapter 3), the researchers answered about "directions of development of their research environments" and "bottlenecks in accomplishing their research." Of the 387 aggregate subjects, there were no responses from 59, and a total of 328 did answer the questions; of these, 127 were researchers from "universities," 128 from "government," and 73 from "industry."

According to the results of the survey, most of the researchers working in multidisciplinary research areas, and particularly most of the researchers employed in universities or their affiliated organizations (classified as "universities") answered that their "present research environment is lacking in research facilities, personnel, and funding," and that they "would like to find ways to improve their research environment by taking advantage of research promotion systems, joint research, and so forth." In Question II.3) the intention was to ask about "(future-oriented, positive) development directions of the research environment," but very few answered about future-oriented, positive development directions; most of the opinions expressed were about how the researchers would like to improve upon the current inadequacies in their research environments. Among these there were also many researchers who are completely losing their enthusiasm about improving their research environment; it is a serious problem, as discussed in detail below.

Irrespective of whether the researchers were from private firms ("industry"), national laboratories ("government"), or universities and their affiliated organizations ("universities"), many cited "the lack of personnel" as one of the "bottlenecks in accomplishing research." Among these, however, there was a relatively large number of "government"researchers.

As for the researchers who cited "the lack of research facilities" or "insufficient funding" as one of the "bottlenecks in accomplishing research," there was an overwhelmingly larger number from "universities" than from "government" and "industry."

Below we will give a detailed report of the survey results.

(1) Responses About "The Bottlenecks in Accomplishing Research That Are Related to the Research Environment"

Many of the researchers working in multidisciplinary areas cited the fact that their "research environment is lacking in research facilities, personnel, and funding" as the "bottleneck in accomplishing research." In particular, 30% of the researchers from "universities" (38 people) said that their "research environment is lacking in research facilities, personnel, and funding." This is an overwhelmingly high percentage in comparison with "government" (16%; 21 people) and "industry" (12%; 9 people). Because the format of the question was whether their "research environment is lacking in research facilities, personnel, and funding," there are probably quite a few researchers who would answer that only one or two of these things are lacking, so it is thought that more would actually answer that their "research environment is lacking in research facilities, personnel, funding."

(a) Lack of Personnel

Of the researchers who cited the "lack of personnel" as a "bottleneck in accomplishing research," 73% were "government" researchers (94 people). Close to 70% of the researchers from "universities" (69%; 87 people) and "industry" (67%; 49 people) also gave the same answer. Among "government" researchers there were many complaints about the "desperate lack of personnel," "the conspicuous aging of researchers and the inability to secure young researchers," "adequate funding and facilities, but never enough people," and "the lack of capabilities of joint researchers." Researchers from "universities" pointed out the "lack of personnel" in the same way as "government" researchers, pointing out particularly the "lack of young assistants and the lack of young technical officials with specialized skills." Other indications in the "personnel aspect" that we noticed were "a decrease in the number of graduate students going on to pursue doctorates," "inadequacies in the post-doctorate system," and "the conservative tendencies of students who hesitate about getting into interdisciplinary areas." In "universities," too, differences arise between "having a considerable number of personnel such as graduate students" and "especially lacking in personnel" depending on whether or not there is a graduate school. In "industry" there are also many complaints about the "lack of personnel," but in the cases where research themes are not valued very much in the firm, it seems that the inadequate allocation of personnel is a factor.

(b) Economic Inadequacies

Of the researchers who cited the "lack of money" as a "bottleneck in accomplishing research," the most were from "universities" (62%; 79 people), and few were from "government" (45%; 58 people) and "industry" (26%; 19 people). In "universities," even if many people inevitably cite the lack of money for purchasing large equipment, there was a surprisingly large number who complained about the extreme inadequacy of ordinary expenditures and traveling expenses. The problem is fundamental at low levels, and is serious: "there has been no change in ordinary expenditures for 20 years"; "a lot research can be done in university labs with a few million yen in yearly

funding, but nowadays it is tough to raise even a few million yen for yearly expenses"; "just 450,000 yen in research expenditures and 50,000 for traveling expenses is extremely inadequate"; "the amounts of scientific research expenditures are too little"; etc.

(c) Lack of Facilities and Equipment

Most of the researchers who cited "lack of equipment and facilities" as a "bottleneck in accomplishing research" were from "universities" (54%; 68 people). There was not much difference between the numbers of researchers from "government" (37%; 47 people) and "industry" (34%; 25 people) who gave this reply.

(d) Other

There was a smaller percentage of researchers from "industry" than from "universities" and "government" that cited inadequate research equipment and facilities, personnel, and funding as a "bottleneck." But there were a few researchers from "industry" who mentioned "bottlenecks" such as "the difficulty of research themes for which no commercialization scenario can be drawn," "the importance given to economy and investment efficacy of research expenditures," and that "affiliated firms are oriented more towards development than basic research."

In "universities" there were many researchers who said, "There is not enough time for research because we spend so much time on education and office work." Many researchers from "industry" and "government" made the same kind of point: "Because so much time is spent on miscellaneous duties and other such non-research work, there is not enough time for doing research."

A similar point was brought up by a few "government" researchers who cited "the vertical management system of governmental agencies" as a "bottleneck."

(2) Responses About "Directions of Development of "Research Environments"

Regarding the inadequacy of their present research environments, many researchers said that they "would like to find ways to improve their research environment by taking advantage of research promotion systems, joint research, and so forth."

However, from the text of the responses it is apparent that improving the research environment is difficult, even if much effort is put forth. Some comments are, for example: "Although there is the need to think about expanding all aspects of the research environment, the situation is one where it can only be dealt with now and then" ("universities"). "To compensate for the lack of personnel, we are adopting efficient analysis and measurement methods, even if it means somewhat of a sacrifice in sensibility and accuracy. If the funds are there, we would like to automate our instrumentation to make it more labor-saving. We are also thinking about farming out the work as commissioned analyses" ("government"). "We would like to increase our personnel, but in actuality that is difficult" ("government"). "We will make

up for the lack of personnel by using trainees and foreign students, and by hiring outside contractors to do trial manufacturing" ("government").

There were also many who answered that they try to compensate for the inadequacies of their research environment by means of joint research. For example: "With some research we have to resort to joint efforts with industry that also involves providing services to the firms" ("universities"). "We would like to broadly conduct joint research to compensate for the inadequacies of our research environment" ("universities"). "Because we lack personnel, we would like to set up systems for joint research with government and industry" ("universities"). "Because we have few personnel, we will tie up with universities and firms. Because our development expenditures are small, we will tie up with firms" ("government"). "We will do joint research and will take part in applying outside equipment and facilities, and personnel in our own research" ("industry").

Examples of responses about promoting joint research from a more positive standpoint are: "We will promote joint research because we will need the advice of experts from other fields" ("universities"). "We will start up study societies with researchers from other fields" ("universities").

Although the above responses show that researchers in tough situations would like to somehow or other steadily improve their research environments, there are also many researchers who are losing their enthusiasm altogether. There were hopeless replies, too: "Research equipment and facilities, and personnel will have to change into research that is as unnecessary as possible" ("universities"). "I don't even feel like thinking about future directions of development towards improving the research environment" ("universities"). Then there were those who seemed to take a philosophical view in their responses: "Improvements are thought to be difficult at the present time" ("government"). "Whether it be equipment and facilities, personnel, or funding, there is no basis for thinking about long-term developmental directions. We can only use what we can, haphazardly" ("universities"). "Although I am hopeful about the future, there is hardly any equipment, research subsidies are in name only, and research funds are also meager. But, the research will continue" ("government"). The problem is very serious.

(3) Conclusion

Looking just at the responses to questionnaires, as discussed above, the research environments in which the average researchers that are oriented towards multidisciplinary areas are placed, and particularly the research environments in "government" and "universities" that should be leading S&T, are in a situation that does not warrant satisfaction. (This is not limited to multidisciplinary research areas but can also be said about average researchers throughout Japan.) In some cases there is even misery. Of course, in a few, very rare cases it is said that "research facilities and equipment are adequate, and there is no lack of personnel or funding" ("universities"), and "at least, for the research topics I am now working on, it is better than in other research organizations" ("industry"). Thus, there is no doubt that some leading researchers are in environments that are well-endowed thanks to

the researchers' understanding of their research organization, various research promotion systems, and so forth. Nevertheless, if at the foot of a vast mountain we think at first that we can scale the high peak that rises above us, the fact that the research environment of the general researcher does not warrant satisfaction is a serious problem for Japan, which aims to establish itself as a scientific and technological nation.

3.3.4 State of Utilization of Research Promotion Systems (Valid responses: 360, No response: 27)

Figure 3.3.4-1 and Table 3.3.4-1 show the aggregate results of responses to Question II.3-(7) in Attached Figure 2, "State of Utilization of Research Promotion Systems." The choices were:

1. Currently utilizing such system(s) (abbreviated to "now utilizing")
2. Would like to use, but cannot use because we were left out of the selection (abbreviated to "left out of selection")
3. If there is an appropriate system, will use it (abbreviated to "will use if there is an appropriate system")
4. No need whatsoever (abbreviated to "no need)

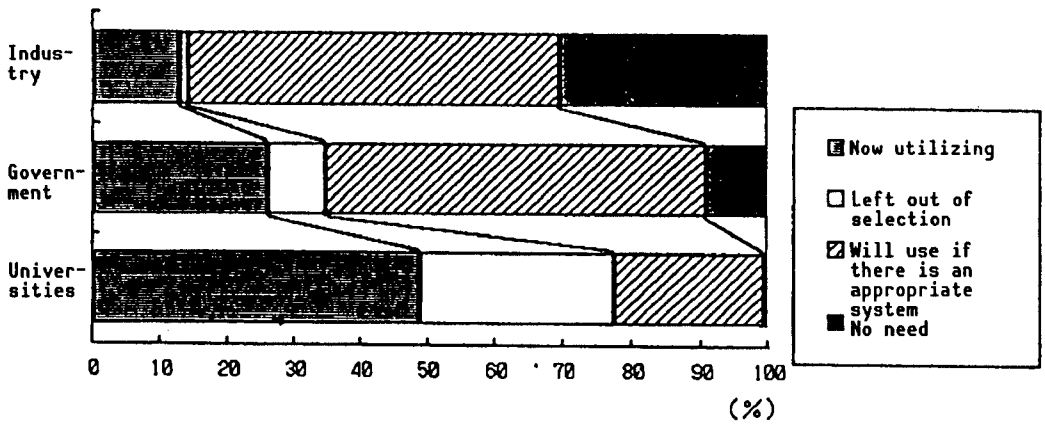


Figure 3.3.4-1 State of Utilization of Research Promotion Systems (Valid responses: 360; No responses: 27)

Most of the researchers who responded "will use if there is an appropriate system" and "no need" were from "industry." Conversely, most of those that responded "now utilizing" and "left out of the selection" were from "universities." Most "government" researchers responded "will use if there is an appropriate system."

Concrete examples of promotion systems that researchers utilize are systems attributable to public organizations, such as the Scientific Research Grants and Coordination Funds for Promoting S&T; in addition, the use of private-sector promotion systems was also seen.

Table 3.3.4-1 State of Utilization of Research Promotion Systems
(Upper: Number of responses; Lower: %)

	Industry	Government	Universities	Overall
Now utilizing	11	36	67	114
	13%	26%	49%	32%
Left out of the selection	1	12	39	52
	1%	9%	29%	14%
Will use if there is an appropriate system	47	77	30	154
	55%	56%	22%	43%
Not involved, do not plan to become involved	26	13	1	40
	31%	9%	1%	11%

3.3.5 Current State of Research Encouragement Systems and Topics

This section summarizes that which is thought to be representative of the majority of opinions obtained from questionnaire surveys of general researchers about the current state of and topics in the research promotion systems that will be important in promoting research in multidisciplinary areas. In addition, in Sub-Section (2) we will discuss and summarize that which is representative of the opinions obtained from interviews of knowledgeable persons.

(1) Current State of Research Promotion Systems and Topics, From Questionnaire Surveys

Question II-3)-(1) of the questionnaire form (Attached Figure 2 in Section 3.1.2) brought up seven of the Science and Technology Agency's basic research promotion systems; those surveyed answered this question by describing their wishes with respect to these government policies. Of the 387 aggregate subjects, 203 people did not respond to this question, and 184 people did; 86 of those that responded were from "universities," 64 from "government", and 34 from "industry." Below we will go through the list of representative opinions, in order of those for which there were the most responses.

(a) Stronger PR Activities for Basic Research Promotion Systems (Pointed out in 67 responses)

The opinions most expressed were about the lack of PR: "I wish these systems were publicized more because I do not know much (anything) about them." "I cannot comment because I do not know much about these systems." Of those that gave some kind of opinion, 41% of those from "universities" (36 people), 38%

from "industry" (13 people) and 30% from "government" (18 people) gave opinions about the lack of PR. In this connection, many also said that "if eligible, I would like to apply" and "I wish the STA would create a booklet that summarizes application methods."

Stronger PR activities for basic research promotion systems is thought to be needed.

(b) Tie-Ups With, Coordination of Other Ministries' and Agencies' Research Promotion Systems (Pointed out in 24 responses)

There are also many who voiced their desire for cooperation and coordination with other ministries' and agencies' research promotion systems, and for further opening of the door for applications. Some opinions that were given include: "I would like to see the cultivation of basic research and germination research that goes beyond the barriers of ministries and agencies" ("universities"). "I would like to see tie-ups with the basic technology fostering policies of the Ministry of Posts and Telecommunications and MITI" ("industry"). "I was about to apply, but withdrew because I felt apprehensive about a relationship with the Ministry of Education" ("universities"). "I would like to see the door for applications opened wider, even to those connected with universities" ("universities"). "How about the possibility of private-sector participation?" ("Industry").

(c) Openness and Fairness of Selections (Pointed out in 22 responses)

There were also many opinions about the fairness of selections: "I wish the selections were more open, and the deciding factors were something I could comply with (now I do not comply.)" ("universities"). "I would like to see the selections conducted objectively" ("industry"). "Make the evaluation system strict. Select the themes with impartiality" ("government"). Irrespective of whether the researchers come from "government," "industry," or "universities," overall there are strong calls to "offer systems publicly" and "to widen the range of openings." Among these there is also the opinion, "If my application is rejected I would like to be told why, in concrete terms. If possible, I would like the government to give researchers the chance to object to the rejection of their application. Telling researchers why they are rejected will also lead to fostering applicants" ("universities").

(d) Support for Research for which Ratings are not Decided, and for Researchers without Proven Track Records (Pointed out in 18 responses)

There were a considerable number of those who voiced the opinion that "the tendency is for the benefits of existing systems to be limited to researchers who have already proven themselves, and their associates" ("government," "industry," and "universities"). There were many opinions such as: "Even if the researcher does not have a record of accomplishments, I would like to see positive research support if he has a good proposal" ("industry," and "universities"). "Support that starts after the ratings are decided has no meaning" ("government"). "Setting fixed standards and qualifications for the applicants will not further the systems for promoting basic research"

("government"). "I wish someone would create a system that could be used by the ranks of young university assistants" ("universities"). "I wish someone would create a system for supporting post-doctorate students" ("universities").

(e) Encouraging Small-Scale Research, Widening the Research Support Base (Pointed out in 14 responses)

Opinions calling for the promotion of small-scale research, and for broadening the base of research support included: "I wish there was more of a balance in the promotion of large-scale research and small-scale research" ("government"). "I would like to see somewhat broader support for small science because it can be good even if it is meager" ("universities"). "Overemphasis on large-scale research is dangerous" ("government"). "I would like the kind of support that would allow me to buy a little more general-purpose equipment" ("universities"). "Because a small amount of money is sufficient support for a single research project, I would like to see support for as many researchers as possible" ("universities" and "government"). "I wish there could be research exchange with relatively small-scale budgets" ("government").

(f) Simplifying Applications, Reports, and Budget Management (Pointed out in 14 responses)

There were a few opinions here and there calling for simplification of duties and budget management: "I wish applications and reports were made more simple because when they take a lot of time, the research gets pithy" ("universities"). "Because there is too strong of an awareness that tax money is being used, audits are too strict and often are an obstacle to free research, so I wish the government would think about the methods, including budget management" ("industry"). "I wish that constraints were not attached to the way research support funds are used (the distinctions of personnel expenses, equipment expenses, and traveling expenses)" ("industry"). "I would like to see a system for employing research assistants" ("universities"). "Budgets are put into effect too late" ("government").

(g) Importance of Basic Research, Perfecting Promotion Systems(Pointed out in 5 responses)

"Because basic research is important, I wish it was promoted more" ("government"). "I wish the outlays for science did not get used up for technology" (two responses, "government"). "I would like to see a more replete system for promoting basic research" (two responses, "universities").

Perhaps what was pointed out in these responses is taken too much for granted, but it is nevertheless thought to be important.

(h) Promoting International Exchange (4 responses)

There were opinions calling for the promotion of international exchange: "If there were systems where not only Japanese researchers but also foreign

researchers were eligible, researchers would receive better stimulation from that exchange" ("government"). "I would like to see international centers for basic research established where Japanese and foreign researchers from each field of specialization would gather to carry out joint basic research" ("industry"). "I am for more positive dispatching of researchers overseas" ("government").

(i) For Researchers With Proven Track Records, Systems for Promoting Research Without Relying on Applications (3 responses)

There were opinions opposite to those expressed above in (c) and (d): "Isn't there a way to distributing support to those researchers with proven track records without relying on applications? Foundations in the United States choose who to support in committees. In leading-edge research, predictions do not hold good, so judgments based on past results are better" ("government"). "I would like to see a reduction in the labor involved in making budget requests. I wish budgets could be granted to those people and groups who have brought about results without them having to speak up about it" ("government").

(j) Other

Other opinions expressed were: "Most important is to expand the scale of budgets for basic research fields enough so that Japan, a large economic power, can continue to develop into the future" ("government"). "Not just economical provisions for the research environment, such as equipment purchases and so forth, but also personnel, research places, and freedom are desired" ("government" and "industry"). "I would like to see study societies created and systems in which researchers can participate freely" ("universities").

(2) Current State of Research Promotion Systems and Topics, From Interviews

Many of those interviewed pointed out that the biggest bottleneck encountered by researchers when they attempt to open up new fields is that there is no system for going beyond existing fields, university courses, and the framework between ministries and agencies in order to provide support for research in new fields.

For example:

- Although there are scholarship/endowment funds and money for commissioned research as ways for university researchers to obtain outside funding, funds cannot be appropriated for projects that do not qualify for either of those, and other ministries and agencies cannot become sponsors. With these and other such constraints, the money cannot be put to practical use as support for research that is in the idea stage.

- With university course systems, funds cannot be obtained when, for example, researchers who want to do research in biochemistry are needed in clinical medicine.

• To get research funding the recommendation of an academic society is needed. Getting adequate support requires the participation of several academic societies, and consequently a lot of time is spent in conferences sponsored by the academic societies.

As one example, there is apparently a desire for expansion of systems like the "Creative S&T Promotion System" that promote basic, multidisciplinary research and allow researchers from many different fields to come together.

(ii) Problems In Promoting Germination Research

Regarding the support of young researchers or of germination research, there have been many complaints that in the current state of affairs there are some inadequacies and that there are problems in employing that support:

• At the very minimum idea research requires on the order of 10 billion yen in investments; systems that provide this magnitude of support must be expanded.

• Sums of money that can be sufficient for a single researcher operating within a single promotion system are needed.

• It will be hard to cultivate young researchers with small amounts of money for young people's germination research. The most desirable situation is one where insightful leaders wisely employ young people in the research that is carried out; investments in amounts that correspond to such a setup are necessary (concretely, the Scientific Research System and the Priority Basic Research System).

On the other hand, the opinion was also put forth that

• Researchers that just think about getting funding will degenerate mentally. It is not a matter of just thinking about providing the funding, but opportunities for basic study must also be provided.

(iii) Problems with Lengths of Research Time in the Support Systems, and the Importance of Multi-Channeling (Utilization of Multiple Support Systems)

As for the length of time needed for a researcher to carry out his research, the general opinion is that five years is not quite long enough. That is, although this view takes into consideration the "Creative S&T Promotion System" and the "Coordination Funds for S&T Promotion" (both of which allow five years for research projects), the opinion is that if it takes about two years to get the experimental equipment up and running, and then another year or so to fine tune it, then getting satisfactory research data will end up taking about a year, and the experimental equipment that was so painstakingly put together should not be wasted. With regard to how many years it actually takes to get satisfaction, some researchers feel that after the research passes through several stages a decade will be needed: about three years are needed until the basic experiments begin, then seven or eight years until corporations will be interested. However, it was unanimous that time limits

should be set on research projects. Also, in order not to invite semi-fixed research areas and aging researchers, everybody recognizes the need for setting appropriate time limits on research. And, in the sense of efficiently investing in research, it is not a ten-year-long period of continuous support that is desired, but rather a setup where support systems with three- to five-year time limits can be used in stages; i.e., the so-called multi-channeling of support systems (multiple support systems with completely different objectives, time limits, and amounts of money) are desired.

The need for multi-channeling was also in expressed in the view that there should be multi-channeling in systems so that for the same research theme, several applications for support could be made to several different research promotion systems. This is an appropriate demand for coping with the current situation, where a single source of funding is not enough. Also, in the aspect of the amount of funding, even if a structure of one research promotion system for one researcher was achieved, multi- channeling is needed in the sense that it would widen the range of support for the individuality of researchers (research themes): arrangements must be made for several different research promotion systems so that researchers could apply for support from a system that corresponds to the nature of their research theme, or, if the importance of a research theme that corresponds to even just one of many systems is recognized, support from that system could be employed.

(b) Opinions on the Promotion of Basic Research

(i) Activating Mutual Exchange Among Researchers

The importance of mutual exchange among researchers, including overseas exchange, is thought to be recognized by all; it is not just the problem of the outflow of excellent researchers overseas, and waiting for the arguments for embarking solely upon basic research. In order to activate exchange, hard potential, such as equipment and facilities that researchers find attractive, must be raised, and soft repletion, where mutual exchange among researchers is possible, is also desired; this would set time limits on the research periods for single research themes, and would make it easier to bring in personnel from the outside.

(ii) Self-Sufficiency of Research Organizations, and Activation

In connection with ideal models for research organizations, there is the opinion that, national research organizations must be independent from all the ministries and agencies and must have the right to make budget appeals. Opinions about other forms of research organizations express the desire for joint government-private research organizations that are not constrained by public finance laws, National Public Service Laws, and so forth. This kind of research organization would provide places for research that answer the needs of researchers, while on the other hand, would set limits on the length of time for a given research theme. Doing it in this way would activate researcher exchange and would make theme selection more flexible. The general opinion is that the administration should not manage researchers; rather research organizations should stand on their own feet and activate exchange.

(iii) Relative Importance of Research Objectives

There were many who voiced objections to the administration creating the flow of research:

• The grand plan for the long future of the nation is for enterprises, who are thinking about future profits, to cultivate research themes without partners.

• When researchers flirt too much with the question of "what uses will their research have," research seeds that have originality will wither. There are examples of research labs that went downhill because they overemphasized being goal-oriented.

Among these there was also a contrasting opinion:

• The important things are the common concepts of what the research is for, and what the applications are. Before setting up a system for promoting research, a basic sense of values is needed.

However, what is unanimous on both side is the following opinion:

• Research is people. There must be a setup where research can be carried out by leaders, who have an overall philosophy and an eye for looking at people, that make full use of the concepts of each researcher.

This "overall philosophy" is also thought to include being goal-oriented. There was also the opinion that there is a need for a Japanese version of the U.S. Gordon Conference or the European Jacques Monot Conference (both are places for information exchange among leading-edge researchers) as a way of grasping the flow of basic research.

(c) The Image of the Ideal Research Support System

From the opinions obtained by means of interview surveys we will try to summarize the image of the ideal system for promoting basic research.

(i) Form of the System

The aim is a research period of ten years. The premise for that is either 1) a method whereby young researchers would participate for a limited period of time in the long-term research themes of prominent researchers; 2) a method of placing time limits on themes and researchers; or 3) a combination of the first two methods.

As for the way in which support would be provided, phased investments are preferred: for about the first three years, millions of yen per year until ideas start sprouting, and 10 to 30 million yen per year of support during the stage when goals are established (even if that research is at the nebulous level); at that point the research would be evaluated; then the next step would be to make arrangements for a large-scale promotion system. This phased investment would not necessarily require continuous investment from the same promotion system. Rather, a flexible way of coping is considered necessary;

e.g., preparations would be made for multiple promotion systems (multi-channeling) so that other appropriate systems could be utilized to correspond with the state of progress during each step of the research, and with changes in the evaluations of the research.

(ii) Screening Methods When Adopting a Theme

The ideal way to screen the research themes that are applied for is to avoid popularity contests: after an arbitrary decision by a single reviewer who is suitable for the research theme, or after a peer review by a few people, the person in charge would also arbitrarily decide whether or not the theme should be adopted. (Although fairness cannot be ignored, the view that the stress should instead be on individuality was prominent.) As for the qualifications of the applicant, the system would be lenient towards the degree of academic standing that the applicant acquired (doctorate); no bones would be made about the number of times the applicant took the platform at academic meetings or about his record of past accomplishments, such as the number of papers published. There was also the opinion that there is no need for age limits as part of the screening, when considering the fact that there are individual differences in the ways that researchers bring forth their research results. Based on the idea that the investment is in a person more so than in a research theme, the reviewer would interview the researcher. (The screening should not be based on just the application, the contents of which are strategically biased.) Accordingly, the number of research themes that one reviewer screens must be reduced to about ten. If rigorous screening can be done in this way, screening that lacks in objectiveness, e.g., age limits, will be unnecessary.

(iii) Reviewers

There were three different opinions about the reviewer's age: that his age should be overlooked; that he should be in the same age group as that of the researcher, with the same sensibilities; and that he should be a senior scientist who will not be swayed by fads. However, almost all agreed that the system must be one where the reviewer is evaluated himself. That is, the system must be such that the reviewer stays on (on a part-time basis) until the research theme that was chosen comes to an end and the final evaluation is done.

(iv) Evaluation When the Research Ends

It goes without saying that evaluations must never be driven by private considerations. The reviewer will take an honest look at the researcher; if it is experimental research, the reviewer will rate the lab and the research equipment. Then the reviewer himself must ascertain whether or not the research that should be evaluated is having an important impact, including international academic societies. (For this reason, as in the case of the screening when the theme is adopted, the number of research themes that a single reviewer examines must be necessarily limited.)

As for the interim reviews while the research is still going on, there was the opinion that if a rigorous evaluation can be conducted, that alone will bring forth good results; then on the other hand there was also the contrasting view that good results are more likely to come out when the research is left alone until the end. There is also the view that, in the case where a rigorous evaluation is carried out, the evaluation should be done by people within the same research organization because it is difficult to have outside people, who know nothing about the background behind the research, perform the evaluation.

Summary

During the first year of this survey, as described in detail in Parts I and II, we interviewed knowledgeable people, sent questionnaires to general researchers and the offices of academic societies, and surveyed various kinds of documentation. From this information we got a grasp on the current state of multidisciplinary research areas in Japan and the directions of development.

In Chapter 1 of Part II we discussed the methods we used to implement interviews of knowledgeable people, questionnaire surveys of general researchers and offices of academic societies, and surveys of various kinds of documentation.

In Section 2.1 of Chapter 2 we listed specific information that was obtained in this survey: examples of study societies and workshops in multidisciplinary research areas, examples of research themes, and keypersons involved in those. In Section 2.2, based on the interviews, questionnaire surveys, and documentation surveys, and giving full consideration to global and international needs, we selected from the areas of advanced multidisciplinary research nine representative research areas that are thought to be important now and in the future. Then in Section 2.3 we discussed the current state of affairs and topics in each of those areas. In Sections 2.4 and 2.5 we created directories of researchers and lists of research theme names for each of the nine research areas. The nine representative areas of multidisciplinary research are 1) intelligent materials, 2) frontier measurement and control technology, 3) new genetic manipulation technology, 4) new neuroscience and technology, 5) biomolecular S&T, 6) temporal bioscience and technology, 7) new global environmental S&T, 8) recycling S&T, and 9) computational S&T.

In Chapter 3, from the questionnaire surveys of general researchers working in multidisciplinary areas, we summarized the current state of research in those areas, the bottlenecks encountered in carrying out that research, and the current state of research promotion systems. According to the questionnaire surveys, the research environments in which average researchers who are oriented towards multidisciplinary research are placed are in a state that does not warrant satisfaction from researchers, especially those researchers from "government" and "universities" who should be leading S&T. (This is something that can be said broadly about the average researcher in Japan, regardless of his research area.) Many of those who responded to the questionnaires said that they "would like to find ways to improve their research environment by taking advantage of research promotion systems, joint research, and so forth." Actually, 32% of all researchers (49% of those from

"universities," 36% from "government," and 11% from "industry") now utilize some kind of research promotion system. There were many opinions that pointed out the problems and expressed hope for improvements in the current state of research promotion systems. From now on ways must be found to further improve research promotion systems.

When first planning the survey we intended to conduct a survey of the current state of multidisciplinary research areas and directions of that development by getting a grasp on the current state of activity in various study societies and the processes of their formation. Then in the first phase of the survey we tried to list the study societies, survey the general outlook of those groups, and classify them. In the course of the survey, though, we found that in many areas of multidisciplinary research there are no activities of study societies and other such groups; on the contrary, once a study society is established, the research theme is no longer a novel, leading-edge theme. This was pointed out by many of the knowledgeable people we interviewed and also by many of the members of the survey promotion committee. Therefore, in the first year of the survey we had to change tracks along the way from a survey centered on study societies to a survey centered on research themes.

In the second year of the survey we plan to take up two or three of the nine representative areas of advanced multidisciplinary research that were mentioned above; then, with examples of that research, we will investigate the developmental processes of advanced multidisciplinary areas.

- END -

Foreign Broadcast Information Service (FBIS) and Joint Publications Research Service (JPRS) publications contain political, military, economic, environmental, and sociological news, commentary, and other information, as well as scientific and technical data and reports. All information has been obtained from foreign radio and television broadcasts, news agency transmissions, newspapers, books, and periodicals. Items generally are processed from the first or best available sources. It should not be inferred that they have been disseminated only in the medium, in the language, or to the area indicated. Items from foreign language sources are translated; those from English-language sources are transcribed. Except for excluding certain diacritics, FBIS renders personal names and place-names in accordance with the romanization systems approved for U.S. Government publications by the U.S. Board of Geographic Names.

Headlines, editorial reports, and material enclosed in brackets [ ] are supplied by FBIS/JPRS. Processing indicators such as [Text] or [Excerpts] in the first line of each item indicate how the information was processed from the original. Unfamiliar names rendered phonetically are enclosed in parentheses. Words or names preceded by a question mark and enclosed in parentheses were not clear from the original source but have been supplied as appropriate to the context. Other unattributed parenthetical notes within the body of an item originate with the source. Times within items are as given by the source. Passages in boldface or italics are as published.

SUBSCRIPTION/PROCUREMENT INFORMATION

The FBIS DAILY REPORT contains current news and information and is published Monday through Friday in eight volumes: China, East Europe, Central Eurasia, East Asia, Near East & South Asia, Sub-Saharan Africa, Latin America, and West Europe. Supplements to the DAILY REPORTs may also be available periodically and will be distributed to regular DAILY REPORT subscribers. JPRS publications, which include approximately 50 regional, worldwide, and topical reports, generally contain less time-sensitive information and are published periodically.

Current DAILY REPORTs and JPRS publications are listed in *Government Reports Announcements* issued semimonthly by the National Technical Information Service (NTIS), 5285 Port Royal Road, Springfield, Virginia 22161 and the *Monthly Catalog of U.S. Government Publications* issued by the Superintendent of Documents, U.S. Government Printing Office, Washington, D.C. 20402.

The public may subscribe to either hardcover or microfiche versions of the DAILY REPORTs and JPRS publications through NTIS at the above address or by calling (703) 487-4630. Subscription rates will be provided by NTIS upon request. Subscriptions are available outside the United States from NTIS or appointed foreign dealers. New subscribers should expect a 30-day delay in receipt of the first issue.

U.S. Government offices may obtain subscriptions to the DAILY REPORTs or JPRS publications (hardcover or microfiche) at no charge through their sponsoring organizations. For additional information or assistance, call FBIS, (202) 338-6735,or write to P.O. Box 2604, Washington, D.C. 20013. Department of Defense consumers are required to submit requests through appropriate command validation channels to DIA, RTS-2C, Washington, D.C. 20301. (Telephone: (202) 373-3771, Autovon: 243-3771.)

Back issues or single copies of the DAILY REPORTs and JPRS publications are not available. Both the DAILY REPORTs and the JPRS publications are on file for public reference at the Library of Congress and at many Federal Depository Libraries. Reference copies may also be seen at many public and university libraries throughout the United States.